As filed with the Securities and Exchange Commission on September 25, 2006

Registration No. 333-135821

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 2
to

FORM S-1

REGISTRATION STATEMENT
Under
The Securities Act of 1933

CADENCE PHARMACEUTICALS, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**2834**	**41-2142317**
(State or other jurisdiction of incorporation or organization)	*(Primary Standard Industrial Classification Code Number)*	*(I.R.S. Employer Identification Number)*

12481 High Bluff Drive, Suite 200
San Diego, CA 92130
(858) 436-1400

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Theodore R. Schroeder
President and Chief Executive Officer
Cadence Pharmaceuticals, Inc.
12481 High Bluff Drive, Suite 200
San Diego, CA 92130
(858) 436-1400

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information contained in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion
Preliminary Prospectus dated September 25, 2006

PROSPECTUS

Shares

Common Stock

This is our initial public offering. We are offering shares of common stock.

We expect the initial public offering price to be between $ and $ per share. Currently, no public market exists for our common stock. After pricing of the offering, we expect that our common stock will be quoted on the Nasdaq Global Market under the symbol "CADX."

Investing in our common stock involves risks that are described in the "Risk Factors" section beginning on page 8 of this prospectus.

	Per Share	Total
Public offering price	$	$
Underwriting discount	$	$
Proceeds, before expenses, to us	$	$

The underwriters may also purchase up to an additional shares of common stock from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus to cover overallotments.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The shares of common stock will be ready for delivery on or about , 2006.

Merrill Lynch & Co.

Deutsche Bank Securities

Pacific Growth Equities, LLC

JMP Securities

The date of this prospectus is , 2006.

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You should rely only on the information contained in this prospectus. We have not, and the underwriters have not, authorized anyone to provide you with information different from or in addition to that contained in this prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: Neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

PROSPECTUS SUMMARY

This summary does not contain all of the information you should consider before buying shares of our common stock. You should read the entire prospectu carefully, especially the "Risk Factors" section and our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in shares of our common stock. Unless the context requires otherwise, references in this prospectus to "Cadence," "we," "us" and "our" refer to Cadenc Pharmaceuticals, Inc.

Cadence Pharmaceuticals, Inc.

Our Company

We are a biopharmaceutical company focused on in-licensing, developing and commercializing proprietary product candidates principally for use in the hospital setting. Since our inception in 2004, we have in-licensed rights to two Phase III product candidates, both of which have been studied in prior Phase III clinical trials conducted by our licensors. We have in-licensed the exclusive U.S. and Canadian rights to IV APAP, an intravenous formulation of acetaminophen that is currently marketed in Europe for the treatment of acute pain and fever by Bristol-Myers Squibb Company, or BMS. We believe that IV APAP is the only stable, pharmaceutically-acceptable intravenous formulation of acetaminophen. We have also in-licensed the exclusive North American and European rights to omiganan pentahydrochloride 1% aqueous gel, or Omigard™, for the prevention and treatment of device-related, surgical wound-related and burn-related infections. We believe that the hospital setting is a concentrated, underserved market for pharmaceuticals and anticipate building our own, hospital-focused sales force as our product candidates approach potential U.S. Food and Drug Administration, or FDA, approval. We intend to build a leading franchise in the hospital setting, continuing to focus on products that are in late-stages of development, currently commercialized outside the United States, or approved in the United States but with significant commercial potential for proprietary new uses or formulations.

The Hospital Market

Large, multinational pharmaceutical companies have generally decreased marketing efforts focused on hospital-use drugs, instead focusing on drugs that can be marketed in the larger outpatient setting. We believe this reduced emphasis on the hospital marketplace presents us with an excellent opportunity to in-license, acquire, develop and commercialize products that address unmet medical needs in the hospital setting. We believe the concentrated nature of the hospital marketplace will allow for our expansion into other therapeutic areas without substantial investment in additional commercial infrastructure.

According to data from IMS Health Inc., or IMS, an independent marketing research firm, approximately $28 billion was spent on promotional activities by the pharmaceutical industry in 2004. Of this amount, IMS estimates that only $1 billion was directed towards hospital-based physicians and directors of pharmacies. In contrast, U.S. hospitals and clinics accounted for approximately $54 billion or 21% of U.S. pharmaceutical sales in 2005, according to IMS. Furthermore, we believe pharmaceutical sales to acute care hospitals are highly concentrated among a relatively small number of large institutions. For example, according to Wolters Kluwer Health, an independent marketing research firm, only 2,000 of the approximately 5,000 acute care hospitals in the United States represent more than 80% of injectable analgesic sales. We believe the relative lack of promotional efforts directed toward the highly concentrated hospital marketplace makes it an underserved and compelling opportunity, especially for a biopharmaceutical company commercializing its products directly through its own dedicated sales force.

Our Product Candidates

IV APAP for the Treatment of Acute Pain and Fever

We are developing IV APAP in the U.S. market for the treatment of acute pain and fever. According to IMS, over 500 million units of injectable analgesics, typically used to treat acute pain, were sold in the United States in 2005. Opioids represent the majority of unit volume in the market but are

associated with a variety of unwanted side effects including sedation, nausea, vomiting, constipation, cognitive impairment and respiratory depression. Ketorolac a non-steroidal anti-inflammatory drug, or NSAID, is the only non-opioid injectable analgesic available in the United States for the treatment of acute pain. However, ketorolac carries strong warnings from the FDA for various side effects, including an increased risk of bleeding — a particularly troubling side-effect in the surgical setting.

Acetaminophen was first available for sale in the United States in 1955 when it was introduced under the brand name Tylenol. Acetaminophen is the most widely used drug for pain relief and the reduction of fever in the United States and is currently available in over 600 pharmaceutical products. Historically, poor stability in aqueous solutions and inadequate solubility of acetaminophen prevented the development of an intravenous dosage form. The patent protection for IV APAP extends through various dates in 2017 to 2021. Our patent protection for IV APAP is limited to a specific intravenous formulation of acetaminophen and extends through various dates in 2017 to 2021. There are currently no patents covering the acetaminophen molecule itself in the territories licensed to us, which include the United States and Canada.

IV APAP has previously been studied in six completed Phase III trials by BMS principally to support a Marketing Authorization Application in Europe for multiple indications, including pain and fever in both adults and children. Since its introduction in Europe in mid-2002, over 100 million doses of IV APAP have been administered to patients, and it has become the market share leader among injectable analgesics, with 2005 sales of more than $140 million according to IMS. In the fourth quarter of 2006, we expect to initiate the remaining Phase III clinical trial requirements for potential approval in the United States. We expect these Phase III clinical trial results to be available in the first half of 2008 and, if positive, to subsequently submit a new drug application, or NDA, for IV APAP in the second half of 2008. However, we cannot be certain that the FDA will not require additional trials or that IV APAP will ever receive regulatory approval in the United States.

Omigard for the Prevention of Intravascular Catheter-Related Infections

We are currently developing Omigard for the prevention of intravascular catheter-related infections. According to the February 2004 *Catheter: Global Markets & Technologies* report from Theta Reports, eight million central venous catheters, or CVCs, were sold in the United States in 2003, and unit sales are projected to grow to 11 million by 2007. Although CVCs have become an important part of medical care, they can give rise to dangerous and costly complications, including: local catheter site infections, or LCSIs, which are infections at the catheter insertion site; catheter colonization, which is the growth of microorganisms on the portion of the catheter below the skin surface; and catheter-related bloodstream infections, or CRBSIs, which are infections in the bloodstream caused by microorganisms associated with the catheter. The Centers for Disease Control and Prevention estimates that there are 250,000 CRBSIs each year in the United States. The attributable mortality rate of CRBSIs is approximately 12% to 25% with an average marginal cost to the healthcare system of $25,000 per infection. Currently, topical antiseptics are the primary agent used to cleanse the skin surface around the catheter insertion site prior to insertion. However, the utility of these antiseptics is limited, principally due to their short duration of antimicrobial activity.

Omigard is a topical antimicrobial that has been demonstrated to be rapidly bactericidal and fungicidal with prolonged duration of activity against microorganisms commonly found on the skin surface, including multi-drug resistant microorganisms such as methicillin-resistant *staphylococcus aureus*, or MRSA. Importantly, resistance to Omigard has not been induced in the laboratory after extensive study, nor has Omigard demonstrated potential to induce cross-resistance to other antimicrobial therapeutics. We have in-licensed the patents and the exclusive development and commercialization rights to Omigard in North America and Europe for the prevention of device-related, surgical wound-related and burn-related infections from Migenix Inc. The patent protection for Omigard extends through various dates in 2017 to 2022.

Omigard has previously been studied in a large, completed Phase III trial that demonstrated statistically significant outcomes for the prevention of LCSI and catheter colonization. The presence of an LCSI may result in replacement of the catheter and/or administration of antibiotics, both of which create additional costs to hospitals and have the potential for adverse safety outcomes. In addition, catheter colonization is well correlated with CRBSIs, according to a published review of clinical trials. However, despite the favorable, statistically significant results for prevention of LCSI and catheter colonization, the study did not show statistical significance for the primary endpoint, the prevention of CRBSIs. After in-licensing Omigard, we reached agreement with the FDA through the special protocol assessment, or SPA, process on the trial design, endpoints and statistical analysis plan for a single confirmatory Phase III clinical trial with a primary endpoint of prevention of LCSIs. The SPA process provides for official FDA evaluation of a proposed Phase III clinical trial protocol and generally provides a product sponsor with a binding agreement from the FDA that the design and analysis of the trial are adequate to support a license application submission if the trial is performed according to the SPA. We initiated this Phase III clinical trial in August 2005 and expect the results to be available in the second half of 2007 and, if positive, to subsequently submit an NDA for Omigard in the first half of 2008.

Our Strategy

Our goal is to be a leading biopharmaceutical company focused on the development and commercialization of proprietary pharmaceuticals principally for use in the hospital setting. Specifically, we intend to:

- *Obtain regulatory approval for our Phase III hospital product candidates.* We have designed our Phase III clinical programs in an effort to reduce clinical development risk, facilitate regulatory approval and optimize marketing claims. To that end, we plan to resume a U.S. Phase III program later this year for IV APAP previously initiated by BMS, and we expect to submit an NDA in the second half of 2008 based on the previously completed trials and any further trials that may be required by the FDA. In addition, we have reached a written agreement with the FDA through the SPA process for a single confirmatory Phase III study of Omigard for the prevention of LCSIs.
- *Build a highly leverageable sales organization targeting hospitals.* We intend to build a commercial organization focused on promoting our products principally to hospitals in the United States. We believe that both IV APAP and Omigard can be effectively promoted by our own sales force targeting key hospitals in the United States. Importantly, we believe the number of institutions in the hospital marketplace is relatively limited and a small number of these institutions account for a substantial portion of the prescribing activity. The concentrated nature of this market creates the opportunity for significant marketing synergies as we intend to leverage our sales force across multiple therapeutic categories in the hospital. Outside the United States, we intend to establish strategic partnerships for the commercialization of our products where we have commercialization rights.
- *Expand our product portfolio through acquiring or in-licensing additional late-stage, hospital-focused products with well-understood risk profiles.* We will seek additional opportunities to acquire or in-license products to more fully exploit our clinical, regulatory, manufacturing, sales and marketing capabilities. We believe that our focus on the hospital market enables us to evaluate a broader range of products across multiple therapeutic areas for possible acquisition. We focus on products that are in late-stages of development, currently commercialized outside the United States, or approved in the United States but with significant commercial potential for proprietary new uses, including new indications, dosage forms or delivery systems.
- *Pursue additional indications and commercial opportunities for our product candidates.* We will seek to maximize the value of IV APAP, Omigard and any other product candidates we may in-license, acquire or develop by pursuing other indications and commercial

opportunities for such candidates. For example, we have rights to develop and commercialize Omigard for additional indications related to the prevention and treatment of device-related, surgical wound-related and burn-related infections.

Risk Factors

We are a development stage company with no revenues, and our operations to date have generated substantial and increasing needs for cash. Our net loss was $7.5 million in 2005, and as of June 30, 2006, we had an accumulated deficit of $45.5 million. Our business and our ability to execute on our business strategy are subject to a number of risks that you should be aware of before you decide to buy our common stock. In particular, you should consider the following risks, which are discussed more fully in "Risk Factors" beginning on page 8:

- we are largely dependent on the success of our only two product candidates, IV APAP and Omigard, and we cannot be certain that our planned clinical development programs will be sufficient to support NDA submissions or that either product candidate will receive regulatory approval or be successfully commercialized;
- delays in the commencement, enrollment or completion of clinical testing for either of our product candidates could result in increased costs to us and delay or limit our ability to obtain regulatory approval;
- even if our product candidates are approved by regulatory authorities, we expect intense competition in the hospital marketplace for our targeted indications;
- the patent rights that we have in-licensed covering IV APAP are limited to a specific intravenous formulation of acetaminophen, and our market opportunity for this product candidate may be limited by the lack of patent protection for the active ingredient itself and other formulations that may be developed by competitors; and
- we will require substantial additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our development programs and commercialization efforts.

Corporate Information

We were incorporated in Delaware on May 26, 2004. Our principal executive offices are located at 12481 High Bluff Drive, Suite 200, San Diego, California 92130, and our telephone number is (858) 436-1400. Prior to November 2004, we were named Strata Pharmaceuticals, Inc. Our website address is http://www.cadencepharm.com. The information on, or accessible through, our website is not part of this prospectus.

The U.S. Patent and Trademark Office has issued a Notice of Allowance in connection with our intent-to-use trademark application for the mark CADENCE™, covering pharmaceutical preparations for the treatment or prevention of diseases or infections of the body's major organs, including the heart, lungs, liver and kidneys; pharmaceutical preparations for the treatment or prevention of diseases of the body's systems, including the immune system and the cardiovascular system; and pharmaceutical preparations to treat or manage pain, anesthesia, surgical and medical procedures. A Notice of Allowance is a notice issued by the U.S. Patent and Trademark Office to an intent-to-use application once all steps of the application process have been completed. Once the Notice of Allowance has been issued, the applicant has six months to file a statement of use or an extension, showing that it is using the mark in commerce, in order for the U.S. Patent and Trademark Office to issue a certificate of registration. We are developing commercial names for our product candidates, and have applied for U.S. trademark registration for Omigard™. This prospectus also contains trademarks of others, including Bactroban®, Betadine®, BioPatch®, DepoDur®, Dermagraft®, Habitrol®, Lotensin®, Neosporin®, Perfalgan®, Pro-Dafalgan®, Toradol® and Tylenol®.

THE OFFERING

Common stock offered	shares
Common stock to be outstanding after this offering	shares
Use of proceeds	We expect to use the net proceeds from this offering to fund clinical trials and other research and development activities, and to fund working capital, capital expenditures and other general corporate purposes. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products.
Risk factors	See "Risk Factors" and other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.
Proposed Nasdaq Global Market symbol	CADX

The number of shares of common stock to be outstanding after this offering is based on 88,182,195 shares outstanding as of June 30, 2006, and excludes:

- 5,769,471 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2006 at a weighted average exercise price of $0.38 per share;
- 385,000 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2006 at a weighted average exercise price of $1.00 per share; and
- shares of common stock reserved for future issuance under our 2006 equity incentive award plan, which will become effective on the day prior to the day on which we become subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act (including 1,678,789 shares of common stock reserved for future grant or issuance under our 2004 equity incentive award plan, which shares will be added to the shares to be reserved under our 2006 equity incentive award plan upon the effectiveness of th 2006 equity incentive award plan).

Except as otherwise indicated, all information in this prospectus assumes:

- no exercise by the underwriters of their option to purchase up to an additional shares of common stock to cover over-allotments;
- the filing of our amended and restated certificate of incorporation and amended and restated bylaws upon completion of this offering;
- the conversion of all outstanding shares of our preferred stock into 79,630,455 shares of common stock upon completion of this offering; and
- a one-for- reverse stock split of our common stock to be effected before the completion of this offering.

SUMMARY FINANCIAL DATA

The following table summarizes certain of our financial data. The summary financial data are derived from our audited financial statements for the period from May 26, 2004 (inception) through December 31, 2004, and the year ended December 31, 2005. Data are also derived from our unaudited financial statements for the six-month periods ended June 30, 2005 and 2006, and for the period from May 26, 2004 (inception) through June 30, 2006. The data should be read together with our financial statements and related notes, "Selected Financial Data," and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this prospectus. The pro forma as adjusted balance sheet data gives effect to the conversion of all outstanding shares of our preferred stock into 79,630,455 shares of our common stock and our sale of shares of our common stock in this offering at the initial offering price of $ per share, after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

	Period from May 26, 2004 (Inception) Through December 31, 2004	Year Ended December 31, 2005	Six Months Ended June 30,		Period from May 26, 2004 (Inception) Through June 30, 2006
			2005	2006	
	(In thousands, except per share amounts)				
Statement of Operations Data:					
Operating expenses:					
Research and development	$ 2,233	$ 6,126	$ 2,402	$ 33,574	$ 41,934
Marketing	41	240	142	317	598
General and administrative	877	1,412	540	1,488	3,777
Total operating expenses	3,151	7,778	3,084	35,379	46,309
Loss from operations	(3,151)	(7,778)	(3,084)	(35,379)	(46,309)
Other income (expense):					
Interest income	9	255	14	553	818
Interest expense	—	—	—	(44)	(44)
Total other income	9	255	14	509	774
Net loss	$ (3,142)	$ (7,523)	$ (3,070)	$ (34,870)	$ (45,535)
Basic and diluted net loss per share(1)	$ (0.86)	$ (1.63)	$ (0.68)	$ (7.01)	
Shares used to compute basic and diluted net loss per share(1)	3,658	4,624	4,527	4,974	
Pro forma basic and diluted net loss per share(1)		$ (0.36)		$ (0.59)	
Shares used to compute pro forma basic and diluted net loss per share(1)		20,649		58,711	

(1) See Note 1 of Notes to Financial Statements for an explanation of the method used to compute the historical and pro forma net loss per share and the number of shares used in the computation of the per share amounts.

	As of June 30, 2006	
	Actual	Pro Forma As Adjusted(1)
	(In thousands)	
Balance Sheet Data:		
Cash and cash equivalents	$ 42,881	$
Working capital	37,476	
Total assets	46,355	
Long-term debt, less current portion	5,968	
Deficit accumulated during the development stage	(45,535)	
Total stockholders' equity	34,428	

(1) Each $1.00 increase or decrease in the assumed initial public offering price of $ would increase or decrease, respectively, the amount of cash and cash equivalents, working capital, total assets and total stockholders' equity by $, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the following risk factors, as well as the other information in this prospectus, before deciding whether to invest in shares of our common stock. The occurrence of any of the following risks could harm our business, financial condition, results of operations or growth prospects. In that case, the trading price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Our Business and Industry

We are largely dependent on the success of our two product candidates, IV APAP and Omigard, and we cannot be certain that either of these product candidates will receive regulatory approval or be successfully commercialized.

We currently have no drug products for sale and we cannot guarantee that we will ever have marketable drug products. The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products are subject to extensive regulation by the U.S. Food and Drug Administration, or FDA, and other regulatory authorities in the United States and other countries, which regulations differ from country to country. We are not permitted to market our product candidates in the United States until we receive approval of a new drug application, or NDA, from the FDA. We have not submitted an NDA or received marketing approval for either of our product candidates. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. We currently have only two product candidates, and our business success currently depends entirely on their successful development and commercialization.

We have not developed either of our product candidates independently. We recently in-licensed exclusive rights to IV APAP, an intravenous formulation of acetaminophen that is currently marketed in Europe for the treatment of acute pain and fever by Bristol-Myers Squibb Company, or BMS. We intend to conduct six clinical trials to provide the FDA with data to support multiple dose efficacy for soft tissue surgery, efficacy for fever and safety in adults and children, based on the preliminary feedback we received from the FDA in our meeting in August 2006. In July 2004, we in-licensed the rights to our only other product candidate, omiganan pentahydrochloride 1% aqueous gel, or Omigard, which is currently being evaluated in a single Phase III clinical trial for the prevention of local catheter site infections, or LCSIs, and will require the successful completion of this Phase III clinical trial before we are able to submit an NDA to the FDA for approval. Our clinical development programs for IV APAP and Omigard may not lead to commercial products if we fail to demonstrate that the product candidates are safe and effective in clinical trials and we may therefore fail to obtain necessary approvals from the FDA and similar foreign regulatory agencies, or because we may have inadequate financial or other resources to advance these product candidates through the clinical trial process. Any failure to obtain approval of IV APAP or Omigard would have a material and adverse impact on our business.

If clinical trials of our current or future product candidates do not produce results necessary to support regulatory approval in the United States or elsewhere, we will be unable to commercialize these products.

To receive regulatory approval for the commercial sale of IV APAP, Omigard or any other product candidates that we may in-license or acquire, we must conduct, at our own expense, adequate and well controlled clinical trials to demonstrate efficacy and safety in humans. Clinical testing is expensive, takes many years and has an uncertain outcome. Clinical failure can occur at any stage of the testing. Our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical and/or non-clinical testing. For example, Migenix Inc., or Migenix, the licensor for our Omigard product candidate, together with its former collaborator, Fujisawa Healthcare, Inc., or Fujisawa, completed enrollment in a Phase III trial in February 2003 that demonstrated statistically significant results for the secondary endpoints of the trial: the prevention of LCSIs and catheter colonization, which is the growth of microorganisms on the portion of the catheter below the skin

surface. However, the trial did not show statistical significance for the primary endpoint, the prevention of catheter-related bloodstream infections, or CRBSIs.

After the termination of the collaboration between Migenix and Fujisawa in January 2004, we in-licensed the rights to Omigard from Migenix in July 2004 and subsequently reached an agreement under the special protocol assessment, or SPA, process with the FDA concerning the protocol for our own Phase III clinical trial for Omigard. In connection with the SPA for Omigard, the FDA agreed that a single confirmatory Phase III trial will be required for approval of Omigard and that the prevention of LCSIs will be the sole primary efficacy endpoint. However, we cannot be certain that our ongoing Phase III trial for Omigard will demonstrate statistical significance or otherwise demonstrate sufficient efficacy and safety to support the filing of an NDA or ultimately lead to regulatory approval. Furthermore, despite having completed the SPA process, the FDA's agreement with us on the trial protocol remains subject to future public health concerns unrecognized at the time of the FDA's protocol assessment.

Our failure to adequately demonstrate the efficacy and safety of IV APAP, Omigard or any other product candidates that we may in-license or acquire would prevent receipt of regulatory approval and, ultimately, the commercialization of that product candidate.

Because the results of earlier clinical trials are not necessarily predictive of future results, IV APAP, Omigard or any other product candidate we advance into clinical trials may not have favorable results in later clinical trials or receive regulatory approval.

Success in clinical testing and early clinical trials does not ensure that later clinical trials will generate adequate data to demonstrate the efficacy and safety of the investigational drug. A number of companies in the pharmaceutical industry, including those with greater resources and experience, have suffered significant setbacks in Phase III clinical trials, even after promising results in earlier clinical trials.

In March 2006, we in-licensed the rights to IV APAP from BMS, which is currently marketing IV APAP in Europe and other parts of the world under the brand name Perfalgan. BMS has completed nine clinical trials, mostly in Europe, primarily in support of European regulatory approvals for this product candidate. However, we do not know at this time what regulatory weight, if any, the U.S. and Canadian regulatory agencies will give to these clinical data in supplementing clinical data generated by us for potential regulatory approval of IV APAP in the United States and Canada. The FDA and foreign regulatory agencies may reject these clinical trial results if they determine that the clinical trials were not conducted in accordance with requisite regulatory standards and procedures. Furthermore, we have not audited or verified the accuracy of the primary clinical data provided by BMS and cannot determine their applicability to our regulatory filings. Even though BMS has obtained marketing approval in Europe and other territories for IV APAP, we must conduct additional adequate and well controlled clinical trials in the United States to demonstrate IV APAP's safety and efficacy in specific indications to gain regulatory approval in the United States. We may not be able to demonstrate the same safety and efficacy for IV APAP in our planned Phase III clinical trial as was demonstrated previously by BMS.

Our other product candidate, Omigard, is a novel antimicrobial peptide and is not yet approved in any jurisdiction. No antimicrobial peptide has been approved by the FDA, including two antimicrobial peptides with mechanisms of action similar to Omigard that were studied in Phase III clinical trials. Although Omigard has been studied in more than 750 patients, all of the patients studied were enrolled in trials conducted or sponsored by Migenix or Fujisawa. Since in-licensing rights to Omigard from Migenix in July 2004, we have initiated a Phase III clinical trial in which we are still seeking to enroll the target patient population. We do not expect to complete enrollment in this Phase III clinical trial until the second half of 2007. Similar to IV APAP, we have obtained electronic databases from the completed Phase III trials sponsored by Migenix and Fujisawa, and are currently analyzing these data. We have not audited or verified the accuracy of the primary clinical data provided by our licensor and its former collaborator and cannot determine their applicability to our regulatory filings. Although the Phase III clinical trial for Omigard conducted by Migenix and Fujisawa demonstrated favorable, statistically significant results for the prevention of LCSIs and catheter colonization, secondary endpoints in their trial,

we may not observe similar results in our ongoing Phase III clinical trial. Furthermore, the earlier Phase III clinical trial failed to show statistical significance for the primary endpoint of that trial, the prevention of CRBSIs. While we will measure the prevention of CRBSIs as a secondary endpoint in our ongoing Phase III clinical trial for Omigard, our trial is not designed to demonstrate statistical significance for this secondary endpoint. Although we are targeting a different primary endpoint in our trial, the prevention of LCSIs, it is possible that we will experience similar, unexpected results. Failure to satisfy a primary endpoint in a Phase III clinical trial would generally mean that a product candidate would not receive regulatory approval without a further successful Phase III clinical trial.

The data collected from our clinical trials may not be adequate to support regulatory approval of IV APAP, Omigard or any other product candidates that we may in-license or acquire. Moreover, all clinical data reported is taken from databases that may not have been fully reconciled against medical records kept at the clinical sites. Despite the results reported by others in earlier clinical trials for our product candidates, we do not know whether any Phase III or other clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market our product candidates.

Delays in the commencement or completion of clinical testing could result in increased costs to us and delay or limit our ability to obtain regulatory approval for our product candidates.

Delays in the commencement or completion of clinical testing could significantly affect our product development costs. We do not know whether planned clinical trials for IV APAP will begin on time or be completed on schedule, if at all. Similarly, we may not complete enrollment for our ongoing Phase III clinical trial for Omigard on schedule, or at all. The commencement and completion of clinical trials requires us to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs for the same indication as our product candidates or may not be eligible to participate in or may be required to withdraw from a clinical trial as a result of changing standards of care. The commencement and completion of clinical trials can be delayed for a variety of other reasons, including delays related to:

- reaching agreements on acceptable terms with prospective clinical research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining regulatory approval to commence a clinical trial;
- obtaining institutional review board approval to conduct a clinical trial at a prospective site;
- recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including competition from other clinical trial programs for the same indication as our product candidates; and
- retaining patients who have initiated a clinical trial but may be prone to withdraw due to the treatment protocol, lack of efficacy, personal issues, side effects from the therapy or who are lost to further follow-up.

In addition, a clinical trial may be suspended or terminated by us, the FDA or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues or any determination that a trial presents unacceptable health risks; or

- lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties.

Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to institutional review boards for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in the completion of, or if we terminate, our clinical trials, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Even if we are able to ultimately commercialize our product candidates, other therapies for the same indications may have been introduced to the market and established a competitive advantage.

We expect intense competition in the territories in which we have rights to our product candidates, and new products may emerge that provide different or better therapeutic alternatives for our targeted indications.

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of our product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. There can be no assurance that developments by others will not render our product candidates obsolete or noncompetitive. Furthermore, new developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical industry at a rapid pace. These developments may render our product candidates obsolete or noncompetitive.

We intend to develop IV APAP for the treatment of acute pain in the hospital setting, which will compete with well established injectable drugs for this and similar indications, including opioids such as morphine, fentanyl, meperidine and hydromorphone, each of which is available generically from several manufacturers, as well as an extended release injectable formulation of morphine, DepoDur, currently marketed by an affiliate of Endo Pharmaceuticals Holdings Inc. Ketorolac, an injectable non-steroidal anti-inflammatory drug, or NSAID, is also available generically from several manufacturers and used to treat acute pain. During the time that it will take us to obtain regulatory approval for IV APAP, if at all, we anticipate that several additional products may be developed for the treatment of acute pain, including other injectable NSAIDs, novel opioids, new formulations of currently available opioids, long-acting local anesthetics and new chemical entities as well as alternative delivery forms of various opioids and NSAIDs.

We are also developing our Omigard product candidate for the prevention of intravascular catheter-related infections in the hospital setting. If approved, Omigard will compete with well established topical products that are currently used in practice to prevent these infections as well as BioPatch, a device marketed by Johnson & Johnson, which has been approved for wound dressing and prevention of catheter-related infections. Other competitive products may be under development.

In addition, competitors may seek to develop alternative formulations of our product candidates that address our targeted indications that do not directly infringe on our in-licensed patent rights. For example, we are aware of several U.S. and Canadian patents and patent applications covering various potential injectable formulations of acetaminophen, including intravenous formulations, as well as methods of making and using these potential formulations. Furthermore, analogs of Omigard have been developed by others that are not covered by patents licensed to or owned by us. The commercial opportunity for our product candidates could be significantly harmed if competitors are able to develop alternative

formulations outside the scope of our in-licensed patents. Compared to us, many of our potential competitors have substantially greater:

- capital resources;
- development resources, including personnel and technology;
- clinical trial experience;
- regulatory experience;
- expertise in prosecution of intellectual property rights; and
- manufacturing, distribution and sales and marketing experience.

As a result of these factors, our competitors may obtain regulatory approval of their products more rapidly than we are able to or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, useful and less costly than ours and may also be more successful than us in manufacturing and marketing their products. We also expect to face similar competition in our efforts to identify appropriate collaborators or partners to help develop or commercialize our product candidates in markets outside the United States.

If any of our product candidates for which we receive regulatory approval do not achieve broad market acceptance, the revenues that we generate from their sales will be limited.

The commercial success of our product candidates for which we obtain marketing approval from the FDA or other regulatory authorities will depend upon the acceptance of these products by the medical community and coverage and reimbursement of them by third-party payors, including government payors. The degree of market acceptance of any of our approved products will depend on a number of factors, including:

- limitations or warnings contained in a product's FDA-approved labeling, including potential limitations or warnings for IV APAP that may be more restrictive than oral formulations of acetaminophen;
- changes in the standard of care for the targeted indications for either of our product candidates could reduce the marketing impact of any superiority claims that we could make following FDA approval;
- limitations inherent in the approved indication for either of our product candidates compared to more commonly-understood or addressed conditions, including, in the case of Omigard, the ability to promote Omigard to hospitals and physicians who may be more focused on an indication specifically for the prevention of CRBSIs compared to the prevention of LCSIs, the primary endpoint in our ongoing Phase III clinical trial; and
- potential advantages over, and availability of, alternative treatments, including, in the case of IV APAP, a number of products already used to treat acute pain in the hospital setting, and in the case of Omigard, a number of competitive topical products as well as a device that has been approved for wound dressing and prevention of catheter-related infections.

Our ability to effectively promote and sell our product candidates in the hospital marketplace will also depend on pricing and cost effectiveness, including our ability to produce a product at a competitive price and our ability to obtain sufficient third-party coverage or reimbursement. Since many hospitals are members of group purchasing organizations, which leverage the purchasing power of a group of entities to obtain discounts based on the collective buying power of the group, our ability to attract customers in the hospital marketplace will also depend on our ability to effectively promote our product candidates to group purchasing organizations. We will also need to demonstrate acceptable evidence of safety and efficacy as well as relative convenience and ease of administration. Market acceptance could be further limited

depending on the prevalence and severity of any expected or unexpected adverse side effects associated with our product candidates. If our product candidates are approved but do not achieve an adequate level of acceptance by physicians, health care payors and patients, we may not generate sufficient revenue from these products, and we may not become or remain profitable. In addition, our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful.

The decreasing use of the comparator product in our clinical trial for Omigard may limit our ability to complete the trial in a timely manner and hinder the competitive profile of this product candidate.

The SPA that we agreed to with the FDA for our ongoing Phase III clinical trial for Omigard requires that Omigard be compared to 10% povidone-iodine, a topical antiseptic used to sterilize catheter insertion sites. Although the SPA generally provides us with a binding agreement from the FDA that, assuming positive results, the design and analysis of our ongoing Omigard trial are adequate to support an NDA filing, all SPAs are subject to future public health concerns unrecognized at the time of protocol assessment.

After we established the SPA and commenced our clinical trial, many hospitals, particularly in the United States, began increasing use of another topical antiseptic, chlorhexidine, as the standard of care to sterilize catheter insertion sites. Although we believe 10% povidone-iodine continues to be used by a sufficient number of hospitals to support continued enrollment of patients in our Phase III clinical trial for Omigard, this changing standard of care limits the number of potential clinical trial sites available to us. Accordingly, it may be difficult for us to maintain the clinical trial sites that we have already retained for the Omigard trial if any of these institutions elects to replace our comparator product with chlorhexidine, and it may take us longer than anticipated to identify and reach terms with additional hospitals to serve as clinical trial sites for the trial. Delays in the completion of enrollment or clinical testing for our ongoing Phase III clinical trial for Omigard and any other studies we may conduct to compare Omigard to chlorhexidine or another topical antiseptic could significantly affect our product development costs, our prospects for regulatory approval and our ability to compete. Furthermore, the decreasing use of 10% povidone-iodine in favor of chlorhexidine could reduce the marketing impact of any superiority claims that we could make following FDA approval. For example, hospitals and physicians may be reluctant to adopt the use of Omigard as a single agent for the prevention of local catheter site infections. Even if Omigard is approved by the FDA, if this product candidate does not achieve an adequate level of acceptance by physicians, health care payors and patients, we may be unable to generate sufficient revenues to recover our development costs or otherwise sustain and grow our business.

Even if our product candidates receive regulatory approval, they may still face future development and regulatory difficulties.

Even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. Any of these restrictions or requirements could adversely affect our potential product revenues. For example, the label ultimately approved for IV APAP, Omigard or any other product candidates that we may in-license or acquire, if any, may include a restriction on the term of its use, or it may not include one or more of our intended indications.

Our product candidates will also be subject to ongoing FDA requirements for the labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information on the drug. In addition, approved products, manufacturers and manufacturers' facilities are subject to continual review and periodic inspections. If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If our product candidates

fail to comply with applicable regulatory requirements, such as current Good Manufacturing Practices, or cGMPs, a regulatory agency may:

- issue warning letters or untitled letters;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- impose other civil or criminal penalties;
- suspend regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require a product recall.

Even if our product candidates receive regulatory approval in the United States, we may never receive approval or commercialize our products outside of the United States.

Our rights to IV APAP are limited to the United States and Canada, and our rights to Omigard are limited to North America and Europe. In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the United States as well as other risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed above regarding FDA approval in the United States. As described above, such effects include the risks that our product candidates may not be approved for all indications requested, which could limit the uses of our product candidates and have an adverse effect on product sales and potential royalties, and that such approval may be subject to limitations on the indicated uses for which the product may be marketed or require costly, post-marketing follow-up studies.

We have never marketed a drug before, and if we are unable to establish an effective sales and marketing infrastructure, we will not be able to successfully commercialize our product candidates.

In the United States, we plan to build our own sales force to market our products directly to physicians, nurses, hospitals, group purchasing organizations and third-party payors. We currently do not have significant internal sales, distribution and marketing capabilities. In order to commercialize any of our product candidates, we must either acquire or internally develop sales and marketing capabilities, or enter into collaborations with partners to perform these services for us. The acquisition or development of a hospital-focused sales and marketing infrastructure for our domestic operations will require substantial resources, will be expensive and time consuming and could negatively impact our commercialization efforts, including delay any product launch. Moreover, we may not be able to hire a sales force that is sufficient in size or has adequate expertise. If we are unable to establish our sales and marketing capability or any other capabilities necessary to commercialize any products we may develop, we will need to contract with third parties to market and sell our products. If we are unable to establish adequate sales and marketing capabilities, whether independently or with third parties, we may not be able to generate any product revenue, may generate increased expenses and may never become profitable.

Our product candidates may have undesirable side effects that could delay or prevent their regulatory approval or commercialization.

Undesirable side effects caused by our product candidates could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our product candidates and generating revenues from their sale. For example, the adverse events related to IV APAP observed in clinical trials completed to date include transient liver enzyme evaluations, nausea or vomiting and pain or local skin reactions at the injection site. When used outside the current guidelines for administration, acetaminophen has the potential to cause liver toxicity. While administration of acetaminophen in intravenous form is not expected to result in an increased risk of toxicity to the liver compared with an equivalent dose of acetaminophen administered orally, we cannot be certain that increased liver toxicity or other drug-related side effects will not be observed in future clinical trials or that the FDA will not require additional trials or impose more severe labeling restrictions due to liver toxicity or other concerns. Drug-related adverse events observed in clinical trials completed to date for Omigard have been limited to local skin reactions, including redness, swelling, bleeding, itching, bruising and pain. In addition, while these drug-related adverse events have all been related to the skin, including the catheter insertion site, we cannot be certain that other drug-related side effects will not be reported in clinical trials or thereafter.

If either of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by the product:

- regulatory authorities may require the addition of labeling statements, specific warnings or a contraindication;
- regulatory authorities may withdraw their approval of the product;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase our commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from its sale.

If the government or third-party payors fail to provide coverage and adequate coverage and payment rates for our future products, if any, or if hospitals choose to use therapies that are less expensive, our revenue and prospects for profitability will be limited.

In both domestic and foreign markets, our sales of any future products will depend in part upon the availability of coverage and reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare, managed care providers, private health insurers and other organizations. In particular, many U.S. hospitals receive a fixed reimbursement amount per procedure for certain surgeries and other treatment therapies they perform. Because this amount may not be based on the actual expenses the hospital incurs, hospitals may choose to use therapies which are less expensive when compared to our product candidates. Accordingly, IV APAP, Omigard or any other product candidates that we may in-license or acquire, if approved, will face competition from other therapies and drugs for these limited hospital financial resources. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of hospitals, other target customers and their third-party payors. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Governments continue to propose and pass legislation designed to reduce the cost of healthcare. In the United States, we expect that there will continue to be federal and state proposals to implement similar governmental controls. For example, in December 2003, Congress enacted a limited prescription drug benefit for Medicare beneficiaries in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. Under this program, drug prices for certain prescription drugs are negotiated by drug plans, with the goal to lower costs for Medicare beneficiaries. In some foreign markets, the government controls the pricing of prescription pharmaceuticals. In these countries, pricing negotiated with governmental authorities can take six to 12 months or longer after the receipt of regulatory marketing approval for a product. Cost control initiatives could decrease the price that we would receive for any products in the future, which would limit our revenue and profitability. Accordingly, legislation and regulations affecting the pricing of pharmaceuticals might change before our product candidates are approved for marketing. Adoption of such legislation could further limit reimbursement for pharmaceuticals.

If we breach any of the agreements under which we license rights to our product candidates from others, we could lose the ability to continue the development and commercialization of our product candidates.

In March 2006, we entered into an exclusive license agreement with BMS relating to our IV APAP product candidate for the United States and Canada, and in July 2004, we entered into an exclusive license agreement with Migenix relating to our Omigard product candidate for North America and Europe. Because we have in-licensed the rights to our two product candidates from third parties, if there is any dispute between us and our licensors regarding our rights under these license agreements, our ability to develop and commercialize these product candidates may be adversely affected. Any uncured, material breach under these license agreements could result in our loss of exclusive rights to the related product candidate and may lead to a complete termination of our product development efforts for the related product candidate.

If BMS breaches the underlying agreement under which we sublicense the rights to our IV APAP product candidate, we could lose the ability to develop and commercialize IV APAP.

Our license for IV APAP is subject to the terms and conditions of a license from SCR Pharmatop to BMS, under which BMS originally licensed the intellectual property rights covering IV APAP. If BMS materially breaches the terms or conditions of this underlying license from SCR Pharmatop, and neither BMS nor we adequately cure that breach, or BMS and SCR Pharmatop otherwise become involved in a dispute, the breach by BMS or disputes with SCR Pharmatop could result in a loss of, or other material adverse impact on, our rights under our license agreement with BMS. While we would expect to exercise all rights and remedies available to us, including seeking to cure any breach by BMS, and otherwise seek to preserve our rights under the patents licensed by SCR Pharmatop, we may not be able to do so in a timely manner, at an acceptable cost or at all. Any uncured, material breach under the license from SCR Pharmatop to BMS could result indirectly in our loss of exclusive rights to our IV APAP product candidate and may lead to a complete termination of our product development and any commercialization efforts for IV APAP.

We rely on third parties to conduct our clinical trials, including our planned Phase III clinical program for IV APAP and our ongoing Phase III clinical trial for Omigard. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates on our anticipated timeline or at all.

We intend to rely primarily on third-party CROs to oversee our clinical trials for our IV APAP and Omigard product candidates, and we depend on independent clinical investigators, medical institutions and contract laboratories to conduct our clinical trials. Although we rely on CROs to conduct our clinical trials, we are responsible for ensuring that each of our clinical trials is conducted in accordance with its investigational plan and protocol. Moreover, the FDA requires us to comply with regulations and standards, commonly referred to as good clinical practices, or GCPs, for conducting, monitoring, recording

and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. Our reliance on CROs does not relieve us of these responsibilities and requirements. CROs and investigators are not our employees, and we cannot control the amount or timing of resources that they devote to our programs. If our CROs or independent investigators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, it will delay the approval of our FDA applications and our introductions of new products. The CROs with which we contract for execution of our clinical trials play a significant role in the conduct of the trials and the subsequent collection and analysis of data. Failure of the CROs to meet their obligations could adversely affect clinical development of our product candidates. Moreover, these independent investigators and CROs may also have relationships with other commercial entities, some of which may have competitive products under development or currently marketed. If independent investigators and CROs assist our competitors, it could harm our competitive position. If any of these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the clinical data is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for IV APAP, Omigard or future product candidates.

If the manufacturers upon whom we rely fail to produce our product candidates in the volumes that we require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the development and commercialization of, or be unable to meet demand for, our products and may lose potential revenues.

We do not manufacture any of our product candidates, and we do not currently plan to develop any capacity to do so. We do not yet have agreements established regarding commercial supply of either of our product candidates and may not be able to establish or maintain commercial manufacturing arrangements on commercially reasonable terms for IV APAP, Omigard or any other product candidates that we may in-license or acquire. Any problems or delays we experience in preparing for commercial-scale manufacturing of a product candidate may result in a delay in FDA approval of the product candidate or may impair our ability to manufacture commercial quantities, which would adversely affect our business. For example, our manufacturers will need to produce specific batches of our product candidates to demonstrate acceptable stability under various conditions and for commercially viable lengths of time. We and our contract manufacturers will need to demonstrate to the FDA and other regulatory authorities this acceptable stability data for our product candidates, as well as validate methods and manufacturing processes, in order to receive regulatory approval to commercialize IV APAP, Omigard or any other product candidate. Furthermore, if our commercial manufacturers fail to deliver the required commercial quantities of bulk drug substance or finished product on a timely basis and at commercially reasonable prices, we would likely be unable to meet demand for our products and we would lose potential revenues.

We currently have what we believe are adequate clinical supplies of our Omigard product candidate. We entered into a clinical supply agreement with Lawrence Laboratories, an affiliate of BMS, under which Lawrence Laboratories has manufactured a single batch of clinical supplies of IV APAP and a single batch of placebo. With these batches, we believe we will have adequate clinical supplies of our IV APAP product candidate and placebo. The term of the clinical supply agreement generally extends until the earlier of the receipt by us of regulatory approval for IV APAP or December 31, 2008. In addition, the clinical supply agreement could terminate upon mutual written consent of the parties, the termination of the IV APAP agreement or our dissolution. The clinical supply agreement may also be terminated by either party upon written notice to the other party of an uncured, material breach. We are currently negotiating with suppliers for the potential commercial supply of the finished drug product for IV APAP. We do not have any long-term commitments from our suppliers of clinical trial material or guaranteed prices for our product candidates or placebos. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production

costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Our manufacturers may not perform as agreed. If our manufacturers were to encounter any of these difficulties, our ability to provide product candidates to patients in our clinical trials would be jeopardized.

In addition, all manufacturers of our product candidates must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. We have little control over our manufacturers' compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of any quantities supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

Our future growth depends on our ability to identify and acquire or in-license products and if we do not successfully identify and acquire or in-license related product candidates or integrate them into our operations, we may have limited growth opportunities.

We in-licensed the rights to each of our two current product candidates, IV APAP and Omigard, from third parties who conducted the initial development of each product candidate. An important part of our business strategy is to continue to develop a pipeline of product candidates by acquiring or in-licensing products, businesses or technologies that we believe are a strategic fit with our focus on the hospital marketplace. Future in-licenses or acquisitions, however, may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention to develop acquired products or technologies;
- incurrence of substantial debt or dilutive issuances of securities to pay for acquisitions;
- higher than expected acquisition and integration costs;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. In particular, we may compete with larger pharmaceutical companies and other competitors in our efforts to establish new collaborations and in-licensing opportunities. These competitors likely will have access to greater financial resources than us and may have greater expertise in identifying and evaluating new opportunities. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts.

We will need to increase the size of our organization, and we may experience difficulties in managing growth.

As of June 30, 2006, we had 24 full-time employees. We will need to continue to expand our managerial, operational, financial and other resources in order to manage and fund our operations and clinical trials, continue our development activities and commercialize our product candidates. To support this growth, we expect to hire approximately 20 additional employees within the next 12 months at an estimated cost of $2.5 million. We are not in a position to provide a meaningful estimate of our staffing needs beyond the next 12 months. Our management, personnel, systems and facilities currently in place may not be adequate to support this future growth. Furthermore, our staffing estimates are based on assumptions that may prove to be wrong. Our need to effectively manage our operations, growth and various projects requires that we:

- manage our clinical trials effectively, including our planned Phase III clinical program for IV APAP, which will be conducted at numerous clinical trial sites, and our ongoing Phase III clinical trial for Omigard, which is being conducted at numerous clinical sites;
- manage our internal development efforts effectively while carrying out our contractual obligations to licensors and other third parties; and
- continue to improve our operational, financial and management controls, reporting systems and procedures.

We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our development and commercialization goals.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel.

We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Diego, California area. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the product acquisition, development, regulatory and commercialization expertise of our senior management, particularly Theodore R. Schroeder, our President and Chief Executive Officer, James B. Breitmeyer, M.D., Ph.D., our Executive Vice President, Development and Chief Medical Officer, and William R. LaRue, our Senior Vice President, Chief Financial Officer, Treasurer and Secretary. If we lose one or more of these key employees, our ability to implement our business strategy successfully could be seriously harmed. Replacing key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel. Although we have employment agreements with Mr. Schroeder, Dr. Breitmeyer and Mr. LaRue, these agreements are terminable at will at any time with or without notice and, therefore, we may not be able to retain their services as expected.

In addition, we have scientific and clinical advisors who assist us in our product development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with ours.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for a product candidate and may have to limit its commercialization.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval expose us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers or others using, administering or selling our products. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- decreased demand for our product candidates;
- impairment of our business reputation;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- loss of revenues; and
- the inability to commercialize our product candidates.

We have obtained limited product liability insurance coverage for our clinical trials with a $10 million annual aggregate coverage limit and additional amounts in selected foreign countries where we are conducting clinical trials. However, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Recent proposed legislation may permit re-importation of drugs from foreign countries into the United States, including foreign countries where the drugs are sold at lower prices than in the United States, which could materially adversely affect our operating results and our overall financial condition.

Legislation has been introduced in Congress that, if enacted, would permit more widespread re-importation of drugs from foreign countries into the United States, which may include re-importation from foreign countries where the drugs are sold at lower prices than in the United States. Such legislation, or similar regulatory changes, could decrease the price we receive for any approved products which, in turn, could materially adversely affect our operating results and our overall financial condition. For example, BMS markets IV APAP in Europe and other countries principally under the brand name Perfalgan. Although Perfalgan is not labeled for sale in the United States and we have an exclusive license from BMS and its licensor to develop and sell our product candidate in the United States, it is possible that hospitals and other users may in the future seek to import Perfalgan rather than purchase IV APAP in the United States for cost-savings or other reasons. We would not receive any revenues from the importation and sale of Perfalgan into the United States.

Our business involves the use of hazardous materials and we and our third-party manufacturers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our third-party manufacturers' activities and, to a lesser extent, our own activities involve the controlled storage, use and disposal of hazardous materials, including the components of our product

candidates and other hazardous compounds. We and our manufacturers are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that the safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state or federal authorities may curtail our use of these materials and interrupt our business operations.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing clinical trials for IV APAP or Omigard could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liability and the further development of our product candidates may be delayed.

Risks Related to Intellectual Property

The patent rights that we have in-licensed covering IV APAP are limited to a specific intravenous formulation of acetaminophen, and our market opportunity for this product candidate may be limited by the lack of patent protection for the active ingredient itself and other formulations that may be developed by competitors.

The active ingredient in IV APAP is acetaminophen. There are currently no patents covering the acetaminophen molecule itself in the territories licensed to us, which include the United States and Canada. As a result, competitors who obtain the requisite regulatory approval can offer products with the same active ingredient as IV APAP so long as the competitors do not infringe any process or formulation patents that we have in-licensed from BMS and its licensor, SCR Pharmatop. We are aware of a number of third-party patents in the United States that claim methods of making acetaminophen. If a supplier of the active pharmaceutical ingredient, or API, for our IV APAP product candidate is found to infringe any of these method patents covering acetaminophen, our supply of the API could be delayed and we may be required to locate an alternative supplier. We are also aware of several U.S. and Canadian patents and patent applications covering various potential injectable formulations of acetaminophen as well as methods of making and using these potential formulations. In addition, Injectapap, a formulation of acetaminophen for intramuscular injection was approved by the FDA for the reduction of fever in adults in March 1986 but was withdrawn from the market by McNeil Pharmaceutical in July 1986. Although we are not aware of any announcement regarding the reasons for Injectapap's withdrawal, we believe it was likely withdrawn from the market due to product-related concerns either related to the intramuscular injection mode of administration or the sodium bisulfite in the formulation.

The number of patents and patent applications covering products in the same field as IV APAP indicates that competitors have sought to develop and may seek to market competing formulations that may not be covered by our licensed patents and patent applications. In addition, the Canadian patent applications that we have in-licensed have yet to be examined by the Canadian Patent Office. Thus, they may issue with claims that cover less than the corresponding in-licensed U.S. patents, or simply not issue at all. The commercial opportunity for our IV APAP product candidate could be significantly harmed if competitors are able to develop an alternative formulation of acetaminophen outside the scope of our in-licensed patents.

The patent rights that we have in-licensed covering Omigard are limited in scope and limited to specific territories.

We have an exclusive license from Migenix for Omigard in North America and Europe for the licensed field, although currently there are issued patents only in the United States and certain European countries. Canadian applications are pending; however, the claims that ultimately issue in Canada may be narrower than the protection obtained in the United States and Europe or may simply not issue at all. In addition, no patent protection has been sought in Mexico. Accordingly, the manufacture, sale and use of Omigard in Mexico by a competitor cannot be prevented. Furthermore, analogs of Omigard have been developed by others that are not covered by patents licensed to us. At least some of these analogs are covered by third-party patents. It is possible that competitors having rights to these third-party patents may develop competing products having the same, similar or better efficacy compared to Omigard.

Furthermore, our license agreement with Migenix may be construed to cover only the use of Omigard for the licensed field, which is the treatment of burn-related, surgical wound-related, or device-related infections. Thus, Migenix or third-party licensees of Migenix may be able to market Omigard for other uses, including treatment of non-surgery related wound infections. We may be unable to prevent physicians from using any such competitive Omigard product off-label for the field licensed to us. Furthermore, the license covers only omiganan pentahydrochloride and its pharmaceutical formulations. Although the license agreement may prevent Migenix from developing a competing product for use in the licensed field, the agreement may not prevent Migenix from licensing a competing product, such as another salt of omiganan, to a third-party for use in the licensed field. Accordingly, we may face competition from a third-party licensee of Migenix using a different salt form of omiganan than our Omigard product candidate.

We depend on our licensors for the maintenance and enforcement of our intellectual property and have limited control, if any, over the amount or timing of resources that our licensors devote on our behalf.

We depend on our licensors, BMS and Migenix, to protect the proprietary rights covering IV APAP and Omigard. Regarding IV APAP, either BMS or its licensor, SCR Pharmatop, depending on the patent or application, is responsible for maintaining issued patents and prosecuting patent applications. Regarding Omigard, Migenix is responsible for maintaining issued patents and prosecuting patent applications. We have limited, if any, control over the amount or timing of resources that our licensors devote on our behalf or the priority they place on maintaining these patent rights and prosecuting these patent applications to our advantage. SCR Pharmatop is under a contractual obligation to BMS to diligently prosecute their patent applications and allow BMS the opportunity to consult, review and comment on patent office communications. However, we cannot be sure that SCR Pharmatop will perform as required. Should BMS decide it no longer wants to maintain any of the patents licensed to us, BMS is required to afford us the opportunity to do so at our expense. However, we cannot be sure that BMS will perform as required. If BMS does not perform, and if we do not assume the maintenance of the licensed patents in sufficient time to make required payments or filings with the appropriate governmental agencies, we risk losing the benefit of all or some of those patent rights. For patents and applications licensed from Migenix, Migenix is obligated to use commercially reasonable efforts to obtain and maintain patent rights covering Omigard in North America and Europe. If Migenix intends to abandon prosecution or maintenance of any patents or applications, they are obligated to notify us, and at that time, we will be granted an opportunity to maintain and prosecute the patents and applications. In such a case, Migenix is required to transfer all necessary rights and responsibilities to facilitate our maintenance and prosecution of the patents and applications. Similar to BMS, however, we cannot be certain that Migenix will perform its contractual obligations as required or that we will be able to adequately assume the prosecution or maintenance of the Omigard-related patents and applications.

As part of a financing transaction, Migenix has pledged as collateral to its lenders the patents and patent applications covering Omigard. While we believe our license agreement with Migenix would survive any foreclosure on these patents and patent applications, we cannot be sure that the lenders will have

adequate expertise or resources to properly perform Migenix's obligations to us under the license agreement, including maintaining and prosecuting the patents and patent applications.

While we intend to take actions reasonably necessary to enforce our patent rights, we depend, in part, on our licensors to protect a substantial portion of our proprietary rights. In the case of the IV APAP patents, BMS has the first right to prosecute a third-party infringement of the SCR Pharmatop patents, and has the sole right to prosecute third-party infringement of the BMS patents. We will have the ability to cooperate with BMS in third-party infringement suits involving the SCR Pharmatop patents. In certain instances, we may be allowed to pursue the infringement claim ourselves. With respect to Omigard, we have the first right to prosecute a third-party for infringement of the in-licensed Migenix patents provided the infringing activities are in North America or Europe and relate primarily to the licensed field of use. Migenix is obligated to reasonably cooperate with any such suit.

Our licensors may also be notified of alleged infringement and be sued for infringement of third-party patents or other proprietary rights. We may have limited, if any, control or involvement over the defense of these claims, and our licensors could be subject to injunctions and temporary or permanent exclusionary orders in the United States or other countries. Our licensors are not obligated to defend or assist in our defense against third-party claims of infringement. We have limited, if any, control over the amount or timing of resources, if any, that our licensors devote on our behalf or the priority they place on defense of such third-party claims of infringement. Finally, Migenix is not obligated to defend or assist in our defense of a third-party infringement suit relating to our Omigard product candidate; however, Migenix has the right to control the defense and settlement that relates to the validity and enforceability of claims in the in-licensed Migenix patents.

For a third-party challenge to the SCR Pharmatop in-licensed patents relating to IV APAP, we will have some ability to participate in either SCR Pharmatop's or BMS's defense thereof. In the case that neither party elects to defend the third-party challenge, then we may have the opportunity to defend it. For a third-party challenge to the in-licensed BMS patents relating to IV APAP, BMS has the sole right to defend such challenge. If it chooses not to, we may have the right to renegotiate or terminate the license regarding the in-licensed BMS patents.

Because of the uncertainty inherent in any patent or other litigation involving proprietary rights, we or our licensors may not be successful in defending claims of intellectual property infringement by third parties, which could have a material adverse affect on our results of operations. Regardless of the outcome of any litigation, defending the litigation may be expensive, time-consuming and distracting to management.

Because it is difficult and costly to protect our proprietary rights, we may not be able to ensure their protection.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for IV APAP, Omigard or any other product candidates that we may in-license or acquire and the methods we use to manufacture them, as well as successfully defending these patents against third-party challenges. We will only be able to protect our technologies from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical or biotechnology patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents.

The degree of future protection for our proprietary rights is uncertain, because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- our licensors might not have been the first to make the inventions covered by each of our pending patent applications and issued patents;
- our licensors might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our product candidates or technologies;
- it is possible that none of the pending patent applications licensed to us will result in issued patents;
- the issued patents covering our product candidates may not provide a basis for commercially viable active products, may not provide us with any competitive advantages, or may be challenged by third parties;
- we may not develop additional proprietary technologies that are patentable; or
- patents of others may have an adverse effect on our business.

Patent applications in the United States are maintained in confidence for at least 18 months after their earliest effective filing date. Consequently, we cannot be certain that our licensors were the first to invent or the first to file patent applications on some of our product candidates. In the event that a third party has also filed a U.S. patent application relating to our product candidates or a similar invention, we may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office to determine priority of invention in the United States. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a material adverse effect on our U.S. patent position. Furthermore, we may not have identified all U.S. and foreign patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies that affect our drug market.

In addition, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans, and in these countries patent protection may not be available at all to protect our drug candidates. Even if patents issue, we cannot guarantee that the claims of those patents will be valid and enforceable or provide us with any significant protection against competitive products, or otherwise be commercially valuable to us.

We also rely on trade secrets to protect our technology, particularly where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. While we use reasonable efforts to protect our trade secrets, our licensors, employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

If our licensors or we fail to obtain or maintain patent protection or trade secret protection for IV APAP, Omigard or any other product candidate we may in-license or acquire, third parties could use our proprietary information, which could impair our ability to compete in the market and adversely affect our ability to generate revenues and achieve profitability.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in any litigation would harm our business.

Our ability to develop, manufacture, market and sell IV APAP, Omigard or any other product candidates that we may in-license or acquire depends upon our ability to avoid infringing the proprietary

rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the general fields of pain treatment and prevention of infections and cover the use of numerous compounds and formulations in our targeted markets. For instance, we are aware of European Patent No. 1 089 755 B1 granted in February 2004 and assigned to N.V. Nutricia of the Netherlands. This patent is in force in various European countries, and the claims may be broad enough in scope to cover our Omigard product candidate if we choose to commercialize it in Europe. We are investigating potential invalidity defenses in Europe centered around Migenix's earlier-filed patent application, PCT Patent Application Publication No. WO 98/07745. However, we cannot predict the outcome of any invalidity defense, and it is possible that we may determine it prudent to seek a license from N.V. Nutricia to avoid extended litigation and other disputes. We cannot be sure that a license would be available to us on commercially reasonable terms, or at all. Similarly, we are aware of a patent application pending in the United States that is the equivalent to N.V. Nutricia's European patent, specifically, U.S. Patent Application No. 09/720,278. Because this patent application has neither published nor issued, it is too early to tell if the claims of this application will present similar issues for Omigard in the United States. We are also aware of a patent application pending in Canada that is the equivalent to N.V. Nutricia's European patent, specifically, Canadian Patent Application No. 2332127. Because this patent application has not issued, it is too early to tell if the claims of this application will present similar issues for Omigard in Canada. However, similar to the European patent, if the U.S. or Canadian patent applications issue with a scope that is broad enough to cover our Omigard product candidate and we and Migenix are unable to assert successful defenses to any patent claims, we may be unable to commercialize Omigard, or may be required to expend substantial sums to obtain a license to the other party's patent. While we believe there may be multiple grounds to challenge the validity of the European patent, and these grounds may be applicable to the U.S. and Canadian applications should they issue as patents, the outcome of any litigation relating to this European patent and the U.S. and Canadian patent applications, or any other patents or patent applications, is uncertain and participating in such litigation would be expensive, time-consuming and distracting to management. Because of the uncertainty inherent in any patent or other litigation involving proprietary rights, we and Migenix may not be successful in defending intellectual property claims by N.V. Nutricia or other third parties, which could have a material adverse affect on our results of operations. Regardless of the outcome of any litigation, defending the litigation may be expensive, time-consuming and distracting to management. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that IV APAP or Omigard may infringe. There could also be existing patents of which we are not aware that IV APAP or Omigard may inadvertently infringe.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third party claims that we infringe on their products or technology, we could face a number of issues, including:

- infringement and other intellectual property claims which, with or without merit, can be expensive and time consuming to litigate and can divert management's attention from our core business;
- substantial damages for past infringement which we may have to pay if a court decides that our product infringes on a competitor's patent;
- a court prohibiting us from selling or licensing our product unless the patent holder licenses the patent to us, which it is not required to do;
- if a license is available from a patent holder, we may have to pay substantial royalties or grant cross licenses to our patents; and
- redesigning our processes so they do not infringe, which may not be possible or could require substantial funds and time.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Risks Related to Our Finances and Capital Requirements

We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

We are a development stage company with a limited operating history. We have focused primarily on in-licensing and developing our two product candidates, IV APAP and Omigard, with the goal of supporting regulatory approval for these product candidates. We have financed our operations almost exclusively through private placements of preferred stock and have incurred losses in each year since our inception in May 2004. Net losses were $3.1 million in 2004, $7.5 million in 2005 and $34.9 million for the first six months of 2006. The net loss for the first six months of 2006 was principally attributed to our expense related to the $25.0 million licensing fee for IV APAP paid to BMS and clinical trial and regulatory expenses. As of June 30, 2006, we had an accumulated deficit of $45.5 million. These losses, among other things, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our development expenses as well as clinical product manufacturing expenses to increase in connection with our ongoing and planned Phase III clinical trials for our product candidates. In addition, if we obtain regulatory approval for IV APAP or Omigard, we expect to incur significant sales, marketing and outsourced manufacturing expenses as well as continued development expenses. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

We currently have no source of revenue and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from our development-stage product candidates, and we do not know when, or if, we will generate any revenue. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- successfully complete our ongoing and planned clinical trials for IV APAP and Omigard;
- obtain regulatory approval for either of our two product candidates;
- assuming these regulatory approvals are received, manufacture commercial quantities of our product candidates at acceptable cost levels; and
- successfully market and sell any approved products.

Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product. We also do not anticipate that we will achieve profitability for at least several years after generating material revenues, if ever. If we are unable to generate revenues, we will not become profitable and may be unable to continue operations without continued funding.

Our short operating history makes it difficult to evaluate our business and prospects.

We were incorporated in May 2004 and have only been conducting operations with respect to our IV APAP product candidate since March 2006 and our Omigard product candidate since July 2004. Our operations to date have been limited to organizing and staffing our company, in-licensing our two product candidates and initiating product development activities for our two product candidates. We have not yet demonstrated an ability to obtain regulatory approval for or successfully commercialize a product candidate. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

We will need additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing products for use in the hospital setting, conducting clinical trials, establishing outsourced manufacturing relationships and successfully manufacturing and marketing drugs that we may develop is expensive. We will need to raise additional capital to:

- fund our operations and continue to conduct adequate and well-controlled clinical trials to provide clinical data to support regulatory approval of marketing applications;
- continue our development activities;
- qualify and outsource the commercial-scale manufacturing of our products under cGMP; and
- commercialize IV APAP, Omigard or any other product candidates that we may in-license or acquire, if any of these product candidates receive regulatory approval.

We believe that our existing cash, cash equivalents and short-term investments will be sufficient to meet our projected operating requirements through at least June 30, 2007. We have based this estimate on assumptions that may prove to be wrong, and we could spend our available financial resources much faster than we currently expect. Our future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress and cost of our clinical trials and other product development programs for IV APAP, Omigard and any other product candidates that we may in-license or acquire;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with our product candidates;
- the cost and timing of completion of an outsourced commercial manufacturing supply for each product candidate;
- the costs and timing of regulatory approval;
- the costs of establishing sales, marketing and distribution capabilities;
- the effect of competing technological and market developments; and
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies, but we currently have no commitments or agreements relating to any of these types of transactions.

Until we can generate a sufficient amount of product revenue, if ever, we expect to finance future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements, as well as through interest income earned on cash balances. We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our development programs or our commercialization efforts.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- the timing of milestone payments required under our license agreements for IV APAP and Omigard;
- our execution of other collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- our addition or termination of clinical trials or funding support;
- variations in the level of expenses related to our two existing product candidates or future development programs;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting our product candidates or those of our competitors; and
- if either of our product candidates receives regulatory approval, the level of underlying hospital demand for our product candidates and wholesalers' buying patterns.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership will be diluted. If we raise additional funds through licensing arrangements, it may be necessary to relinquish potentially valuable rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us. Any debt financing we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. For example, in February 2006, we entered into a $7.0 million loan and security agreement with Silicon Valley Bank and Oxford Finance Corporation which contains a variety of affirmative and negative covenants, including required financial reporting, limitations on the disposition of assets other than in the ordinary course of business, limitations on the incurrence of additional debt and other requirements. To secure our performance of our obligations under the loan and security agreement, we pledged substantially all of our assets other than intellectual property assets, to the lenders. Our failure to comply with the covenants in the loan and security agreement could result in an event of default that, if not cured or waived, could result in the acceleration of all or a substantial portion of our debt.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the Nasdaq Global Market, have imposed various new requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these new compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more

time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, commencing in fiscal 2008, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management and our independent registered public accounting firm to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. Our testing, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses. Our compliance with Section 404 will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Moreover, if we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would require additional financial and management resources.

Risks Relating to Securities Markets and Investment in Our Stock

There may not be a viable public market for our common stock.

Prior to this offering, there has been no public market for our common stock, and there can be no assurance that a regular trading market will develop and continue after this offering or that the market price of our common stock will not decline below the initial public offering price. The initial public offering price will be determined through negotiations between us and the representatives of the underwriters and may not be indicative of the market price of our common stock following this offering. Among the factors considered in such negotiations are prevailing market conditions, certain of our financial information, market valuations of other companies that we and the representatives of the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant. See “Underwriting” for additional information.

As a new investor, you will experience immediate and substantial dilution in the net tangible book value of your shares.

The initial public offering price of our common stock in this offering is considerably more than the net tangible book value per share of our outstanding common stock. Investors purchasing shares of common stock in this offering will pay a price that substantially exceeds the value of our assets after subtracting liabilities. As a result, investors will:

- incur immediate dilution of $ per share, based on an assumed initial public offering price of $ per share, the midpoint of our expected public offering price range; and
- contribute % of the total amount invested to date to fund our company based on an assumed initial offering price to the public of $ per share, the mid point of our expected public offering price range, but will own only % of the shares of common stock outstanding after the offering.

To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors.

We believe that our existing cash, cash equivalents and short-term investments will be sufficient to meet our projected operating requirements through at least June 30, 2007. However, because we will need to raise additional capital to fund our clinical development programs, among other things, we may conduct substantial additional equity offerings. These future equity issuances, together with the exercise of outstanding options or warrants and any additional shares issued in connection with acquisitions, will result in further dilution to investors.

We expect that the price of our common stock will fluctuate substantially.

The initial public offering price for the shares of our common stock sold in this offering has been determined by negotiation between the representatives of the underwriters and us. This price may not reflect the market price of our common stock following this offering. The price of our common stock may decline. In addition, the market price of our common stock is likely to be highly volatile and may fluctuate substantially due to many factors, including:

- the results from our clinical trial programs, including our planned Phase III clinical program for IV APAP and our ongoing Phase III clinical trial for Omigard;
- the results of clinical trial programs for IV APAP and Omigard being performed by others;
- FDA or international regulatory actions, including failure to receive regulatory approval for any of our product candidates;
- failure of any of our product candidates, if approved, to achieve commercial success;
- announcements of the introduction of new products by us or our competitors;
- market conditions in the pharmaceutical and biotechnology sectors;
- developments concerning product development results or intellectual property rights of others;
- litigation or public concern about the safety of our potential products;
- actual and anticipated fluctuations in our quarterly operating results;
- deviations in our operating results from the estimates of securities analysts or other analyst comments;
- additions or departures of key personnel;
- third-party coverage and reimbursement policies;
- developments concerning current or future strategic collaborations; and
- discussion of us or our stock price by the financial and scientific press and in online investor communities.

The realization of any of the risks described in these “Risk Factors” could have a dramatic and material adverse impact on the market price of our common stock. In addition, class action litigation has often been instituted against companies whose securities have experienced periods of volatility in market price. Any such litigation brought against us could result in substantial costs and a diversion of management’s attention and resources, which could hurt our business, operating results and financial condition.

Our management team may invest or spend the proceeds of this offering in ways in which you may not agree or in ways which may not yield a return.

Our management will have broad discretion over the use of proceeds from this offering. The net proceeds from this offering will be used to fund clinical trials and other research and development activities, and to fund working capital, capital expenditures and other general corporate purposes. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products. We have no present understandings, commitments or agreements with respect to any such in-licenses, acquisitions or investments and no portion of the net proceeds has been allocated for any specific transaction. Our management will have considerable discretion in the application of the net proceeds, and

you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or market value. Until the net proceeds are used, they may be placed in investments that do not produce significant income or that lose value.

Future sales of our common stock may depress our stock price.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have outstanding shares of common stock based on the number of shares outstanding as of June 30, 2006. This includes the shares that we are selling in this offering, which may be resold in the public market immediately. Of the remaining shares, shares are currently restricted as a result of securities laws or lock-up agreements but will be available for resale in the public market as described in the "Shares Eligible for Future Sale" section of this prospectus. As a result of the lock-up agreements between our underwriters and our security holders and the provisions of Rule 144, Rule 144(k) and Rule 701 under the Securities Act, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

- shares will be eligible for sale on the date of this prospectus;
- shares will be eligible for sale upon the expiration of the lock-up agreements beginning 180 days after the date of this prospectus;
- shares will be eligible for sale, upon exercise of vested options, upon the expiration of the lock-up agreements, beginning 180 days after the date of this prospectus;
- shares will be eligible for sale, upon exercise of outstanding warrants, upon the expiration of the lock-up agreements, beginning 180 days after the date of this prospectus; and
- the remaining restricted shares will be eligible for sale from time to time thereafter upon expiration of their respective one-year holding periods.

Moreover, after this offering, holders of approximately 83,555,455 shares of common stock and the holders of warrants to purchase 385,000 shares of our common stock will have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. These rights will continue following this offering and will terminate seven years following the completion of this offering, or for any particular holder with registration rights, at such time following this offering when all securities held by that stockholder subject to registration rights may be sold pursuant to Rule 144 under the Securities Act. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to the lock-up agreements described in the "Underwriting" section of this prospectus.

Our executive officers and directors and their affiliates will exercise control over stockholder voting matters in a manner that may not be in the best interests of all of our stockholders.

Immediately following this offering, our executive officers and directors and their affiliates will together control approximately % of our outstanding common stock. As a result, these stockholders will collectively be able to significantly influence all matters requiring approval of our stockholders, including the election of directors and approval of significant corporate transactions. The concentration of ownership may delay, prevent or deter a change in control of our company even when such a change may be in the best interests of all stockholders, could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws, which are to become effective at the closing of this offering, contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations;
- a requirement of approval of not less than 66²/₃% of all outstanding shares of our capital stock entitled to vote to amend any bylaws by stockholder action, or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval.

In addition, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These and other provisions in our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors, including to delay or impede a merger, tender offer or proxy contest involving our company. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

We have never paid dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.

We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. Furthermore, our loan and security agreement with Silicon Valley Bank and Oxford Finance Corporation restricts our ability to pay dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We may become involved in securities class action litigation that could divert management's attention and harm our business.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements, including statements regarding the progress and timing of clinical trials, the safety and efficacy of our product candidates, the goals of our development activities, estimates of the potential markets for our product candidates, estimates of the capacity of manufacturing and other facilities to support our products, projected cash needs and our expected future revenues, operations and expenditures. The forward-looking statements are contained principally in the sections entitled “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business.” These statements relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. These risks and uncertainties include, among others:

- our ability to successfully complete clinical development of our only two product candidates, IV APAP and Omigard, on expected timetables, or at all, which includes enrolling sufficient patients in our clinical trials and demonstrating the safety and efficacy of these product candidates in such trials;
- the content and timing of submissions to and decisions made by the FDA and other regulatory agencies, including foreign regulatory agencies, demonstrating to the satisfaction of the FDA and such other agencies the safety and efficacy of our product candidates;
- intense competition in our markets and the ability of our competitors, many of whom have greater resources than we do, to offer different or better therapeutic alternatives than our product candidates;
- market acceptance of and future development and regulatory difficulties relating to any product candidates for which we do receive regulatory approval;
- our ability to develop sales, distribution and marketing capabilities or enter into agreements with third parties to sell, distribute and market any of our product candidates that may be approved for sale;
- our ability to obtain coverage and reimbursement for any of our product candidates that may be approved for sale from the government or third-party payors, and the extent of such coverage and reimbursement, and the willingness of hospitals to pay for our product candidates versus less expensive therapies;
- our compliance with the agreements under which we license the rights to our product candidates;
- our reliance on third parties to conduct our clinical trials and manufacture our product candidates;
- our ability to grow our business by identifying and acquiring or in-licensing new product candidates, increasing the size of our organization and attracting and retaining key personnel;
- our and our licensors’ ability to obtain, maintain and successfully enforce adequate patent and other intellectual property protection of our product candidates and the rights relating thereto; and
- our short operating history, our lack of revenue and profitability, our significant historical operating losses and our ability to obtain additional funding to continue to operate our business, which funding may not be available on commercially reasonable terms, or at all.

Forward-looking statements include all statements that are not historical facts. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “predict,” “potential,” or the negative of those terms, and similar expressions and comparable terminology intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. These forward-looking statements represent our estimates and assumptions only as of the date of this prospectus and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this prospectus. The forward-looking statements contained in this prospectus are excluded from the safe harbor protection provided by the Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933, as amended.

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately $ million from the sale of the shares of common stock offered in this offering, based on an assumed initial public offering price of $ per share (the mid-point of the price range set forth on the cover page of this prospectus) and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us. Each $1.00 increase or decrease in the assumed public offering price of $ per share would increase or decrease, the net proceeds to us from this offering by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

The principal purposes for this offering are to fund clinical trials and other research and development activities, including with respect to our two product candidates, to fund our working capital, to make capital expenditures, for other general corporate purposes, to create a public market for our common stock, to increase our ability to access the capital markets in the future and to provide liquidity for our existing stockholders.

We currently expect to use our net proceeds from this offering as follows:

- approximately $58.0 million to fund clinical trials for IV APAP and Omigard and other research and development activities;
- approximately $4.0 million to fund capital expenditures, primarily including equipment associated with the manufacturing of IV APAP; and
- the remainder to fund working capital and other general corporate purposes.

We anticipate that the net proceeds from this offering, together with our existing cash and cash equivalents, will allow us to complete the clinical trials necessary to support NDA filings for IV APAP and Omigard.

We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products. However, we have no current understandings, commitments or agreements to do so.

The amounts and timing of our actual expenditures will depend on numerous factors, including the progress in, and costs of, our clinical trials and other product development programs. We therefore cannot estimate the amount of net proceeds to be used for all of the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock and we do not currently intend to pay any cash dividends on our common stock. We expect to retain future earnings, if any, to fund the development and growth of our business. The payment of dividends by us on our common stock is limited by our loan and security agreement with Silicon Valley Bank and Oxford Finance Corporation. Any future determination to pay dividends on our common stock will be at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements and contractual restrictions.

CAPITALIZATION

The following table sets forth our capitalization as of June 30, 2006:

- on an actual basis; and
- on a pro forma as adjusted basis to reflect the conversion of all outstanding shares of our preferred stock into 79,630,455 shares of common stock and our receipt of the estimated net proceeds from this offering, based on an assumed initial public offering price of $ per share (the mid-point of the price range set forth on the cover page of this prospectus) and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

The pro forma information below is illustrative only and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes appearing elsewhere in this prospectus.

	As of June 30, 2006	
	Actual	Pro Forma as Adjusted(1)
	(In thousands, except share and par value amounts)	
Cash and cash equivalents	$ 42,881	
Long-term debt, less current portion	$ 5,968	
Stockholders' equity:		
Preferred stock, $0.0001 par value actual and pro forma as adjusted; actual — 80,015,455 shares authorized; 79,630,455 issued and outstanding; pro forma as adjusted — 10,000,000 shares authorized; no shares issued and outstanding	—	
Series A-1 convertible preferred stock, actual — 8,085,108 shares authorized, issued and outstanding; pro forma as adjusted — no shares authorized; no shares issued and outstanding	1	
Series A-2 convertible preferred stock, actual — 18,060,347 shares authorized; 17,675,347 issued and outstanding; pro forma as adjusted — no shares authorized; no shares issued and outstanding	2	
Series A-3 convertible preferred stock, actual — 53,870,000 shares authorized, issued and outstanding; pro forma as adjusted — no shares authorized; no shares issued and outstanding	5	
Common stock, $0.0001 par value; actual — 100,000,000 shares authorized; 8,551,740 shares issued and outstanding; pro forma as adjusted — 100,000,000 shares authorized; shares issued and outstanding	1	
Additional paid-in capital	79,954	
Deficit accumulated during the development stage	(45,535)	
Total stockholders' equity	34,428	
Total capitalization	$ 40,396	

(1) Each $1.00 increase or decrease in the assumed public offering price of $ per share would increase or decrease, respectively, the amount of cash and cash equivalents, additional paid-in capital and total capitalization by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

The number of pro forma as adjusted common shares shown as issued and outstanding in the table is based on the number of shares of our common stock outstanding as of June 30, 2006, and excludes:

- 5,769,471 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2006 at a weighted average exercise price of $0.38 per share;
- 385,000 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2006 at a weighted average exercise price of $1.00 per share; and
- shares of our common stock reserved for future issuance under our 2006 equity incentive award plan, which will become effective on the day prior to the day on which we become subject to the reporting requirements of the Exchange Act (including 1,678,789 shares of common stock reserved for future grant or issuance under our 2004 equity incentive award plan, which shares will be added to the shares to be reserved under our 2006 equity incentive award plan upon the effectiveness of the 2006 equity incentive award plan).

DILUTION

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock after this offering. As of June 30, 2006, our historical net tangible book value was $34.4 million, or $0.39 per share of common stock. Our historical net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of shares of our common stock outstanding as of June 30, 2006, after giving effect to the conversion of all outstanding shares of our preferred stock into 79,630,455 shares of our common stock. After giving effect to our sale in this offering of shares of our common stock at an assumed initial public offering price of $ per share (the mid-point of the price range set forth on the cover page of this prospectus) and after deducting estimated underwriting discounts and commissions and estimated offering costs payable by us, our pro forma as adjusted net tangible book value as of June 30, 2006 would have been $ million, or $ per share of our common stock. This represents an immediate increase of net tangible book value of $ per share to our existing stockholders and an immediate dilution of $ per share to investors purchasing shares in this offering. The following table illustrates this per share dilution:

Assumed initial public offering price per share		$
Historical net tangible book value per share as of June 30, 2006	$ 0.39	
Increase per share attributable to investors purchasing shares in this offering		
Pro forma net tangible book value per share, as adjusted to give effect to this offering		
Dilution to investors purchasing shares in this offering		$

Each $1.00 increase or decrease in the assumed public offering price of $ per share would increase or decrease, our pro forma as adjusted net tangible book value by approximately $ million, the pro forma as adjusted net tangible book value per share after this offering by approximately $ per share and the dilution as adjusted to investors purchasing shares in this offering by approximately $ per share, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

If the underwriters exercise their over-allotment option in full, the pro forma net tangible book value per share after giving effect to this offering would be $ per share, and the dilution in pro forma net tangible book value per share to investors in this offering would be $ per share.

The following table summarizes, as of June 30, 2006, the differences between the number of shares of common stock purchased from us, after giving effect to the conversion of our preferred stock into common stock, the total effective cash consideration paid, and the average price per share paid by our existing stockholders and by our new investors purchasing stock in this offering at an assumed initial public offering price of $ per share (the mid-point of the price range set forth on the cover page of this prospectus) before deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us:

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders before this offering	88,182,195	%	$ 79,742,641	%	$ 0.90
Investors purchasing shares in this offering					
Total		100.0%	$	100.0%	$

Each $1.00 increase or decrease in the assumed public offering price of $ per share would increase or decrease total consideration paid by new investors, total consideration paid by all stockholders and the average price per share paid by all stockholders by $ million, $ million and $, respectively, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

If the underwriters exercise their over-allotment option in full, our existing stockholders would own % and our new investors would own % of the total number of shares of our common stock outstanding after this offering.

The above information assumes no exercise of stock options or warrants outstanding as of June 30, 2006. As of June 30, 2006, there were:

- 5,769,471 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2006 at a weighted average exercise price of $0.38 per share;
- 385,000 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2006 at a weighted average exercise price of $1.00 per share; and
- shares of our common stock reserved for future issuance under our 2006 equity incentive award plan, which will become effective on the day prior to the day on which we become subject to the reporting requirements of the Exchange Act (including 1,678,789 shares of common stock reserved for future grant or issuance under our 2004 equity incentive award plan, which shares will be added to the shares to be reserved under our 2006 equity incentive award plan upon the effectiveness of the 2006 equity incentive award plan).

SELECTED FINANCIAL DATA

The following selected statement of operations data for the period from May 26, 2004 (inception) through December 31, 2004, the year ended December 31, 2005 and the balance sheet data as of December 31, 2004 and 2005 have been derived from our audited financial statements included elsewhere in this prospectus. The statement of operations data for the six-month periods ended June 30, 2005 and 2006, the period from May 26, 2004 (inception) through June 30, 2006 and the balance sheet data as of June 30, 2006 have been derived from our unaudited financial statements included elsewhere in this prospectus. The unaudited financial statements have been prepared on a basis consistent with our audited financial statements and, in the opinion of management, contain all adjustments, consisting only of normal recurring adjustments, we consider necessary for the fair presentation of the financial data. The selected financial data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes included elsewhere in this prospectus.

	Period from May 26, 2004 (Inception) Through December 31, 2004	Year Ended December 31, 2005	Six Months Ended June 30,		Period from May 26, 2004 (Inception) Through June 30, 2006
			2005	2006	
	(In thousands, except per share amounts)				
Statement of Operations Data:					
Operating expenses:					
Research and development	$ 2,233	$ 6,126	$ 2,402	$ 33,574	$ 41,934
Marketing	41	240	142	317	598
General and administrative	877	1,412	540	1,488	3,777
Total operating expenses	3,151	7,778	3,084	35,379	46,309
Loss from operations	(3,151)	(7,778)	(3,084)	(35,379)	(46,309)
Other income (expense):					
Interest income	9	255	14	553	818
Interest expense	—	—	—	(44)	(44)
Total other income	9	255	14	509	774
Net loss	$ (3,142)	$ (7,523)	$ (3,070)	$ (34,870)	$ (45,535)
Basic and diluted net loss per share(1)	$ (0.86)	$ (1.63)	$ (0.68)	$ (7.01)	
Shares used to compute basic and diluted net loss per share(1)	3,658	4,624	4,527	4,974	
Pro forma basic and diluted net loss per share(1)		$ (0.36)		$ (0.59)	
Shares used to compute pro forma basic and diluted net loss per share(1)		20,649		58,711	

(1) See Note 1 of Notes to Financial Statements for an explanation of the method used to compute the historical and pro forma net loss per share and the number of shares used in the computation of the per share amounts.

	As of December 31,		As of June 30,
	2004	2005	2006
		(In thousands)	
Balance Sheet Data:			
Cash and cash equivalents and securities available-for-sale	$ 4,271	$ 15,025	$ 42,881
Working capital	4,161	14,405	37,476
Total assets	4,536	15,769	46,355
Long-term debt, less current portion	—	—	5,968
Deficit accumulated during the development stage	(3,142)	(10,665)	(45,535)
Total stockholders' equity	4,422	14,623	34,428

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with "Selected Financial Data" and our financial statements and related notes appearing elsewhere in this prospectus. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including but not limited to those set forth under "Risk Factors" and elsewhere in this prospectus.

Overview

Background

We are a biopharmaceutical company focused on in-licensing, developing and commercializing proprietary product candidates principally for use in the hospital setting. Since our inception in 2004, we have in-licensed rights to two Phase III product candidates, both of which have been studied in prior Phase III clinical trials conducted by our licensors. We have in-licensed the exclusive U.S. and Canadian rights to IV APAP, an intravenous formulation of acetaminophen that is currently marketed in Europe for the treatment of acute pain and fever by Bristol-Myers Squibb Company, or BMS. We believe that IV APAP is the only stable, pharmaceutically-acceptable intravenous formulation of acetaminophen. We have also in-licensed the exclusive North American and European rights to omiganan pentahydrochloride 1% aqueous gel, or Omigard, for the prevention and treatment of device-related, surgical wound-related and burn-related infections.

We believe that the hospital setting is a concentrated, underserved market for pharmaceuticals and anticipate building our own, hospital-focused sales force as our product candidates approach potential U.S. Food and Drug Administration, or FDA, approval. We intend to build a leading franchise in the hospital setting, continuing to focus on products that are in late-stages of development, currently commercialized outside the United States, or approved in the United States but with significant commercial potential for proprietary new uses or formulations.

We were incorporated in May 2004. During 2004, we focused on hiring our management team and initial operating employees and on in-licensing our first product candidate, Omigard. Substantial operations did not commence until September 2004. During 2005, we completed the special protocol assessment, or SPA, for Omigard, and initiated Phase III clinical trials for this product candidate. In March 2006, we in-licensed rights to IV APAP from BMS. Pending further discussions with the FDA concerning our Phase III development program for IV APAP, we plan to initiate the remaining Phase III clinical trial requirements for this product candidate in the fourth quarter of 2006.

We are a development stage company. We have incurred significant net losses since our inception. As of June 30, 2006, we had an accumulated deficit of $45.5 million. These losses have resulted principally from costs incurred in connection with research and development activities, including license fees, costs of clinical trial activities associated with our current product candidates and general and administrative expenses. We expect to continue to incur operating losses for the next several years as we pursue the clinical development and market launch of our product candidates and acquire or in-license additional products, technologies or businesses that are complementary to our own.

Revenues

We have not generated any revenues to date, and we do not expect to generate any revenues from licensing, achievement of milestones or product sales until we are able to commercialize our product candidates ourselves or execute a collaboration arrangement.

Research and Development Expenses

Our research and development expenses consist primarily of license fees, salaries and related employee benefits, costs associated with clinical trials managed by our contract research organizations, or CROs, and costs associated with non-clinical activities, such as regulatory expenses. Our most significant costs are for license fees and clinical trials. The clinical trial expenses include payments to vendors such as CROs, investigators, clinical suppliers and related consultants. Our historical research and development expenses relate predominantly to the in-licensing of IV APAP and Omigard and clinical trials for Omigard. We charge all research and development expenses to operations as incurred because the underlying technology associated with these expenditures relates to our research and development efforts and has no alternative future uses.

We use external service providers and vendors to conduct our clinical trials, to manufacture our product candidates to be used in clinical trials and to provide various other research and development related products and services. A substantial portion of these external costs are tracked on a project basis.

We use our internal research and development resources across several projects and many resources are not attributable to specific projects. A substantial portion of our internal costs, including personnel and facility related costs, are not tracked on a project basis and are included in the "unallocated" category in the table below.

The following summarizes our research and development expenses for the periods indicated:

Product Candidate	Period from May 26, 2004 (Inception) Through December 31, 2004	Year Ended December 31, 2005	Six Months Ended June 30, 2005	Six Months Ended June 30, 2006	Period from May 26, 2004 (Inception) Through June 30, 2006
			(In thousands)		
IV APAP	$ —	$ —	$ —	$ 25,698	$ 25,698
Omigard	2,001	4,802	1,850	6,238	13,041
Unallocated	232	1,324	552	1,638	3,195
	$ 2,233	$ 6,126	$ 2,402	$ 33,574	$ 41,934

At this time, due to the risks inherent in the clinical trial process and given the early stage of our product development programs, we are unable to estimate with any certainty the costs we will incur in the continued development of our product candidates for potential commercialization. Clinical development timelines, the probability of success and development costs vary widely. While we are currently focused on advancing each of our product development programs, our future research and development expenses will depend on the determinations we make as to the scientific and clinical success of each product candidate, as well as ongoing assessments as to each product candidate's commercial potential. In addition, we cannot forecast with any degree of certainty which product candidates will be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

We expect our development expenses to be substantial over the next few years as we continue the advancement of our product development programs. We initiated our Phase III clinical trial program for Omigard in August 2005, and we have not yet commenced our own Phase III clinical trials for IV APAP. We expect to receive results from the ongoing Omigard clinical trial in the second half of 2007. In the fourth quarter of 2006, we expect to initiate the remaining Phase III clinical trial requirements for IV APAP for submission to the FDA and expect these Phase III clinical trial results to be available in the first half of 2008. The lengthy process of completing clinical trials and seeking regulatory approval for our product candidates requires the expenditure of substantial resources. Any failure by us or delay in completing clinical trials, or in obtaining regulatory approvals, could cause our research and development expense to increase and, in turn, have a material adverse effect on our results of operations.

Marketing

Our marketing expenses consist primarily of market research studies, salaries, benefits and professional fees related to building our marketing capabilities. We anticipate increases in marketing expenses as we add personnel and continue to develop and prepare for the potential commercialization of our product candidates.

General and Administrative

Our general and administrative expenses consist primarily of salaries, benefits and professional fees related to our administrative, finance, human resources, legal, business development and internal systems support functions, as well as insurance and facility costs. We anticipate increases in general and administrative expenses as we add personnel, comply with the reporting obligations applicable to publicly-held companies, and continue to build our corporate infrastructure in support of our continued development and preparation for the potential commercialization of our product candidates.

Interest and Other Income

Interest and other income consist primarily of interest earned on our cash, cash equivalents and short-term investments.

Income Taxes

As of December 31, 2005, we had both federal and state net operating loss carryforwards of approximately $8.7 million. If not utilized, the net operating loss carryforwards will begin expiring in 2024 for federal purposes and 2014 for state purposes. As of December 31, 2005, we had both federal and state research and development tax credit carryforwards of approximately $0.3 million and $0.1 million, respectively. The federal tax credits will begin expiring in 2024 unless previously utilized and the state tax credits carryforward indefinitely. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code, substantial changes in our ownership may limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset taxable income. Any such annual limitation may significantly reduce the utilization of the net operating losses before they expire. In each period since our inception, we have recorded a valuation allowance for the full amount of our deferred tax asset, as the realization of the deferred tax asset is uncertain. As a result, we have not recorded any federal or state income tax benefit in our statement of operations.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in conformity with generally accepted accounting principles in the United States. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and related disclosures. Actual results could differ from those estimates.

We believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Research and Development Expenses

A substantial portion of our on-going research and development activities are performed under agreements we enter into with external service providers, including CROs, who conduct many of our research and development activities. We accrue for costs incurred under these contracts based on factors such as estimates of work performed, milestones achieved, patient enrollment and experience with similar contracts. As actual costs become known, we adjust our accruals. To date, our accruals have been within management's estimates, and no material adjustments to research and development expenses have been recognized. We expect to expand the level of research and development activity performed by external

service providers in the future. As a result, we anticipate that our estimated accruals will be more material to our operations in future periods. Subsequent changes in estimates may result in a material change in our accruals, which could also materially affect our results of operations.

Stock-Based Compensation

Effective January 1, 2006, we adopted Statement of Financial Accounting Standards, or SFAS, No. 123(R), *Share-Based Payment*, which revises SFAS No. 123, *Accounting for Stock-Based Compensation* and supersedes Accounting Principles Board, or APB, Opinion No. 25, *Accounting for Stock Issued to Employees.* SFAS No. 123(R) requires that share-based payment transactions with employees be recognized in the financial statements based on their fair value and recognized as compensation expense over the vesting period. Prior to SFAS No. 123(R), we disclosed the pro forma effects of applying SFAS No. 123 under the minimum value method. We adopted SFAS No. 123(R) effective January 1, 2006, prospectively for new equity awards issued subsequent to December 31, 2005. The adoption of SFAS No. 123(R) in the first quarter of 2006 did not result in the recognition of additional stock-based compensation expense.

Under SFAS No. 123(R), we calculate the fair value of stock option grants using the Black-Scholes option-pricing model. The assumptions used in the Black-Scholes model were 6.06-6.08 years for the expected term, 70% for the expected volatility, 4.36-5.08% for the risk free rate and 0% for dividend yield for the six months ended June 30, 2006. Future expense amounts for any particular quarterly or annual period could be affected by changes in our assumptions.

The weighted average expected option term for 2006 reflects the application of the simplified method set out in SEC Staff Accounting Bulletin, or SAB, No. 107 which was issued in March 2005. The simplified method defines the life as the average of the contractual term of the options and the weighted average vesting period for all option tranches.

Estimated volatility for fiscal 2006 also reflects the application of SAB No. 107 interpretive guidance and, accordingly, incorporates historical volatility of similar public entities.

As of June 30, 2006, we had approximately $1.5 million of unrecognized share-based compensation costs related to nonvested equity awards. As of June 30, 2006, we had outstanding vested options to purchase 341,768 shares of our common stock and unvested options to purchase 5,427,703 shares of our common stock with an intrinsic value of and , respectively, based on an estimated initial public offering price of per share.

Prior to January 1, 2006, we applied the intrinsic-value-based method of accounting prescribed by APB Opinion No. 25 and related interpretations. Under this method, if the exercise price of the award equaled or exceeded the fair value of the underlying stock on the measurement date, no compensation expense was recognized. The measurement date was the date on which the final number of shares and exercise price were known and was generally the grant date for awards to employees and directors. If the exercise price of the award was below the fair value of the underlying stock on the measurement date, then compensation cost was recorded, using the intrinsic-value method, and was generally recognized in the statements of operations over the vesting period of the award.

The fair value of our common stock has been established by our board of directors and took into consideration contemporaneous independent valuations of the Company's common stock beginning in March 2006. We have applied the guidance in the American Institute of Certified Public Accountants, or AICPA, Audit and Accounting Practice Aid Series, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, to determine the fair value of our common stock for purposes of setting the exercise prices of stock options granted to employees and others. This guidance emphasizes the importance of the operational development in determining the value of the enterprise. As a development stage enterprise, we are at an early stage of existence, primarily focused on development with an unproven business model. To date, we have been funded primarily by venture capitalists with a history of funding start-up, high-risk entities with the potential for high returns in the event the investments are successful.

Prior to the licensing of IV APAP in March 2006, we valued our common stock at a nominal amount when we were considered to be in a very early stage of development (stages 1 and 2) as defined in the AICPA guidance, where the preferences of the preferred stockholders, in particular the liquidation preferences, are very meaningful. We utilized an asset-based approach for enterprise value and allocated such value to preferred and common stock based on the current value method. The significant estimates used in the asset-based approach consisted of the valuation of our assets and liabilities, which we determined were substantially the same as their fair market values. Since the fair market value of our net assets, including project costs incurred, was less than the liquidation value of our preferred stock, no significant value was assigned to our common stock under the current value method, which allocates value based on liquidation preferences. We did not obtain a contemporaneous independent valuation prior to 2006 as we were focused on product development and fund raising and believed our board of directors, all of whom are related parties, had the requisite experience at valuing early stage companies.

Subsequent to our licensing of IV APAP but prior to the initiation of our initial public offering process on June 14, 2006, based on a contemporaneous independent valuation performed by an unrelated valuation specialist, we increased our common stock valuation to $0.34 per share. Our valuation utilized a market-based approach for enterprise value and allocated such value to preferred and common stock based on an option pricing model. This approach is consistent with the AICPA guidance based on our stage of development following our in-licensing of rights to IV APAP. The determination of enterprise value was based on our Series A-3 preferred stock financing, in which greater than 50% of the investors consisted of new investors to Cadence. The increase in our common stock valuation primarily related to the in-licensing of IV APAP and the advancement of our business model which led to the utilization of a market-based approach.

Subsequent to the initiation of our initial public offering process, based on a contemporaneous independent valuation performed by an unrelated valuation specialist, we increased our common stock valuation to $0.80 per share. Our valuation utilized a market-based approach for enterprise value and allocated such value to preferred and common stock based on an option pricing model. The determination of enterprise value was based on an equal weighting of our Series A-3 preferred stock financing and valuation ranges provided by the underwriters for this offering. The valuation point selected from the underwriters' valuation ranges was discounted by 40% to reflect the lack of marketability that was determined based on put-option analysis and published data regarding marketability discounts in initial public offerings. The increase in our common stock valuation primarily related to the prospect of an initial public offering at higher valuations than our Series A-3 preferred stock financing.

Since we utilized an asset-based approach in our very early stage of development and moved to a market-based approach upon the in-licensing of IV APAP, the probability of successful development of our product candidates was not a specific variable used in our valuation approaches. However, this probability was considered in the price paid for our Series A-3 preferred stock and the valuation ranges provided by the underwriters, which are specific factors included in our valuation approaches.

Equity instruments issued to non-employees are recorded at their fair value as determined in accordance with SFAS No. 123(R) and Emerging Issues Task Force 96-18, *Accounting for Equity Instruments That are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods and Services*, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period.

Results of Operations

Comparison of six months ended June 30, 2006 and 2005

Research and Development Expenses. Research and development expenses increased to $33.6 million for the six months ended June 30, 2006 from $2.4 million for the comparable period during 2005. This increase of $31.2 million primarily was due to:

- an increase of $25.7 million in our IV APAP program primarily as a result of a $25.0 million license fee which was immediately expensed as in-process research and development;
- an increase of $4.4 million in our Omigard program as a result of clinical trial and related costs for a Phase III clinical trial initiated in August 2005; and
- an increase of $1.1 million in unallocated expenses as a result of increased salaries and related personnel costs from increased research and development staff to support our clinical and regulatory efforts related to both Omigard and IV APAP.

Marketing Expenses. Marketing expenses increased to $0.3 million for the six months ended June 30, 2006 from $0.1 million for the comparable period during 2005. This increase of $0.2 million primarily was due to higher market research and branding and personnel costs in 2006.

General and Administrative Expenses. General and administrative expenses increased to $1.5 million for the six months ended June 30, 2006 from $0.5 million for the comparable period during 2005. This increase of $1.0 million primarily was due to legal fees related to the IV APAP license agreement and our new facility lease, other professional fees and consulting fees.

Interest Income. Interest income increased to $553,000 for the six months ended June 30, 2006 from $14,000 for the comparable period during 2005. This increase of $539,000 primarily was due to the increase in average cash and investment balances as a result of preferred stock sales and higher interest rates in 2006.

Interest Expense. Interest expense increased to $44,000 for the six months ended June 30, 2006 from zero for the comparable period during 2005. This increase of $44,000 was primarily due to non-cash interest expense related to the warrants issued to Silicon Valley Bank and Oxford Finance Corporation in connection with their February 2006 commitment to lend us $7.0 million.

Comparison of year ended December 31, 2005 to the period from May 26, 2004 (inception) through December 31, 2004

Research and Development Expenses. Research and development expenses increased to $6.1 million for the year ended December 31, 2005 from $2.2 million for the period from May 26, 2004 (inception) through December 31, 2004. This increase of $3.9 million primarily was due to:

- an increase of $2.8 million in our Omigard program as a result of clinical trial and related costs offset by a decrease in license fees; and
- an increase of $1.1 million in unallocated expenses as a result of increased salaries and related personnel costs from increased research and development staff to support our initial clinical and regulatory efforts.

Marketing Expenses. Marketing expenses increased to $240,000 for the year ended December 31, 2005 from $41,000 for the period from May 26, 2004 (inception) through December 31, 2004. This increase of $199,000 primarily was due to market research, branding and personnel costs in 2005.

General and Administrative Expenses. General and administrative expenses increased to $1.4 million for the year ended December 31, 2005 from $0.9 million for the period from May 26, 2004 (inception) through December 31, 2004. This increase of $0.5 million primarily was due to salaries and

related costs as we expanded our general and administrative functions to support our operations, as well as legal fees, other professional fees and consulting fees.

Interest Income. Interest income increased to $256,000 for the year ended December 31, 2005 from $9,000 for the period from May 26, 2004 (inception) through December 31, 2004. This increase of $247,000 primarily was due to the increase in average cash and investment balances and interest rates in 2005.

Liquidity and Capital Resources

Since inception, our operations have been financed primarily through the private placement of equity securities. Through June 30, 2006, we received net proceeds of approximately $79.5 million from the sale of shares of our preferred and common stock as follows:

- from July 2004 to June 2006, we issued and sold a total of 8,551,740 shares of common stock for aggregate net proceeds of $0.6 million;
- from July 2004 to August 2004, we issued and sold a total of 8,085,108 shares of Series A-1 preferred stock for aggregate net proceeds of $7.5 million;
- from June 2005 to September 2005, we issued and sold 17,675,347 shares of Series A-2 preferred stock for aggregate net proceeds of $17.6 million; and
- in March 2006, we issued and sold a total of 53,870,000 shares of Series A-3 preferred stock for aggregate net proceeds of $53.8 million.

In February 2006, we entered into a $7.0 million loan and security agreement with Silicon Valley Bank and Oxford Finance Corporation to provide us with growth capital. We drew down $7.0 million in June 2006 and have no further credit available under this agreement. We are required to make interest only payments on the loan balance for the first six months of the loan, and beginning February 2007, we are required to make the first of 30 equal monthly principal and interest payments. Interest accrues on all outstanding amounts at the fixed rate of 11.47%. The loan is collateralized by substantially all of our assets other than intellectual property. We are subject to prepayment penalties. Under the terms of the agreement, we are precluded from entering into certain financing and other transactions, including disposing of certain assets and paying dividends, and are subject to various non-financial covenants.

In conjunction with the loan and security agreement, we issued warrants to the lenders to purchase 385,000 shares of Series A-2 preferred stock at an exercise price of $1.00 per share.

As of June 30, 2006, we had $42.9 million in cash and cash equivalents. We have invested a substantial portion of our available cash funds in money market funds placed with reputable financial institutions for which credit loss is not anticipated. We have established guidelines relating to diversification and maturities of our investments to preserve principal and maintain liquidity.

Our operating activities used net cash in the amount of $31.1 million in the six months ended June 30, 2006, $6.9 million for the year ended December 31, 2005 and $3.1 million for the period from May 26, 2004 (inception) through December 31, 2004. The increase in net cash used in operating activities from 2004 to 2005 primarily was due to an increase in our net loss as a result of increased expenses related to the clinical development of Omigard and increased salaries and overhead of company personnel. The increase in net cash used in operating activities from 2005 to 2006 primarily was due to an increase in our net loss as a result of increased expenses related to the license fee paid for IV APAP. We cannot be certain if, when or to what extent we will receive cash inflows from the commercialization of our product candidates. We expect our development expenses to be substantial and to increase over the next few years as we continue the advancement of our product development programs.

As a biopharmaceutical company focused on in-licensing, developing and commercializing proprietary pharmaceutical product candidates, we have entered into license agreements to acquire the rights to develop and commercialize our two product candidates, IV APAP and Omigard. Pursuant to

these agreements, we obtained exclusive licenses to the patent rights and know-how for selected indications and territories. Under the IV APAP agreement, we paid to BMS a $25.0 million up-front fee and may be required to make future milestone payments totaling up to $50.0 million upon the achievement of various milestones related to regulatory or commercial events. Under the Omigard agreement, we paid to Migenix Inc. an aggregate of $2.0 million in the form of an up-front fee, including the purchase of 617,284 shares of Migenix common stock, and may be required to make future milestone payments totaling up to $27.0 million upon the achievement of various milestones related to regulatory or commercial events. Under both agreements, we are also obligated to pay royalties on any net sales of the licensed products.

Our future capital uses and requirements depend on numerous forward-looking factors. These factors include but are not limited to the following:

- the progress of our clinical trials, including expenses to support the trials and milestone payments that may become payable to BMS or Migenix;
- our ability to establish and maintain strategic collaborations, including licensing and other arrangements;
- the costs involved in enforcing or defending patent claims or other intellectual property rights;
- the costs and timing of regulatory approvals;
- the costs of establishing sales or distribution capabilities;
- the success of the commercialization of our products; and
- the extent to which we in-license, acquire or invest in other indications, products, technologies and businesses.

We believe that our existing cash, cash equivalents and short-term investments will be sufficient to meet our projected operating requirements through at least June 30, 2007.

Until we can generate significant cash from our operations, we expect to continue to fund our operations with existing cash resources generated from the proceeds of offerings of our equity securities and our existing borrowings under our loan and security agreement. In addition, we may finance future cash needs through the sale of additional equity securities, strategic collaboration agreements and debt financing. However, we have drawn down all available amounts under our existing loan and security agreement, and we may not be successful in obtaining strategic collaboration agreements or in receiving milestone or royalty payments under those strategic collaboration agreements. In addition, we cannot be sure that our existing cash and investment resources will be adequate, that additional financing will be available when needed or that, if available, financing will be obtained on terms favorable to us or our stockholders. Having insufficient funds may require us to delay, scale-back or eliminate some or all of our development programs, relinquish some or even all rights to product candidates at an earlier stage of development or renegotiate less favorable terms than we would otherwise choose. Failure to obtain adequate financing also may adversely affect our ability to operate as a going concern. If we raise additional funds by issuing equity securities, substantial dilution to existing stockholders would likely result. If we raise additional funds by incurring additional debt financing, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to operate our business.

Contractual Obligations and Commitments

The following table describes our long-term contractual obligations and commitments as of December 31, 2005:

	Payments Due by Period				
	Total	Less Than 1 Year	1 - 3 Years	4-5 Years	After 5 Years
			(In thousands)		
Long-term debt obligations(1)	$ —	$ —	$ —	$ —	$ —
Operating lease obligations(2)	147	147	—	—	—
License obligations(3)	—	—	—	—	—
Total	$ 147	$ 147	$ —	$ —	$ —

(1) Long-term debt obligations do not include $7.0 million of indebtedness incurred in June 2006 under our loan and security agreement with Silicon Valley Bank and Oxford Finance Corporation.

(2) In May 2006, we entered into a six-year operating lease for 23,494 square feet of office space. Operating lease obligations do not include $6.7 million of non-cancelable operating lease payments related to this lease. Future minimum payments under the operating lease total $0.2 million, $1.0 million, $1.1 million, $1.1 million, $1.2 million, $1.2 million and $0.9 million for the years ending December 31, 2006, 2007, 2008, 2009, 2010, 2011 and 2012, respectively.

(3) License obligations do not include additional payments of up to $77.0 million due upon the occurrence of certain milestones related to regulatory or commercial events. We may also be required to pay royalties on any net sales of the licensed products. License payments may be increased based on the timing of various milestones and the extent to which the licensed technologies are pursued for other indications. These milestone payments and royalty payments under our license agreements are not included in the table above because we cannot, at this time, determine when or if the related milestones will be achieved or the events triggering the commencement of payment obligations will occur.

We also enter into agreements with third parties to manufacture our product candidates, conduct our clinical trials and perform data collection and analysis. Our payment obligations under these agreements depend upon the progress of our development programs. Therefore, we are unable at this time to estimate with certainty the future costs we will incur under these agreements.

Related Party Transactions

For a description of our related party transactions, see the “Certain Relationships and Related Party Transactions” section of this prospectus.

Off-Balance Sheet Arrangements

We have not engaged in any off-balance sheet activities.

Quantitative and Qualitative Disclosures About Market Risk

Our cash and cash equivalents as of June 30, 2006 consisted primarily of cash and money market funds. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because the majority of our investments are in short-term marketable securities. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. Some of the securities that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the value of the investment to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of our investment will probably decline. To minimize this risk, we intend to continue to maintain our portfolio of cash equivalents and short-term investments in a variety of securities including commercial paper, money market funds and government and non-government debt securities, all with various maturities. In general, money market funds are not subject to market risk because the interest paid on such funds fluctuates with the prevailing interest rate.

BUSINESS

Overview

We are a biopharmaceutical company focused on in-licensing, developing and commercializing proprietary product candidates principally for use in the hospital setting. Since our inception in 2004, we have in-licensed rights to two Phase III product candidates. We have in-licensed the exclusive U.S. and Canadian rights to IV APAP, an intravenous formulation of acetaminophen that has previously been studied in six completed Phase III trials and is currently marketed in Europe for the treatment of acute pain and fever by Bristol-Myers Squibb Company, or BMS. We believe that IV APAP is the only stable, pharmaceutically-acceptable intravenous formulation of acetaminophen. We intend to initiate Phase III development for the treatment of acute pain in the fourth quarter of 2006 and Phase III development for the treatment of fever in the first half of 2007. We also in-licensed the exclusive North American and European rights to omiganan pentahydrochloride 1% aqueous gel, or Omigard, for the prevention and treatment of device-related, surgical wound-related and burn-related infections. We are currently conducting a Phase III trial of Omigard for the prevention of local catheter site infections, or LCSI, to confirm the results observed for the prevention of LCSI, a secondary endpoint, in a large, completed Phase III trial. We believe that the hospital setting is a concentrated, underserved market for pharmaceuticals and anticipate building our own, hospital-focused sales force as our products approach potential U.S. Food and Drug Administration, or FDA, approval. We intend to build a leading franchise in the hospital setting, continuing to focus on products that are in late-stages of development, currently commercialized outside the United States or approved in the United States but with significant commercial potential for proprietary new uses or formulations.

Our current portfolio consists of the following product candidates:

- *IV APAP for the treatment of acute pain and fever.* We are developing IV APAP in the U.S. market for the treatment of acute pain and fever. According to IMS Health, Inc., or IMS, an independent marketing research firm, over 500 million units of injectable analgesics, typically used to treat pain, were sold in the United States in 2005. Opioids such as morphine, meperdine, hydromorphone and fentanyl represent the majority of unit volume in the market but are associated with a variety of unwanted side effects including sedation, nausea, vomiting, constipation, cognitive impairment and respiratory depression. Ketorolac, a non-steroidal anti-inflammatory drug, or NSAID, is the only non-opioid injectable analgesic available for the treatment of acute pain in the United States. However, ketorolac carries strong warnings from the FDA for various side effects, including an increased risk of bleeding — a particularly troubling side-effect in the surgical setting.

  In March 2006, we in-licensed the patents and the exclusive development and commercialization rights to IV APAP in the United States and Canada from BMS. IV APAP has been marketed outside the United States for approximately four years. Since its introduction in Europe in mid-2002, over 100 million doses of IV APAP have been administered to patients, and it has become the market share leader among injectable analgesics with 2005 sales of more than $140 million according to IMS. With approval in over 40 countries, the addition of IV APAP to our product pipeline is consistent with our strategy to in-license and develop pharmaceutical candidates with well-understood risk profiles. In the fourth quarter of 2006, we expect to initiate the remaining Phase III clinical trial requirements. We expect these Phase III clinical trial results to be available in the first half of 2008 and, if positive, to subsequently submit a new drug application, or NDA, in the second half of 2008.

- *Omigard for the prevention of intravascular catheter-related infections.* We are developing Omigard for the prevention of intravascular catheter-related infections in the United States and Europe. According to the February 2004 *Catheter: Global Markets & Technologies* report from Theta Reports, eight million central venous catheters, or CVCs, were sold in the United States in 2003, and unit sales are projected to grow to 11 million by 2007. Although

CVCs have become an important part of medical care, they can give rise to dangerous and costly complications, including: LCSIs, which are infections at the catheter insertion site; catheter colonization, which is the growth of microorganisms on the portion of the catheter below the skin surface; and catheter-related bloodstream infections, or CRBSIs, which are infections in the bloodstream caused by microorganisms associated with the catheter. The Centers for Disease Control and Prevention, or the CDC, estimates that there are 250,000 CRBSIs each year in the United States. The attributable mortality rate of CRBSIs is approximately 12% to 25% with an average marginal cost to the healthcare system of $25,000 per infection. Currently, topical antiseptics are the primary agent used to cleanse the skin surface around the catheter insertion site prior to insertion. However, the utility of these antiseptics is limited, principally due to the relatively short duration of antimicrobial activity.

Omigard is a topical antimicrobial that has been demonstrated to be rapidly bactericidal and fungicidal with prolonged duration of activity against all microorganisms commonly found on the skin surface including multi-drug resistant microorganisms such as methicillin-resistant *staphylococcus aureus*, or MRSA. Importantly, resistance to Omigard has not been induced in the laboratory after extensive study nor has Omigard demonstrated potential to induce cross-resistance to other antimicrobial therapeutics. In July 2004, we in-licensed the patents and the exclusive development and commercialization rights to Omigard in North America and Europe for the prevention of device-related, surgical wound-related and burn-related infections.

Omigard has previously been studied in a large, completed Phase III trial that demonstrated statistically significant outcomes for the prevention of LCSIs and catheter colonization. The presence of an LCSI may result in replacement of the catheter and/or administration of antibiotics, both of which create additional costs to hospitals and have the potential for adverse safety outcomes. In addition, catheter colonization is well correlated with CRBSIs, according to a published review of clinical trials. In August 2005, we initiated a confirmatory Phase III clinical trial with a primary endpoint, the prevention of LCSIs. We reached agreement with the FDA on the trial design, endpoints and statistical analysis plan received through the special protocol assessment, or SPA, process. We expect these Phase III results to be available in the second half of 2007 and to subsequently submit an NDA for Omigard in the first half of 2008.

- *Other product candidates.* We are also exploring the opportunity to develop new formulations of omiganan pentahydrochloride for the prevention and treatment of other device-related, surgical wound-related and burn-related infections. We are currently preparing preclinical experiments in animal models prior to initiating human clinical trials.

Our Strategy

Our goal is to be a leading biopharmaceutical company focused on the development and commercialization of proprietary pharmaceuticals principally for use in the hospital setting. Our near-term strategy is to focus on completing the development of and commercializing our existing product candidates. Our long-term strategy is to in-license, acquire, develop and commercialize additional product candidates that are in late-stages of development, currently commercialized outside the United States or approved in the United States but with significant commercial potential for proprietary new uses or formulations. Specifically, we intend to:

- *Obtain regulatory approval for our Phase III hospital product candidates, IV APAP and Omigard.* We are applying the expertise of our development teams to conduct and successfully complete the Phase III clinical trials associated with each product candidate. We have designed our Phase III clinical programs in an effort to reduce clinical development risk, facilitate regulatory approval and optimize marketing claims. To that end,

we plan to resume a U.S. Phase III program later this year for IV APAP previously initiated by BMS, and we expect to submit an NDA in the second half of 2008 based on the previously completed trials and any further trials that may be required by the FDA. In addition, we have reached a written agreement with the FDA through the SPA process for a single confirmatory Phase III study of Omigard for the prevention of LCSIs.

- *Build a highly leverageable sales organization targeting hospitals.* We intend to build a commercial organization focused on promoting our products principally to hospitals in the United States. We believe that both IV APAP and Omigard can be effectively promoted by our own sales force targeting key hospitals in the United States. Importantly, the number of institutions comprising the hospital marketplace is relatively limited and we believe a small number of these institutions account for a substantial portion of the prescribing activity. The concentrated nature of this market creates the opportunity for significant marketing synergies as we intend to leverage our sales force across multiple therapeutic categories in the hospital. Outside the United States, we intend to establish strategic partnerships for the commercialization of our products where we have commercialization rights.
- *Expand our product portfolio through acquiring or in-licensing additional late-stage, hospital-focused products with well-understood risk profiles.* We will seek additional opportunities to acquire or in-license products to more fully exploit our clinical, regulatory, manufacturing, sales and marketing capabilities. We believe that our focus on the hospital market enables us to evaluate a broader range of products across multiple therapeutic areas for possible acquisition. In addition, competition from large pharmaceutical companies has generally diminished in the hospital marketplace as greater emphasis has shifted toward larger opportunities in the primary care setting. To reduce the time-to-market and the risks and costs of clinical development, we focus on products that are in late-stages of development, currently commercialized outside the United States or approved in the United States but with significant commercial potential for proprietary new uses or formulations.
- *Pursue additional indications and commercial opportunities for our product candidates.* We will seek to maximize the value of IV APAP, Omigard and any other product candidates we may in-license, acquire or develop by pursuing other indications and commercial opportunities for such candidates. For example, we have rights to develop and commercialize omiganan pentahydrochloride for additional indications related to the prevention and treatment of device-related, surgical wound-related and burn-related infections.

The Hospital Market

Large, multinational pharmaceutical companies have generally decreased marketing efforts focused on hospital-use drugs, instead focusing on drugs that can be marketed in the larger outpatient setting. We believe this reduced emphasis on the hospital marketplace presents us with an excellent opportunity to in-license, acquire, develop and commercialize products that address unmet medical needs in the hospital setting. We believe the concentrated nature of the hospital marketplace will allow for our expansion into other therapeutic areas without substantial investment in additional commercial infrastructure.

According to IMS, approximately $28 billion was spent on promotional activities by the pharmaceutical industry in 2004. Of this amount, IMS estimates that only $1 billion was directed towards hospital-based physicians and directors of pharmacies. This hospital-focused spending represents approximately 3% of total promotional expenditures and has declined from approximately 6% of total spending in 1996. The significant imbalance towards the outpatient market is highlighted by spending on direct-to-consumer campaigns and drug sampling which now make up close to 80% of promotional spending for pharmaceuticals.

Despite these declining promotional expenditures, U.S. hospitals and clinics accounted for approximately $54 billion or 21% of U.S. pharmaceutical sales in 2005, according to IMS. Furthermore, we believe pharmaceutical sales to acute care hospitals are highly concentrated among a relatively small

number of large institutions. For example, according to Wolters Kluwer Health, an independent marketing research firm, only 2,000 of the approximately 5,000 acute care hospitals in the United States represent more than 80% of injectable analgesic sales. The concentration of high-prescribing institutions enables effective promotion of pharmaceuticals utilizing a relatively small, dedicated sales and marketing organization. We believe the relative lack of promotional efforts directed toward the highly concentrated hospital marketplace makes it an underserved and compelling opportunity, especially for a biopharmaceutical company commercializing its products directly through its own dedicated sales force.

We believe a typical sales representative focused on office-based physicians can generally promote only two to three products effectively; whereas, a typical hospital-focused sales representative can effectively promote five to six products. Furthermore, we believe a typical sales representative focused on office-based physicians can effectively reach five to seven physicians per day; whereas, a typical hospital-focused sales representative can reach many more physicians, nurses and pharmacy directors within a given institution. Notably, a hospital-focused sales representative also faces significantly less travel time between sales calls and less wait time in physician offices as a large number of prescribers can be found in a single location. Furthermore, drug sampling generally does not occur in hospitals, which represents a significant cost advantage versus marketing to office-based physicians. A single sales representative can promote products from multiple therapeutic categories to multiple prescribers within the institution.

In addition to hospitals, we intend to promote our products to certain ambulatory care centers, including ambulatory surgery centers and dialysis clinics, which tend to be located in close proximity to a hospital and can be targeted with our hospital sales force. According to Verispan, there are approximately 5,000 outpatient surgery centers in the United States. We estimate that fewer than 500 of these surgery centers represent the high opportunity segment for our products. According to the U.S. General Accounting Office, there are approximately 4,000 dialysis clinics in the United States, of which we believe most are either co-located with a hospital or located in close proximity to a hospital.

In recent years there has also been significant activity by both government agencies and accrediting organizations to hold hospitals accountable for improving patient outcomes across a wide variety of areas, including infection control, pain management, cardiovascular care and others. For example, according to the Association for Professionals in Infection Control and Epidemiology, there are now 13 U.S. states that require hospitals to publicly report their infections rates and there are more than 20 other states that have had legislative activity related to public reporting of infection rates in 2006. These types of initiatives support our view that significant unmet medical needs remain in hospitals today.

Our Product Development Programs

Our current product development programs are focused on late-stage development products principally for use in the hospital setting. Our portfolio consists of the following product candidates:

Product Candidate	Indication	Development Stage in the United States	Development Stage in Europe	Cadence Commercial Rights
IV APAP(1)	Treatment of acute pain — adults	Phase III	Marketed (by BMS)	United States, Canada
	Treatment of acute pain — pediatrics	Phase III	Marketed (by BMS)	United States, Canada
	Treatment of fever — adults	Phase III	Marketed (by BMS)	United States, Canada
	Treatment of fever — pediatrics	Phase III	Marketed (by BMS)	United States, Canada
Omigard	Prevention of local catheter site infections	Phase III	Phase III	North America, Europe

(1) In March 2006, we in-licensed the patents and the exclusive development and commercialization rights to IV APAP in the United States and Canada from BMS. BMS has completed Phase III trials with respect to the above indications, excluding the treatment of fever in adults, for IV APAP in Europe and the United States, which we intend to use in our NDA filing following agreement with the FDA on additional clinical trials needed in the United States for approval. Because the Phase III clinical trial requirements differ in the United States compared to Europe, we are required to complete additional Phase III trials, particularly to demonstrate safety and efficacy from multiple day dosing in additional patient populations, including patients undergoing soft tissue surgery, such as abdominal hysterectomy, and patients with fever. In the fourth quarter of 2006, we expect to initiate the remaining Phase III clinical trial requirements for submission in the United States. We expect these Phase III clinical trial results to be available in the first half of 2008 and, if positive, to submit an NDA in the second half of 2008.

IV APAP for the Treatment of Acute Pain and Fever

Acute Pain Background

Acute pain is generally defined as pain with relatively short duration and recent onset with an easily identifiable cause. It serves to warn the patient of tissue damage and is often sharp initially and followed by aching pain. In the hospital setting, acute pain is generally classified as post-operative or non-operative.

Post-operative pain is a response to tissue damage during surgery that stimulates peripheral nerves, which signal the brain to produce a sensory and emotional response. Post-operative pain may occur not only at the surgical site but also in areas not directly affected by the surgical procedure. The pain may be experienced by an inpatient or outpatient and can be felt after surgical procedures.

Numerous studies reveal that the incidence and severity of post-operative pain is primarily determined by the type of surgery, duration of surgery and the treatment choice following surgery. Post-operative pain is usually greatest with abdominal, head-neck, orthopedic and thoracic surgery and may last up to eight days after the surgical procedure. In comparison, surgical procedures such as arthroscopy, breast biopsy, hernia repair and plastic surgery tend to be less invasive and generally produce minor surgical trauma.

Despite major improvements in surgical techniques and the introduction of novel drugs, the overall treatment of post-operative pain has not substantially improved over the last 20 years. According to the industry research group Datamonitor, up to 75% of patients report inadequate pain relief. Such inadequate pain relief often leads to nausea, vomiting, decreased mobilization and reduced nutritional intake — all of which impede patient recovery — and can lead to infections and blood clots in the legs and lungs — all of which jeopardize patient safety. All of these factors have a major impact on patient care and hospital economic outcomes, including prolonged hospital stays.

Non-operative pain in the hospital is typically associated with diseases, disorders, trauma and other conditions. The most common non-operative pain types among hospitalized patients include pain associated with cancer, trauma, burns, gallstones and cardiovascular events. Other incidences of non-operative pain among hospitalized patients are often related to HIV, pancreatitis, sickle cell disease and other diseases. Inadequate pain management in these patients also leads to poor health and economic outcomes.

Market for Injectable Analgesics

Drugs used to treat pain are collectively known as analgesics. Injectable formulations of analgesics are typically used when patients are unable to take medications by mouth, faster onset of analgesia is required, or it is otherwise more convenient to administer drugs in injectable form. Hospitalized patients may be unable to take medications by mouth for a variety of reasons including post-anesthesia sedation, other forms of sedation, nausea, vomiting, gastrointestinal limitations or other conditions.

According to IMS, the U.S. market for injectable analgesics exceeded 500 million units in 2005. Morphine is the current market leader and accounted for more than 300 million units in 2005. Other injectable opioids such as meperidine, hydromorphone and fentanyl, which are all available in generic forms, accounted for more than 135 million units in 2005. Ketorolac (Toradol), a genericized NSAID, is the only non-opioid injectable analgesic for acute pain available in the United States. According to IMS, injectable ketorolac sold more than 40 million units in 2005.

According to Datamonitor, up to 53 million patients undergo surgical procedures each year in the United States. Datamonitor projects the number of surgical procedures to increase as the elderly population increases and as technological advances allow new surgical procedures to be performed. As such, we expect that the need for safe and effective drugs to treat pain in the post-operative setting will continue to increase.

Limitations of Current Therapies

Only two classes of injectable analgesics, opioids and NSAIDs, are currently available in the United States for the treatment of acute pain.

Opioids have been used as analgesics for over 2,000 years and continue to be the mainstay of post-operative pain management. Opioids activate certain receptors in the central nervous system, which produce analgesia, euphoria and other positive effects. A range of opioids are available in injectable form including morphine, fentanyl, meperidine and hydromorphone.

Opioids, however, are associated with a variety of unwanted side effects including sedation, nausea, vomiting, constipation, headache, cognitive impairment and respiratory depression. Respiratory depression can lead to death if not monitored closely. Side effects from opioids have been demonstrated to reduce quality of life and side-effect-related dosing limitations can result in suboptimal pain relief due to under-dosing. All of these side effects may require additional medications or treatments and can prolong patient stay in the post-anesthesia care unit as well as a patient’s overall stay in the hospital or in an ambulatory surgical center.

Opioid-related side effects also impose significant economic burdens on hospitals and ambulatory surgical centers. For example, nausea and vomiting, common opioid-related side effects, can cause the need for administration of anti-nausea medication, increased monitoring by nurses, increased length of stay

in the post-anesthesia care unit and overall length of stay in the hospital, diverting resources that could otherwise be utilized in revenue-generating activities. Studies have demonstrated increased costs related to post-operative opioid administration from not only increased personnel time and length of stay but also increased supply and drug costs, including drugs to manage the nausea and vomiting.

The only non-opioid injectable analgesic for acute pain available in the United States is the NSAID ketorolac. NSAIDs act as non-selective inhibitors of the enzyme cyclooxygenase, inhibiting both the cyclooxygenase-1, or COX-1, and cyclooxygenase-2, or COX-2, enzymes. The inhibition of COX-2 produces an anti-inflammatory effect resulting in analgesia. Since NSAIDs do not produce respiratory depression or impair gastrointestinal motility, they are considered to be useful alternatives to opioids for the relief of acute pain. Studies have also demonstrated the opioid-sparing potential of ketorolac when used in combination with opioids, as well as resulting decreases in hospital costs. Published studies have shown lower overall per-patient costs ranging from $326 to $2,031 for the patients treated with ketorolac and opioids compared to those treated with opioids alone.

Despite these economic advantages, the use of ketorolac is severely limited in the post-operative period. Non-specific NSAIDs such as ketorolac block COX-1, which plays a major role in the release of prostaglandins to regulate platelet aggregation and protect the lining of the stomach. As a result, bleeding, gastrointestinal and renal complications are significant impediments to the post-operative use of ketorolac. The product carries a black box warning for these side effects. A black box warning is the strongest type of warning that the FDA can require for a drug and is generally reserved for warning prescribers about adverse drug reactions that can cause serious injury or death. The FDA specifically warns that ketorolac should not be used in various patient populations that are at-risk for bleeding, as a prophylactic analgesic prior to major surgery or for intraoperative administration when stoppage of bleeding is critical.

The World Health Organization, or WHO, has established a three-step analgesic ladder for the treatment of pain, which recommends initial treatment with a non-opioid such as acetaminophen, aspirin, or NSAIDs followed by the addition of opioids as pain increases. The WHO analgesic ladder is consistent with the practice of multimodal analgesia, which involves the use of more than one class of drug for pain control to obtain additional analgesia, reduce side effects or both. In the United States, this recommended practice of multimodal analgesia is not fully available to physicians given the current lack of an intravenous formulation of acetaminophen. With the availability of IV APAP in Europe, physicians are able to treat post-operative pain with IV APAP as baseline therapy and use opioids in combination as needed for increasing levels of pain.

Fever

Fever is an increase in internal body temperature above its normal range of 98.6 degrees Fahrenheit. A significant fever is usually defined as an oral or ear temperature of greater than 102 degrees Fahrenheit or a rectal temperature of greater than 103 degrees Fahrenheit. Very high fevers may cause hallucinations, confusion, irritability, convulsions or death. Fever is most often an important immune system response to a viral or bacterial infection since most viruses and bacteria cannot thrive in hot environments. White blood cells release substances called pyrogens that act on the hypothalamus in the brain to raise body temperature.

Hospitalized patients are at especially high risk for developing fever given the potential exposure to various infectious microorganisms, invasive procedures and medications. Surgery is the most common source of fever in the hospital setting, and published incidence rates range from 14% to 91% of post-operative patients. Infections such as wound infections, urinary tract infections and pneumonia are the next most frequent causes. However, deep venous thrombosis, pulmonary emboli, myocardial infarction and medications are also important potential sources of fever. Many patients also present with fever upon arrival at the hospital due to community-acquired infections, underlying diseases, including cancer and HIV, severe sunburn, and often the origin of a fever is unknown.

Fever is also the most common reason parents bring their children to the emergency rooms of hospitals. Pediatric fever is particularly worrisome as approximately 4% of children under age five

experience fever-induced seizures, or febrile seizures. The signs of febrile seizures, which occur when a child's temperature rises or falls rapidly, include loss of consciousness and convulsions.

Acetaminophen, ibuprofen and aspirin are the most commonly used medications to treat fever. The use of ibuprofen, an NSAID, and aspirin are limited due to gastrointestinal side-effects and the risk of bleeding. Ibuprofen is not approved for children under six months of age and is not recommended for patients that are dehydrated or vomiting continuously. Aspirin is contraindicated in children and teenagers with viral infections due to the risk of acquiring Reye's syndrome, a potentially fatal disease.

In the United States, acetaminophen, ibuprofen and aspirin are not available in intravenous dosage form. However, oral delivery of medications is often not possible for hospitalized patients that are unconscious, sedated, fasting, experiencing nausea and vomiting or are otherwise unable to take medications by mouth. Rectal delivery of medications is sometimes possible; however, drug absorption is often erratic, resulting in unpredictable levels of efficacy. Rectal delivery in infants is further complicated by frequent bowel movements which may lead to difficulty determining the amount of medication delivered. It is often more convenient to administer medications in intravenous dosage form, particularly for patients that currently have an intravenous line in place. We believe that the availability of IV APAP in the United States would offer a significant new treatment option for hospitalized patients with fever.

IV APAP

IV APAP has been marketed by BMS in Europe since its launch in France in mid-2002 and subsequent approvals in other countries throughout Europe and other parts of the world. After obtaining these approvals, BMS elected to seek a partner to develop and commercialize IV APAP in the United States and Canada based on a new corporate strategy to focus the company's research and development on 10 specific disease areas, which do not include the treatment of pain. In March 2006, we completed our agreement with BMS to in-license these rights.

Acetaminophen is the most widely used drug for pain relief and the reduction of fever in the United States. The mechanism of action of acetaminophen remains not well understood; however, it is believed that acetaminophen acts in part on central COX enzymes without the peripheral anti-inflammatory effects, platelet inhibition or other side effects associated with NSAIDs. Acetaminophen was discovered in the late 19th century but was not available for sale until 1955 when it was introduced under the brand name Tylenol in the United States. Acetaminophen is currently available in over 600 combination and single ingredient prescription and over-the-counter medicines, including tablet, caplet, orally-dosed liquid suspension, powder and suppository forms for both adults and children.

Historically, poor stability in aqueous solutions and inadequate solubility of acetaminophen prevented the development of an intravenous dosage form. Acetaminophen will decompose in the presence of moisture or water. The rate of decomposition is accelerated as the temperature is increased and upon exposure to light. The stability is also a function of the solution's pH, which creates a further challenge to formulate acetaminophen in an aqueous solution suitable for intravenous administration. We believe that IV APAP is the only stable, pharmaceutically-acceptable intravenous formulation of acetaminophen.

Prior to the introduction of IV APAP in Europe, BMS had developed an intravenous formulation of propacetamol, a prodrug that is rapidly converted in the bloodstream to acetaminophen. This formulation was developed as an alternative approach given the challenges associated with formulating acetaminophen itself in solution. Available in Europe for more than 20 years, intravenous propacetamol was marketed under the brand name Pro-Dafalgan and was generally indicated for the treatment of acute moderate pain and the reduction of fever. Pro-Dafalgan was provided for use as a dried powder to be reconstituted in solution prior to intravenous administration. In healthcare workers reconstituting the drug, there were reported incidences of allergic reactions, including mild allergic reactions on the skin and severe allergic shock from inhalation. Intravenous propacetamol was also associated with pain at the injection site and other local reactions in approximately 50% of patients receiving the drug.

IV APAP was approved in Europe based on clinical data demonstrating that the formulation provides superior analgesic efficacy over placebo and similar analgesic efficacy and bioequivalence to intravenous propacetamol. Well-controlled clinical trials have demonstrated that IV APAP has a safety profile similar to placebo with significantly better tolerability than intravenous propacetamol upon infusion. Pain at the injection site has been demonstrated to be no different than placebo.

IV APAP is the only intravenous formulation of acetaminophen available anywhere in the world and has now been approved in over 40 countries. BMS markets IV APAP in Europe and other countries principally under the brand name Perfalgan. When BMS launched IV APAP, it withdrew intravenous propacetamol from the market. Two strengths of IV APAP are commercially available in these countries in a ready-to-use solution: a 50mL bottle containing 0.5g acetaminophen and a 100mL bottle containing 1g acetaminophen. Both are labeled for administration via a 15-minute intravenous infusion.

In Europe, IV APAP was initially launched in France in mid-2002, followed by Germany and Spain in 2003, the United Kingdom in 2004 and Italy in 2005. Despite this country-by-country launch, according to IMS, IV APAP achieved a 43% dollar share (20% of unit volume) among all injectable analgesics sold in Europe in less than four years. In 2005, IV APAP sold more than 55 million units for total sales exceeding $140 million (U.S. dollars) according to IMS.

We believe the United States represents a substantially larger market opportunity for IV APAP than Europe. According to IMS, over 500 million units of injectable analgesics were sold in the United States in 2005 compared to approximately 320 million in Europe. More significantly, pharmaceutical pricing continues to be higher in the United States on average. Each country in the European Union currently employs direct and other forms of price controls, including reference systems where prices for new drugs are based upon the prices of existing drugs that provide similar therapeutic benefit or prices of drugs in other European countries. According to IMS, the average selling price in Europe was approximately $2.50 (U.S. dollars) per unit.

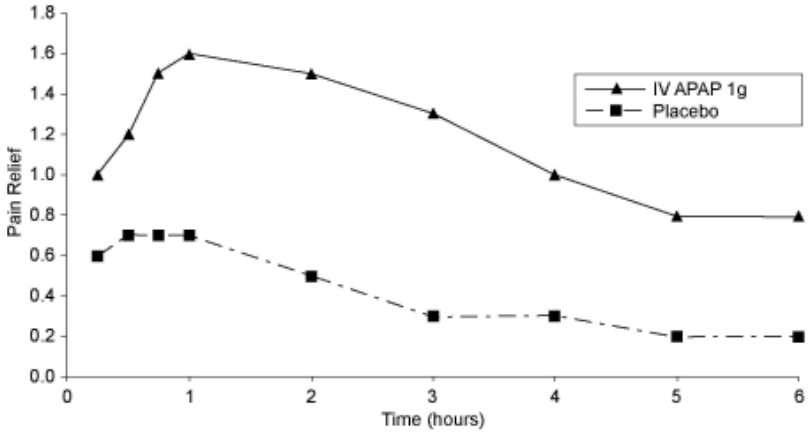
We believe that the key product attributes that will drive adoption include the proven efficacy and established safety profile of acetaminophen, the potential ability to reduce concomitant use of morphine and other opioids, a more convenient dosage form for some patients and a more rapid onset of action.

Clinical Development History

Clinical Overview. There have been 2,241 subjects, including 1,780 subjects that received IV APAP, studied in nine clinical trials completed by BMS, largely submitted to support the Marketing Authorization Application, or MAA, that resulted in European approval. These trials included two Phase I trials, six Phase III trials and one large Phase IV trial. Overall, we believe that the results of these nine studies demonstrate that IV APAP is safe and effective in the treatment of post-operative pain in adults and children. These trials have also demonstrated that IV APAP reduces the consumption of opioids when used in combination.

Clinical Studies for Post-Operative Pain in Adults. One Phase III study evaluated 150 adult subjects with moderate-to-severe pain following total hip and total knee replacements. Subjects were randomized to receive IV APAP, intravenous propacetamol or placebo. We believe this study best demonstrates the efficacy of IV APAP since the patients in the trial were undergoing surgical procedures with more severe levels of pain. On the primary efficacy endpoint, pain relief scores in the patients treated with IV APAP were statistically higher ($p\text{-}value<0.05$) than those treated with placebo and not statistically different than those treated with intravenous propacetamol from 15 minutes to six hours, at which point patients received a second dose. P-values indicate the likelihood that clinical trial results were due to random statistical fluctuations rather than a true cause and effect. The lower the p-value, the more likely there is a true cause-and-effect relationship. Therefore, p-values provide a sense of the reliability of the results of the study in question. Typically, the FDA requires a p-value of less than 0.05 to establish the statistical significance of a clinical trial.

The following graph presents the results for pain relief reported by patients in this Phase III study for post-operative pain in adults following major orthopedic surgery, based on a five point verbal scale, with four representing complete pain relief and zero representing no pain relief:



In addition, this Phase III study demonstrated the following results:

Outcome Measure	Result	p-value
Median time to morphine rescue	3.0 hours for IV APAP vs. 0.8 hours for placebo	<0.001
Reduction in morphine consumption over the 24-hour period	33% reduction (19.1mg) for IV APAP compared to placebo	<0.01

This Phase III study also demonstrated a statistically significant reduction in pain intensity and a statistically significant improvement in patient satisfaction with pain treatment for IV APAP compared to placebo. Drug-related adverse events in this trial were similar to placebo.

Two Phase III studies evaluated a total of 349 adult subjects with moderate-to-severe pain following third molar surgery. Subjects were randomized to receive IV APAP, intravenous propacetamol or placebo. Statistically significant effects versus placebo (*p-value*<0.01) were obtained with IV APAP for all efficacy criteria, including pain relief, pain intensity difference, duration of analgesia and patients' global evaluation. There were no statistically significant differences in treatment-related adverse events between IV APAP and placebo. IV APAP demonstrated similar results on all efficacy parameters compared to intravenous propacetamol with significantly lower incidence of pain at the injection site.

One Phase III study evaluated 163 adult subjects with moderate-to-severe pain following minor gynecologic surgery. Subjects were randomized to receive IV APAP or intravenous propacetamol. IV APAP demonstrated similar results on all efficacy parameters compared to intravenous propacetamol with statistically significantly lower incidence of pain at the injection site.

One Phase IV study evaluated 1,061 subjects with mild-to-moderate pain following surgery. All subjects received up to four doses of IV APAP over a 24-hour period. This trial provided additional data regarding the administration of multiple-doses of IV APAP.

Clinical Studies for Post-Operative Pain in Children. One Phase III study evaluated 183 pediatric subjects with moderate-to-severe pain following surgery for hernia repair. Subjects were randomized to receive IV APAP or intravenous propacetamol. IV APAP demonstrated similar results on all efficacy parameters compared to intravenous propacetamol with significantly lower incidence of pain at the injection site.

Clinical Studies for Fever in Children. One Phase III study evaluated 67 pediatric subjects (age one month to 12 years) with fever of infectious origin. Subjects were randomized to receive IV APAP or intravenous propacetamol. IV APAP demonstrated similar results on all efficacy parameters compared to intravenous propacetamol with statistically significantly lower incidence of pain at the injection site.

Safety Summary. The safety of acetaminophen has been well-established through decades of use in oral, suppository and intravenous formulations. The primary safety concern with acetaminophen is hepatotoxicity, which is well-understood and occurs rarely when acetaminophen is dosed in accordance with the recommended guidelines. In addition, an effective antidote, N-acetylcysteine, is available to treat acetaminophen overdose. We believe there is no evidence that IV APAP poses an increased risk for hepatoxicity or any other adverse event. In fact, in the 1,780 subjects receiving IV APAP in nine clinical trials previously completed by BMS, the product has exhibited a safety profile consistent with published data for oral acetaminophen. This is also consistent with observations from the European post-marketing safety database of IV APAP which covers a time period in which over 100 million doses were administered to patients.

In pharmacokinetic trials, the peak plasma concentration of acetaminophen ranged from 50% to 74% higher for IV APAP compared to oral acetaminophen; however, total plasma concentrations over time were not meaningfully different. Further, these results demonstrated that urinary elimination of acetaminophen metabolites, including metabolites with potential to interact with the liver, was not meaningfully different for IV APAP compared to oral acetaminophen at 12 and 24 hour measurements. Therefore, the study concluded that IV APAP would not be expected to be associated with an increased risk of toxicity to the liver compared with an equivalent dose of acetaminophen administered orally.

Opioid Sparing Summary. The use of IV APAP in clinical trials has consistently been associated with at least a 33% reduction in opioid consumption compared to placebo. In these cases, opioids were available at the discretion of patients utilizing patient controlled analgesia, or PCA, devices.

Clinical Development Plan

We are developing IV APAP based on a targeted indication for the treatment of acute pain, usually in the post-operative setting, and the treatment of fever. We are seeking approval for use in both adults and children for these indications. Our proposed development plan to support this indication integrates the existing body of intravenous propacetamol data, IV APAP data and the data generated by clinical studies of IV APAP to be conducted by us. Under our agreement with BMS, we have rights to reference these BMS data. We intend to submit a 505(b)(2) NDA for IV APAP based on these data sets as well as references to the extensive literature which supports the safety and efficacy of acetaminophen in oral formulations. Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act permits the submission of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference.

In August 2006, we met with the FDA to discuss the clinical trial requirements for submission of a 505(b)(2) NDA for IV APAP. Based on the preliminary feedback from the FDA, we intend to conduct six clinical trials to provide the FDA with additional data to support multiple dose efficacy for soft tissue surgery, efficacy for fever and safety in adults and children. These trials include:

- Phase III trial in female patients with moderate-to-severe pain following total abdominal hysterectomy: this trial will be a randomized, placebo-controlled, double-blind, multi-center study to assess the efficacy and safety of single and multiple doses of IV APAP.
- Phase III trial in adults with fever: this trial will be a randomized, controlled, double-blind study to assess the efficacy and safety of single and multiple doses of IV APAP.
- Pharmacokinetic study in adult subjects: this trial will be a randomized, single center study to assess the pharmacokinetics of single and multiple doses of IV APAP compared to oral acetaminophen in adults.

- Pharmacokinetic study in pediatric subjects: this trial will be a randomized, single center study to assess the pharmacokinetics of single and multiple doses of IV APAP compared to oral acetaminophen in children.
- Safety study in adult subjects: this trial will be an open-label, multi-center study to assess the safety of single and multiple doses of IV APAP in adults.
- Safety study in pediatric subjects: this trial will be an open-label, multi-center study to assess the safety of single and multiple doses of IV APAP in children.

Total enrollment of the six clinical trials will be determined based on additional input expected from the FDA. We intend to initiate the abdominal hysterectomy Phase III trial and the adult pharmacokinetic study in the fourth quarter of 2006. We intend to initiate the other clinical trials in the first half of 2007.

Omigard for the Prevention of Intravascular Catheter-Related Infections

Intravascular Catheter-Related Infections Background

The use of catheters for vascular access has become essential to medical practice. Intravascular catheters are inserted through the skin and advanced so that the tip rests in a vein or artery. Intravascular catheters are typically classified as either peripheral lines which access smaller veins or central lines (such as CVCs, peripherally inserted central catheters and arterial lines) to access larger veins (such as the jugular, femoral and subclavian veins) and arteries. Although such catheters provide necessary access to veins and arteries, their use puts patients at risk for dangerous and costly complications, including LCSIs, catheter colonization and CRBSIs, and, to a lesser degree, infections in other organs including the heart, lungs, brain and bones.

Based on published clinical studies, we estimate that, of patients with a CVC, approximately 10% will develop an LCSI and 20% will develop catheter colonization. This translates into approximately one million LCSIs and two million incidences of catheter colonization in the United States each year. The presence of an LSCI may result in replacement of the catheter and/or administration of antibiotics, both of which create additional costs to hospitals and have the potential for adverse safety outcomes. In addition, catheter colonization is well correlated with CRBSIs, according to a published review of clinical trials.

The CDC estimates that there are more than 250,000 CRBSIs among hospitalized patients and more than 75,000 CRBSIs among hemodialysis patients in the United States each year. Attributable mortality is estimated by the CDC to be 12% to 25% for each CRBSI, which translates into 39,000 to 81,250 deaths annually due to CRBSIs. Further, the CDC estimates that the average cost per infection is estimated to be $25,000 and, for patients in the intensive care unit, is estimated to be up to $56,000.

The additional costs related to infectious complications from CVCs result in an estimated annual burden to the healthcare system exceeding $6 billion. The majority of these costs are shouldered by hospitals due to the reimbursement system. Adopted by Medicare in 1983, the Prospective Payment System for acute hospital inpatient services generally establishes pre-determined reimbursement amounts, or diagnosis-related groups, which are classifications based on the patient’s discharge diagnoses, procedures performed and other patient factors. Similar prospective payment systems were later adopted for certain other Medicare inpatient hospital services, such as rehabilitation and psychiatric hospitals. When the costs of treating a patient fall below or are above these prospective payment amounts, the hospital reaps the respective benefit or bears the respective cost. Therefore, there is a compelling economic incentive for these hospitals to use all available means to reduce infections.

The CDC estimates that hospital-acquired bloodstream infections are the eighth leading cause of death in the United States and that intravascular catheters are the leading cause of hospital-acquired bloodstream infections. Furthermore, a recent study in the New England Journal of Medicine reported that 70% of these infections are antibiotic-resistant, making them more difficult and costly to treat. Consumer

groups, the CDC and the Joint Commission on Accreditation of Healthcare Organizations, or JCAHO, are calling for greater scrutiny and wider reporting of data on hospital-acquired infections. JCAHO or other recognized accreditation is necessary for reimbursement eligibility with Medicare and most insurers. Laws have been passed mandating public reporting of hospital-acquired infection data in Colorado, Connecticut, Florida, Illinois, Maryland, Missouri, New Hampshire, New York, Pennsylvania, South Carolina, Tennessee, Vermont and Virginia. In 2006, more than 20 other states have had some legislative activity related to public reporting of hospital-acquired infections. We believe that the increased scrutiny on catheter-related infections in addition to compelling economic incentives will drive adoption of new products which show an ability to reduce infection rates.

Market for Antimicrobials to Prevent Intravascular Catheter Infections

Theta Reports estimates that nearly 500 million intravascular catheters will be used in the United States in 2006, including approximately 10 million CVCs. Unit sales of CVCs are projected to grow at 9% per year. Outside the United States, Theta Reports estimates that approximately 11 million CVCs will be used in 2006. The number of CVC placements is increasing as the population continues to age and hospitalized patients become increasingly compromised. We estimate that patients with a CVC receive, on average, three to four topical antimicrobial applications during a hospital stay. This translates into more than an estimated 30 million applications in the United States in 2006 for CVCs alone.

The Centers for Medicare and Medicaid Services indicate that there were more than 321,500 patients with end-stage renal disease receiving dialysis at the end of 2004, of which approximately 25% had a CVC. This patient population has been growing at an annual rate of approximately 8% due to the aging population, rise in diabetes, shortage of organ donors and improved technologies enabling longer survival of patients with end-stage renal disease. Patients on hemodialysis receive, on average, three topical antimicrobial applications per week. This translates into more than an estimated 12 million applications in the United States in 2006.

The use of topical antimicrobials to prevent infections associated with other central lines, including arterial lines and peripherally inserted central catheters, also represents a significant market opportunity. According to Theta Reports, there are more than 2 million peripherally inserted central catheters inserted in the United States each year. We estimate there are also approximately 7 million arterials lines inserted in the United States each year.

Limitations of Current Therapies

Microorganisms on the skin surface have been demonstrated to be the leading cause of intravascular device-related infections, including LCSIs and CRBSIs. The same microorganisms on the skin that cause LCSIs can lead to CRBSIs. Given the evidence for the importance of killing microorganisms on the skin surface to prevent the development of intravascular device-related infections, the use of topical antimicrobials is critical. However, currently available products have significant limitations.

The standard of care for skin antisepsis prior to catheter insertion and at dressing changes has been dominated by either povidone-iodine, also known as Betadine, or chlorhexidine, although usage patterns are increasingly favoring chlorhexidine. In 2002, the CDC published guidelines that stated that although chlorhexidine is preferred, povidone-iodine can be used. In 2002, a meta-analysis of eight heterogeneous studies comparing various formulations of chlorhexidine to povidone-iodine for the prevention of catheter-related infections was published. While the meta-analysis indicated a benefit to chlorhexidine, only one of the eight studies on its own demonstrated a statistically significant prevention of CRBSIs. We believe that this change in medical practice despite the lack of robust clinical evidence underscores the desire and willingness of healthcare providers to address this significant unmet need.

Although topical antiseptics tend to have a broad spectrum of antimicrobial activity, duration of activity ranges from minutes to hours after application. These products do not provide sustained antimicrobial coverage throughout the periods between dressing changes (typically every 72-96 hours), and

this lack of sustained antimicrobial activity can put patients at increased risk for acquiring an infection at the catheter insertion site.

In order to address the limited duration of activity associated with topical antiseptics, topical antibiotics have been used, either alone or in combination with topical antiseptics, to confer protection against microbial invasion. Clinical trials have shown benefits attributable to topical antibiotics, but these products have either been associated with increased frequency of fungal infections or emergence of bacterial resistance, including MRSA. These drawbacks have significantly diminished the use of topical antibiotics for the prevention of catheter-related infections. As a result, the market has almost exclusively switched back to the use of topical antiseptics.

There is some limited use of BioPatch, a chlorhexidine-impregnated foam dressing that is placed around the catheter at the insertion site. While this product delivers chlorhexidine to the catheter insertion site over a period of days, it has not been widely adopted reportedly due to difficulty in applying the dressing and the inability to visibly inspect the insertion site through the dressing. Physicians and nurses must lift up the BioPatch to monitor the insertion site for redness, swelling and other leading signs of infection. Such disruption of the dressing has the potential to interfere with the sterility of the site and promote the spread of pathogens.

Other products either in use or in development to reduce catheter-related infections are focused on downstream aspects of the infectious process. Some catheters coated with antiseptics and antibiotics have demonstrated reductions in catheter-related infections. Other new technologies being developed include contamination-resistant hubs, attachable cuffs, new catheter-coatings and antiseptic catheter lock solutions. We believe any use of these products would be in addition to the use of antimicrobial agents on the skin surface to prevent catheter-related infections.

Omigard

Omigard was discovered by researchers at Migenix. Migenix subsequently entered into a collaboration and license agreement with Fujisawa Healthcare, Inc., or Fujisawa. In that agreement, Fujisawa was granted the rights to commercialize Omigard in North America in return for licensing payments, funding of all remaining development costs and establishment of a joint development committee. In January 2004, Migenix reacquired all rights to Omigard from Fujisawa after completion of the first Phase III trial and then, in July 2004, licensed both the North American and European rights to us with the objective of completing the development program and commercializing the product.

Unlike other topical antimicrobials, Omigard exhibits a combination of features that we believe make it an ideal product for the prevention of catheter-related infections. Such features include:

- broad spectrum bactericidal and fungicidal activity;
- activity against resistant strains, including MRSA;
- rapid and prolonged duration of effect;
- resistance to Omigard has not been induced in the laboratory;
- no demonstrated ability to generate cross-resistance to other antimicrobials;
- excellent safety profile; and
- convenient application.

Omigard is effective against a wide variety of bacteria and fungi. The compound has been tested against more than 285 strains of Gram-positive and Gram-negative bacteria as well as more than 75 fungal strains. These studies demonstrate that Omigard has broad bactericidal and fungicidal activity against bacteria and fungi commonly found on the surface of human skin. Further, Omigard has also demonstrated the ability to kill multi-drug resistant microorganisms, including MRSA, and vancomycin-

resistant *enterococcus*, or VRE. The incidence of resistant infections is increasing, and these microorganisms represent a potentially significant threat to the public health.

Omigard has demonstrated not only the ability to kill rapidly but also, unlike the topical antiseptics, a prolonged duration of effect. In preclinical studies with Omigard, most microorganisms were killed after only six minutes of exposure. In skin surface studies, Omigard demonstrated the ability to kill more than 99.9% of microorganisms for at least three days.

In laboratory testing conducted by Migenix, resistance to Omigard, unlike the topical antiseptics, has not been demonstrated, nor has cross-resistance to other antimicrobials been demonstrated. A primary mechanism of action of Omigard is believed to be depolarization of the outer cell membrane of infectious microorganisms, resulting in cell death. Specific receptors within the cell have not been shown to be involved in the disruption of the cell membrane and, therefore, this non-specific mechanism of action decreases the likelihood of the development of resistance.

Omigard presents a benign toxicological profile when administered topically at doses as much as 30 times the planned human dose. The product has been demonstrated to be non-irritating to the skin, non-sensitizing to the skin, and not absorbed through the skin into the bloodstream (based on the inability to detect Omigard in the bloodstream at very low levels) and, therefore, has no meaningful systemic exposure.

Omigard is packaged in a convenient, single unit-of-use plastic squeeze vial. Omigard, which is formulated as a 1% clear viscous, aqueous gel, is applied around the catheter insertion site by squeezing the plastic vial. Unlike the topical antiseptics, Omigard does not have to be scrubbed onto the skin surface. Unlike povidone-iodine, Omigard does not have the potential to stain the skin and clothes of patients and healthcare providers.

Clinical Development History

Migenix completed one Phase I and two Phase II studies of Omigard in a total of 273 subjects. These trials demonstrated no evidence of sensitization, clinically significant irritation or systemic absorption. In addition, the Phase I trial exhibited killing of greater than 99.9% of bacteria and fungi on skin and maintained this level of antimicrobial activity for at least three days.

Migenix and Fujisawa subsequently completed a multi-center, randomized, evaluation committee-blinded Phase III trial that compared Omigard to 10% povidone-iodine in patients receiving CVCs, peripherally inserted central catheters, and/or arterial lines. The study was conducted in 1,407 patients in 27 centers in the United States. The primary efficacy endpoint was to demonstrate the superiority of Omigard over 10% povidone-iodine for the prevention of CRBSIs, as determined by a treatment-blinded evaluation committee. Secondary efficacy endpoints included demonstrating the superiority of Omigard for the prevention of LCSI and catheter colonization.

Treatment with Omigard resulted in a statistically significant prevention in catheter colonization compared to 10% povidone-iodine (*p-value*=0.002). The Omigard group had 21.9% fewer incidences of catheter colonization than the 10% povidone-iodine group.

	Treatment Arm		
Variable	**10% povidone-iodine**	**Omigard**	**p-value**
Catheter colonization present	232/583 (39.8)%	180/578 (31.1)%	0.002

Treatment with Omigard also resulted in a statistically significant prevention in LCSI (*p-value*=0.004). The table below summarizes data for LCSI in the modified intent-to-treat analysis set, which includes only those patients who did not have a bloodstream infection present at baseline. As shown in the table, the Omigard group had 49.2% fewer LCSIs than the 10% povidone-iodine group. Moreover, there was a greater than 50% reduction in the number of patients that had an LCSI and a catheter removed (*p-value*=0.002).

	Treatment Arm		
Variable	**10% povidone-iodine**	**Omigard**	**p-value**
LCSI present	48/699 (6.9)%	24/693 (3.5)%	0.004

Despite these favorable, statistically significant results for the prevention of LCSI and catheter colonization, the study did not show statistical significance for the primary endpoint: the prevention of CRBSI. The table below compares the incidence of CRBSI in the modified intent-to-treat analysis set after treatment with Omigard or 10% povidone-iodine. The rates of failure (development of CRBSI) and indeterminate response were similar for the two treatments arms. There was a 15.4% reduction in the incidence of microbiologically-proven CRBSI in the Omigard group compared to 10% povidone iodine; however, this outcome was not statistically significant.

	Treatment Arm		
Outcome	**10% povidone-iodine**	**Omigard**	**p-value**
Failure	18/699 (2.6)%	15/693 (2.2)%	0.622
Success	635/699 (90.8)%	630/693 (90.9)%	
Indeterminate	46/699 (6.6)%	48/693 (6.9)%	

The definition of CRBSI required an organism isolated from a peripheral blood draw to be genotypically matched to an organism isolated from the catheter tip. In this study, many catheters were lost and the organisms could be not isolated from the catheter tip. Similarly, many patients were administered systemic antibiotics for suspected bloodstream infections but were given such antibiotics prior to taking a blood draw. As a result, the high rate of indeterminate events was observed, which we believe was a significant factor contributing to the lower than expected rate of CRBSI. In addition, the study enrolled a large number of patients that were at relatively low risk for developing a CRBSI, which we believe further decreased the event rate to a point where, as observed, a statistically significant difference for CRBSI between the two treatment arms could not be detected. We believe that the CRBSI endpoint, as defined in the previous study, is not achievable without a very significant increase the number of patients enrolled.

Only 14 patients (2.0%) in each treatment group had adverse events that were considered drug-related. All of these Omigard adverse events were related to the catheter insertion site, and none were serious. Overall, there were no statistically significant differences between the treatment groups for any safety variable.

Clinical Development Plan

In June 2005, we reached agreement on the clinical development plan for Omigard with the FDA under the FDA's SPA process. The SPA process provides for a formal review and written agreement of clinical protocols that are binding on both the FDA and the company sponsor. Through the SPA process, the FDA agreed that a single confirmatory Phase III trial would be required for approval and that LCSI would be the sole primary efficacy endpoint. Secondary endpoints include catheter colonization and other measures of infection.

The presence of an LCSI will typically result in one of several actions being taken by a physician, including administration of systemic or topical antimicrobials and/or removal and replacement of the catheter. The most serious risks from catheter replacement include bleeding from a damaged artery or puncturing of a lung. Further, the same microorganisms on the skin surface that cause LCSIs can cause

CRBSIs. A published review of clinical trials found that catheter colonization is well correlated to CRBSIs.

We have completed a market research study that indicates physicians only modestly favor (73% vs. 65%) a profile of Omigard that demonstrates a statistically significant prevention in LCSIs, catheter colonization and CRBSIs compared to a profile of Omigard that demonstrates a statistically significant prevention in LCSIs and catheter colonization alone. The FDA has communicated to us that LCSI is a clinically relevant indication and, based on these market research findings, we believe that a product indicated for the prevention of LCSIs is also a highly relevant indication to physicians.

The confirmatory Phase III trial that we are conducting according to the SPA, known as the Central Line Infection Reduction Study, or CLIRS trial, is a multi-center, randomized, evaluation committee-blinded study in patients receiving a CVC. The primary efficacy endpoint of the study is to evaluate whether Omigard is superior to 10% povidone-iodine in the prevention of LCSI in patients requiring central venous catheterization. Secondary objectives of the study are to evaluate whether Omigard is superior to 10% povidone-iodine treatment in preventing significant catheter colonization, CRBSI and all-cause bloodstream infections in patients requiring central venous catheterization.

The CLIRS trial is designed to recruit 1,250 patients randomized to receive either Omigard or 10% povidone-iodine. The study began enrollment in August 2005 and is currently being conducted at centers in the United States and Europe. We expect to complete enrollment and have results available in the second half of 2007. Omigard for the prevention of LCSIs was awarded fast track status by the FDA, and we intend to submit an NDA to the FDA in the first half of 2008.

We also intend to submit an MAA to European regulatory authorities in the first half of 2008. We have met with regulatory authorities in several European countries and believe that no additional clinical trials will be required for submission if the ongoing CLIRS trial is successful.

Additional Indications

We intend to pursue a pediatric indication for Omigard for the prevention of catheter-related infections. As in the adult population, CVCs are frequently used in neonates, infants and children with wide variety of conditions. Pediatric CVCs are a significant source of infectious complications in hospitalized children.

We have rights to develop and commercialize omiganan pentahydrochloride for additional indications related to the prevention and treatment of device-related, surgical wound-related and burn-related infections. We believe that omiganan pentahydrochloride may have significant opportunity in these areas. For example, the CDC estimates there are approximately 500,000 post-operative surgical site infections in the United States annually. The CDC also estimates that there are 50,000 hospitalizations from burn injuries and that 10,000 people will die from burn-related infections in the United States every year.

Commercialization Strategy

We intend to build a commercial organization in the United States focused on promoting our products to physicians, nurses and pharmacy directors principally in the hospital setting. We believe that we can achieve our strategic goals by deploying an experienced sales organization supported by an internal marketing infrastructure that targets institutions with the greatest use of pharmaceutical products. We will consider opportunities to partner our products to reach markets outside the United States or to expand our reach to other physician groups outside the hospital where applicable. In particular, we believe that Omigard is an excellent candidate for partnering in countries outside the United States, and we anticipate launching the product in those countries with a partner who has the resources to be competitive in the hospital market.

For the launch of Omigard in the United States, we intend to build our own commercial organization and estimate that a sales force of approximately 75-100 people will reach the top 1,200

institutions, which we believe represents more than 60% of the market opportunity for the product. Sales calls will primarily target intensive care physicians, infectious disease physicians and infection control physicians and nurses. Other targets will include anesthesiologists, surgeons, intensive care and other nurses in the hospital, and physicians and nurses in outpatient dialysis centers. Key elements in the adoption of Omigard will include formulary acceptance followed by trial and usage and, ultimately, adoption to standing orders and protocols within the hospitals and specific units therein. We expect that Omigard will initially be used in combination with topical antiseptics but ultimately may be used as a stand-alone treatment after more widespread use.

For the launch of IV APAP, we intend to expand the sales force to 150-200 people to reach the top 1,800 to 2,000 institutions, which we believe represents more than 80% of the opportunity for both products. The primary target audience will include anesthesiologists and surgeons. Other targets will include certified registered nurse anesthetists, emergency medicine physicians, obstetricians and other physicians throughout the hospital.

Licensing Agreements

IV APAP Agreement

In March 2006, we in-licensed the patents and the exclusive development and commercialization rights to IV APAP in the United States and Canada from BMS. BMS has sublicensed these rights to us under a license agreement with SCR Pharmatop S.A., or Pharmatop.

As consideration for the license, we paid a $25.0 million up-front fee and may be required to make future milestone payments totaling up to $50.0 million upon the achievement of various milestones related to regulatory or commercial events. We are also obligated to pay a royalty on net sales of the licensed products. We have the right to grant sublicenses to our affiliates.

The term of the IV APAP agreement generally extends on a country-by-country basis until the last licensed patent expires, which is expected to occur in 2022. Either party may terminate the IV APAP agreement upon delivery of written notice if the other party commits a material breach of its obligations and fails to remedy the breach within a specified period or upon the occurrence of specified bankruptcy, reorganization, liquidation or receivership proceedings. In addition, BMS may terminate the IV APAP agreement if we breach, in our capacity as a sublicensee, any provision of the agreement between BMS and Pharmatop. The IV APAP agreement will automatically terminate in the event of a termination of the license agreement between BMS and Pharmatop. We may terminate the IV APAP agreement at any time upon specified written notice to BMS after the occurrence of events of default that relate to our territory and would entitle BMS to terminate the Pharmatop license agreement. The events of default include Pharmatop’s inability to maintain specified claims under listed patents, the marketing by a third party of a parenterally-administered product containing acetaminophen, subject to certain conditions, or a successful third party action that deprives Pharmatop of its rights to specified patents. We may also terminate the IV APAP agreement upon specified written notice after an uncured failure by Pharmatop to perform any of its material obligations under the Pharmatop license agreement with respect to our territory that would permit BMS to terminate the Pharmatop license agreement.

Either BMS or Pharmatop may terminate the license agreement between them upon delivery of written notice after an uncured failure by the other party to perform any of its material obligations under the license agreement. BMS may generally terminate the agreement upon written notice to Pharmatop within a specified period so long as all payments due under the agreement to Pharmatop are current. Pharmatop may terminate the agreement upon specified written notice if BMS opposes any of the listed patent applications or challenges the validity or enforceability of any of the listed licensed patents. BMS is also entitled to terminate the Pharmatop agreement upon the occurrence of events of default that relate to the territory described above.

Omigard Agreement

In July 2004, we in-licensed from Migenix the patents and the exclusive development and commercialization rights to omiganan pentahydrochloride for the prevention and treatment of device-related, surgical wound-related and burn-related infections in North America and Europe.

As consideration for the license, we paid a $2.0 million up-front fee, of which $1.9 million was allocated to the value of the acquired technology and $100,000 was attributed to the acquisition of 617,284 shares of Migenix common stock. We may be required to make future milestone payments totaling up to $27.0 million upon the achievement of various milestones related to regulatory or commercial events. We are also obligated to pay a royalty on net sales of the licensed products. We have the right to grant sublicenses to third parties.

The term of the Omigard agreement generally extends until the last licensed patent expires, which is expected to occur in November 2022. Either party may terminate the Omigard agreement upon specified written notice after the other party commits a material breach of its obligations and fails to remedy the breach or upon the cessation of operations of the other party or occurrence of specified bankruptcy, reorganization, liquidation or receivership proceedings involving the other party. We may terminate the Omigard agreement upon written notice if we determine, prior to regulatory approval in the United States, that the product is not reasonably expected to demonstrate safety or efficacy. We may also terminate the Omigard agreement upon specified written notice after receipt of any interim results or the executive summary following database lock of the on-going Phase III trial for Omigard.

Intellectual Property

IV APAP

We are the exclusive licensee of two U.S. patents and two pending Canadian patent applications from Pharmatop, under BMS's license to these patents from Pharmatop. U.S. Patent No. 6,028,222 (Canadian patent application 2,233,924) covers the formulation of IV APAP and expires in August 2017. U.S. Patent No. 6,992,218 (Canadian patent application 2,415,403) covers the process used to manufacture IV APAP and expires in June 2021.

We have also in-licensed the non-exclusive rights to two U.S. patents from BMS. U.S. Patent No. 6,593,331 covers a method of treating pain with acetaminophen and concurrent administration of a hydroxyazapirone and expires in April 2022. US Patent No. 6,511,982 covers a method of treating pain with acetaminophen and concurrent administration of buspirone and expires in June 2020.

Omigard

We are the exclusive licensee of four U.S. patents, two pending U.S. applications, and their international equivalents in North America and Europe for the prevention and treatment of device-related, surgical wound-related, and burn-related infections. U.S. Patent No. 6,180,604 and U.S. Patent No. 6,538,106 cover composition of matter for certain analogues of indolicidin, including Omigard, and expire in August 2017. U.S. Patent No. 6,503,881 covers composition of matter for additional analogues of indolicidin (not including Omigard), pharmaceutical preparations of certain analogues of indolicidin, including Omigard, and methods of using the pharmaceutical preparations for treating microbial infections (including covering routes of administration). U.S. Patent No. 6,503,881 also expires in August 2017. U.S. Patent No. 6,835,536 covers specific pharmaceutical preparations of certain analogues of indolicidin, including Omigard, and methods of treatment by applying pharmaceutical preparations to a target site, including a target site were a medical device is inserted. U.S. Patent No. 6,835,536 expires in November 2022.

Manufacturing

In February 2006, we entered into a clinical supply agreement with Lawrence Laboratories, an affiliate of BMS, under which Lawrence Laboratories has manufactured clinical supplies of IV APAP and

placebo. Under the terms of the agreement, Lawrence Laboratories is obligated to supply us with this single batch of IV APAP and a single batch of placebo at specified prices. With these batches, we believe we will have adequate clinical supplies of our IV APAP product candidate and placebo. The term of the clinical supply agreement generally extends until the earlier of the receipt by us of regulatory approval for IV APAP or December 31, 2008. In addition, the clinical supply agreement terminates upon mutual written consent of the parties, the termination of the IV APAP agreement or our dissolution. Either party may also terminate the clinical supply agreement upon written notice of an uncured, material breach by the other party. For commercial supply, the active pharmaceutical ingredient, or API, acetaminophen is readily available from multiple suppliers. We are currently negotiating with suppliers for commercial supply of the finished drug product for IV APAP.

We have purchased clinical supplies of the API omiganan pentahydrochloride from UCB Bioproducts, which was recently acquired by Lonza Group, Ltd. We have purchased clinical supplies of the Omigard finished drug product from Cardinal Health, Inc. Lonza and Cardinal have produced the clinical supplies which we are using in our Phase III Omigard program. We are currently negotiating with suppliers for commercial supply of the API and finished drug product for Omigard.

Competition

The pharmaceutical industry is subject to intense competition and characterized by extensive research efforts and rapid technological progress. Competition in our industry occurs on a variety of fronts, including developing and bringing new products to market before others, developing new technologies to improve existing products, developing new products to provide the same benefits as existing products at lower cost and developing new products to provide benefits superior to those of existing products. There are many companies, including generic manufacturers as well as large pharmaceutical companies, that have significantly greater financial and other resources than we do, as well as academic and other research institutions that are engaged in research and development efforts for the indications targeted by our product candidates.

IV APAP

Our IV APAP product candidate is being developed for the treatment of acute pain, usually in the hospital setting. A wide variety of competitive products already address this target market, including:

Injectable opioids

- Morphine is the leading product for the treatment of acute post-operative pain, and is available generically from several manufacturers;
- DepoDur, currently marketed by Endo Pharmaceuticals, is an extended release injectable formulation of morphine; and
- other injectable opioids, including fentanyl, meperidine and hydromorphone, each of which is available generically from several manufacturers.

Injectable NSAIDs

- Ketorolac, an injectable NSAID, is available generically from several manufacturers.

Product Candidates

We are also aware of a number of product candidates in development to treat acute pain, including injectable NSAIDs, novel opioids, new formulations of currently available opioids, long-acting local anesthetics and new chemical entities as well as alternative delivery forms of various opioids and NSAIDs. A variety of pharmaceutical and biotechnology companies are developing these new product candidates, including but not limited to Anesiva, Inc (formerly Corgentech Inc.), CeNeS Pharmaceuticals plc, Cumberland Pharmaceuticals

Inc., Durect Corporation, Javelin Pharmaceuticals, Inc., Pfizer Inc., SkyePharma Inc., St. Charles Pharmaceuticals, TheraQuest Biosciences, LLC and Xsira Pharmaceuticals, Inc.

Omigard

We are developing our Omigard product candidate for the prevention of intravascular catheter-related infections. Although there are no approved drugs for this specific indication, a number of topical products are currently used in practice and one device has been approved for wound dressing and prevention of catheter-related infections. These competitive products include:

- topical antiseptics such as povidone-iodine and chlorhexidine, each of which is available generically from several manufacturers;
- Neosporin, a topical antibacterial ointment containing polymyxin, neomycin and bacitracin, available generically from several manufacturers;
- Bactroban, a topical antibacterial containing mupirocin, available generically from several manufacturers; and
- BioPatch, a chlorhexidine-impregnated foam dressing, from Johnson & Johnson that is approved both for wound dressing and the prevention of catheter-related infections.

Other products may be in development; however, we are not aware of any other topical drugs being developed for the prevention of intravascular catheter-related infections.

Government Regulation

Governmental authorities in the United States and other countries extensively regulate the testing, manufacturing, labeling, storage, record-keeping, advertising, promotion, export, marketing and distribution, among other things, of pharmaceutical products. In the United States, the FDA, under the Federal Food, Drug and Cosmetic Act and other federal statutes and regulations, subjects pharmaceutical products to rigorous review. If we do not comply with applicable requirements, we may be fined, the government may refuse to approve our marketing applications or allow us to manufacture or market our products, and we may be criminally prosecuted.

We and our manufacturers and clinical research organizations may also be subject to regulations under other federal, state and local laws, including the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act and import, export and customs regulations as well as the laws and regulations of other countries.

FDA Approval Process

To obtain approval of a new product from the FDA, we must, among other requirements, submit data supporting safety and efficacy as well as detailed information on the manufacture and composition of the product and proposed labeling. The testing and collection of data and the preparation of necessary applications are expensive and time-consuming. The FDA may not act quickly or favorably in reviewing these applications, and we may encounter significant difficulties or costs in our efforts to obtain FDA approvals that could delay or preclude us from marketing our products.

The process required by the FDA before a new drug may be marketed in the United States generally involves the following: completion of preclinical laboratory and animal testing in compliance with FDA regulations, submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin, performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use, and submission and approval of an NDA by the FDA. The sponsor typically conducts human clinical trials in three sequential phases, but the phases may overlap. In Phase I clinical trials, the product is tested in a small number of patients or healthy volunteers, primarily for safety at one or more dosages. In Phase II clinical trials, in addition to safety, the sponsor evaluates the efficacy of the product on targeted indications, and

identifies possible adverse effects and safety risks in a patient population. Phase III clinical trials typically involve testing for safety and clinical efficacy in an expanded population at geographically-dispersed test sites.

Clinical trials must be conducted in accordance with the FDA's good clinical practices requirements. The FDA may order the partial, temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The institutional review board, or IRB, generally must approve the clinical trial design and patient informed consent at each clinical site and may also require the clinical trial at that site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

The applicant must submit to the FDA the results of the preclinical and clinical trials, together with, among other things, detailed information on the manufacture and composition of the product and proposed labeling, in the form of an NDA, including payment of a user fee. The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has 10 months in which to complete its initial review of a standard NDA and respond to the applicant. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months of the PDUFA goal date. If the FDA's evaluations of the NDA and the clinical and manufacturing procedures and facilities are favorable, the FDA may issue either an approval letter or an approvable letter, which contains the conditions that must be met in order to secure final approval of the NDA. If and when those conditions have been met to the FDA's satisfaction, the FDA will issue an approval letter, authorizing commercial marketing of the drug for certain indications. According to the FDA, the median total approval time for NDAs approved during calendar year 2004 was approximately 13 months for standard applications. If the FDA's evaluation of the NDA submission and the clinical and manufacturing procedures and facilities is not favorable, the FDA may refuse to approve the NDA and issue a not approvable letter.

Special Protocol Assessment Process

The special protocol assessment, or SPA, process provides for official FDA evaluation of a proposed Phase III clinical trial protocol and generally provides a product sponsor with a binding agreement from the FDA that the design and analysis of the trial are adequate to support a license application submission if the trial is performed according to the SPA. The FDA's guidance on the SPA process indicates that SPAs are designed to evaluate individual clinical trial protocols primarily in response to specific questions posed by the sponsors. In practice, the sponsor of a product candidate may request an SPA for proposed Phase III trial objectives, designs, clinical endpoints and analyses. A request for an SPA is submitted in the form of a separate amendment to an IND, and the FDA's evaluation generally will be completed within a 45-day review period under applicable PDUFA goals, provided that the trials have been the subject of discussion at an end-of-Phase II and pre-Phase III meeting with the FDA, or in other limited cases. All agreements and disagreements between the FDA and the sponsor regarding an SPA, including the FDA's responses to questions about protocol design, primary efficacy endpoints, study conduct, data analysis and prospective labeling statements must be documented in writing. In limited circumstances, the FDA may agree that a specific finding, such as a particular p-value on the primary efficacy endpoint of a study, will satisfy a specific objective, such as demonstration of efficacy, or support an approval decision. However, final determinations by the FDA are made after a complete review of the applicable NDA and are based on the entire data in the application, and any SPA is subject to future public health concerns unrecognized at the time of protocol assessment.

Section 505(b)(2) New Drug Applications

As an alternate path to FDA approval for new indications or improved formulations of previously-approved products, a company may file a Section 505(b)(2) NDA, instead of a "stand-alone" or "full" NDA. Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, otherwise known as the Hatch-Waxman Amendments. Section 505(b)(2) permits the submission of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. For example, the Hatch-Waxman Amendments permit the applicant to rely upon the FDA's findings of safety and effectiveness for an approved product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new formulation for all or some of the label indications for which the referenced product has been approved, or the new indication sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on the FDA's findings for an already-approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book publication. Specifically, the applicant must certify that: (1) the required patent information has not been filed; (2) the listed patent has expired; (3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patent is invalid or will not be infringed by the manufacture, use or sale of the new product. A certification that the new product will not infringe the already approved product's Orange Book-listed patents or that such patents are invalid is called a paragraph IV certification. If the applicant does not challenge the listed patents, the Section 505(b)(2) application will not be approved until all the listed patents claiming the referenced product have expired. The Section 505(b)(2) application may also not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired.

If the applicant has provided a paragraph IV certification to the FDA, the applicant must also send notice of the paragraph IV certification to the NDA and patent holders once the NDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a legal challenge to the paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of their receipt of a paragraph IV certification automatically prevents the FDA from approving the Section 505(b)(2) NDA until the earliest of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant. For drugs with five-year exclusivity, if an action for patent infringement is initiated after year four of that exclusivity period, then the 30-month stay period is extended by such amount of time so that 7.5 years has elapsed since the approval of the NDA with five-year exclusivity. This period could be extended by six months if the NDA sponsor obtains pediatric exclusivity. Thus, the Section 505(b)(2) applicant may invest a significant amount of time and expense in the development of its products only to be subject to significant delay and patent litigation before its products may be commercialized. Alternatively, if the listed patent holder does not file a patent infringement lawsuit within the required 45-day period, the applicant's NDA will not be subject to the 30-month stay.

Notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(2), over the last few years, certain brand-name pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2) and one pharmaceutical company has sued the FDA on the matter. Although the issues in that litigation are specific to the products involved, if the FDA does not prevail, it may be required to change its interpretation of Section 505(b)(2), which could delay or even prevent the FDA from approving any Section 505(b)(2) NDA that we submit.

Fast Track Designation

A drug designated as a fast track product by the FDA must be intended for the treatment of a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the

condition. Fast track designation does not apply to a product alone, but applies to a combination of the product and specific indication for which it is being studied. A sponsor may submit a request for fast track designation at the time of original submission of its IND, or at any time thereafter prior to receiving marketing approval of its NDA. Fast track status enables the sponsor to have more frequent and timely communication and meetings with the FDA regarding the product development plans. Fast track status may also result in eligibility for NDA priority review, under which the PDUFA review goal for the NDA is six months rather than ten months.

The Hatch-Waxman Act

Under the Hatch-Waxman Act, newly-approved drugs and indications benefit from a statutory period of non-patent marketing exclusivity. The Hatch-Waxman Act provides five-year marketing exclusivity to the first applicant to gain approval of an NDA for a new chemical entity, meaning that the FDA has not previously approved any other new drug containing the same active moiety. Hatch-Waxman prohibits the submission of an abbreviated new drug application, or ANDA, or a Section 505(b)(2) NDA for another version of such drug during the five-year exclusive period; however, as explained above, submission of an ANDA or Section 505(b)(2) NDA containing a paragraph IV certification is permitted after four years, which may trigger a 30-month stay of approval of the ANDA or Section 505(b)(2) NDA. Protection under Hatch-Waxman will not prevent the submission or approval of another full NDA; however, the applicant would be required to conduct its own preclinical and adequate and well-controlled clinical trials to demonstrate safety and effectiveness. The Hatch-Waxman Act also provides three years of marketing exclusivity for the approval of new and supplemental NDAs, including Section 505(b)(2) NDAs, for, among other things, new indications, dosages or strengths of an existing drug, if new clinical investigations that were conducted or sponsored by the applicant are essential to the approval of the application.

Other Regulatory Requirements

We may also be subject to a number of post-approval regulatory requirements. If we seek to make certain changes to an approved product, such as promoting or labeling a product for a new indication, making certain manufacturing changes or product enhancements or adding labeling claims, we will need FDA review and approval before the change can be implemented. While physicians may use products for indications that have not been approved by the FDA, we may not label or promote the product for an indication that has not been approved. Securing FDA approval for new indications or product enhancements and, in some cases, for manufacturing and labeling claims, is generally a time-consuming and expensive process that may require us to conduct clinical trials under the FDA's IND regulations. Even if such studies are conducted, the FDA may not approve any change in a timely fashion, or at all. In addition, adverse experiences associated with use of the products must be reported to the FDA, and FDA rules govern how we can label, advertise or otherwise commercialize our products.

There are current post-marketing safety surveillance requirements that we will need to meet to continue to market an approved product. The FDA also may, in its discretion, require post-marketing testing and surveillance to monitor the effects of approved products or place conditions on any approvals that could restrict the commercial applications of these products.

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal health care program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any health care item or service reimbursable under Medicare, Medicaid or other federally financed health care programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal health care programs.

Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other health care companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

In addition, we and the manufacturers on which we rely for the manufacture of our products are subject to requirements that drugs be manufactured, packaged and labeled in conformity with current good manufacturing practice, or cGMP. To comply with cGMP requirements, manufacturers must continue to spend time, money and effort to meet requirements relating to personnel, facilities, equipment, production and process, labeling and packaging, quality control, record-keeping and other requirements. The FDA periodically inspects drug manufacturing facilities to evaluate compliance with cGMP requirements.

Also, as part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. This practice is regulated by the FDA and other governmental authorities, including, in particular, requirements concerning record-keeping and control procedures.

Outside of the United States, our ability to market our products will also depend on receiving marketing authorizations from the appropriate regulatory authorities. The foreign regulatory approval process includes all of the risks associated with the FDA approval process described above. The requirements governing the conduct of clinical trials and marketing authorization vary widely from country to country.

Third-Party Reimbursement and Pricing Controls

In the United States and elsewhere, sales of pharmaceutical products depend in significant part on the availability of coverage and reimbursement to providers and the consumer from third-party payors, such as government and private insurance plans. Third-party payors are increasingly challenging the prices charged for medical products and services. Our products may not be considered cost effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

In many foreign markets, including the countries in the European Union, pricing of pharmaceutical products is subject to governmental control. In the United States, there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental pricing control. While we cannot predict whether such legislative or regulatory proposals will be adopted, the adoption of such proposals could have a material adverse effect on our business, financial condition and profitability.

Employees

As of June 30, 2006, we had 24 employees, consisting of clinical development, regulatory affairs, manufacturing and program management, administration, business development and marketing. We consider our relations with our employees to be good.

Facilities

We lease approximately 5,928 square feet of space in our headquarters in San Diego, California under a sublease that expired in September 2006. We have entered into a lease that expires in 2012 for approximately 23,494 square feet of space for our new headquarters in San Diego, California which we intend to occupy in September 2006. We intend to sublease approximately 5,800 square feet of our new headquarters for a period of two years. We have no laboratory, research or manufacturing facilities. We believe that our current facilities are adequate for our needs for the immediate future and that, should it be needed, suitable additional space will be available to accommodate expansion of our operations on commercially reasonable terms.

Legal Proceedings

We are not engaged in any legal proceedings.

MANAGEMENT

Executive Officers and Directors

The following table sets forth certain information about our executive officers and directors as of August 31, 2006:

Name	Age	Position
Theodore R. Schroeder	51	President, Chief Executive Officer and Director
James B. Breitmeyer, M.D., Ph.D.	52	Executive Vice President, Development and Chief Medical Officer
William S. Craig, Ph.D.	56	Senior Vice President, Pharmaceutical Development and Manufacturing
Kenneth R. Heilbrunn, M.D.	48	Senior Vice President, Clinical Development
William R. LaRue	55	Senior Vice President, Chief Financial Officer, Treasurer and Secretary
Richard E. Lowenthal	40	Vice President, Regulatory Affairs and Quality Assurance
Mike A. Royal, M.D., J.D.	53	Vice President, Clinical Development, Analgesics
David A. Socks	32	Vice President, Business Development
Cam L. Garner(1)	58	Chairman of the Board of Directors
Brian G. Atwood(2)	53	Director
Samuel L. Barker, Ph.D.	63	Director
Michael A. Berman, M.D.(2)(3)	63	Director
James C. Blair, Ph.D.(1)	67	Director
Alan D. Frazier(1)(3)	55	Director
Alain B. Schreiber, M.D.(2)	51	Director
Christopher J. Twomey(3)	47	Director

(1) Member of the Compensation Committee.
(2) Member of the Nominating/ Corporate Governance Committee.
(3) Member of the Audit Committee.

Executive Officers

Theodore R. Schroeder is one of our co-founders and has served as our President and Chief Executive Officer and as a member of our board of directors since our inception in May 2004. From August 2002 to February 2004, he served as Senior Vice President of North America Sales and Marketing of Elan Pharmaceuticals, Inc., a neuroscience-based pharmaceutical company. From February 2001 to August 2002, Mr. Schroeder served as General Manager of the Hospital Products Business Unit at Elan, a position he also held at Dura Pharmaceuticals, Inc., a specialty respiratory pharmaceutical and pulmonary drug delivery company, from May 1999 to November 2000 until its acquisition by Elan. Prior to joining Dura, Mr. Schroeder held a number of hospital-related sales and marketing positions with Bristol-Myers Squibb Company, a global pharmaceutical company. Mr. Schroeder holds a B.S. in management from Rutgers University.

James B. Breitmeyer, M.D., Ph.D. has served as our Executive Vice President, Development and Chief Medical Officer since August 2006. From December 2001 to August 2006, Dr. Breitmeyer served as Chief Medical Officer and Vice President, Pharmaceutical Operations of Applied Molecular Evolution, a wholly-owned subsidiary of Eli Lilly and Company, a global pharmaceutical company. From February 2000 to July 2001, Dr. Breitmeyer was the President and Chief Executive Officer of the Harvard Clinical

Research Institute. Prior to February 2000, Dr. Breitmeyer held various positions of increasing responsibility including Senior Vice President and Chief Medical Officer of Serono International S.A., a global biopharmaceutical company. Dr. Breitmeyer holds a B.A. in chemistry from the University of California, Santa Cruz, and an M.D. and Ph.D. from Washington University School of Medicine.

William S. Craig, Ph.D. has served as our Senior Vice President, Pharmaceutical Development and Manufacturing since November 2004. From January 2000 to November 2004, Dr. Craig served as Vice President, Research and Product Development of ISTA Pharmaceuticals, Inc., an ophthalmology-focused specialty pharmaceutical company. From 1996 to December 1999, Dr. Craig served as Vice President, Research and Development for Alpha Therapeutics Corporation, a biotechnology company. From 1988 to 1996, he served as Senior Director, Research and Development for Telios Pharmaceuticals, Inc., a biotechnology company. Dr. Craig holds a B.S. in biochemistry from the University of Michigan and a Ph.D. in chemistry from the University of California, San Diego.

Kenneth R. Heilbrunn, M.D. has served as our Senior Vice President, Clinical Development since April 2005. Dr. Heilbrunn has provided us with notice of his resignation effective September 30, 2006. From May 2002 to April 2005, Dr. Heilbrunn served as Vice President of Clinical Development of La Jolla Pharmaceutical Company, an autoimmune disease-focused biopharmaceutical company. From 1998 to April 2002, he held several positions, the most recent of which was Vice President of Clinical Research, at Advanced Tissue Sciences, Inc., a tissue engineering company, where he was responsible for a multicenter Phase III clinical trial which ultimately led to the FDA approval of Dermagraft, a bioengineered human tissue. From 1997 to 1998, Dr. Heilbrunn served as Vice President of Medical Affairs at Hepatix, Inc., a company engaged in the development of a bioengineered liver. From 1994 to 1996, he served as Staff Vice President of Medical Affairs at C.R. Bard, Inc., a manufacturer of healthcare products. From 1989 to 1994, he held several positions in the Medical Affairs department of Ciba-Geigy Pharmaceuticals Division, a pharmaceutical company, the most recent of which was Director for Cardiovascular and Pulmonary Drugs, where he participated in the launch of the nicotine patch, Habitrol, and the antihypertensive drug, Lotensin. From 1986 to 1989, Dr. Heilbrunn served as Staff Internist and, ultimately, Director of the Critical Care unit at the 31st Tactical Air Force Hospital in Homestead, Florida. Dr. Heilbrunn received a B.A. from Brown University and an M.D. from New York Medical College.

William R. LaRue has served as our Senior Vice President, Chief Financial Officer, Treasurer and Secretary since June 2006. From April 2001 to May 2006, Mr. LaRue served as Senior Vice President and Chief Financial Officer of Micromet, Inc., formerly CancerVax Corporation, a biotechnology company focused on the treatment and control of cancer. From March 2000 to February 2001, Mr. LaRue served as Executive Vice President and Chief Financial Officer of eHelp Corporation, a provider of user assistance software. From January 1997 to February 2000, Mr. LaRue served as Vice President and Treasurer of Safeskin Corporation, a medical device company, and from January 1993 to January 1997 he served as Treasurer of GDE Systems, Inc., a high technology electronic systems company. Mr. LaRue received a B.S. in business administration and an M.B.A. from the University of Southern California.

Richard E. Lowenthal has served as our Vice President, Regulatory Affairs and Quality Assurance since November 2004. From November 2002 to November 2004, Mr. Lowenthal served as Senior Director, Worldwide Regulatory Affairs and Drug Safety of Maxim Pharmaceuticals, Inc., a biopharmaceutical company. From December 2001 to November 2002, he served as Vice President of Regulatory Affairs and Quality Assurance of AnGes, MG, Inc., a biopharmaceutical company. From June 1996 to December 2001, Mr. Lowenthal served in various roles in regulatory affairs at Janssen Research Foundation, a division of Johnson & Johnson, most recently as the Global Director of Chemistry, Manufacturing and Control Regulatory Affairs. Prior to joining Janssen, he served as the Director of Regulatory Affairs and Quality Assurance of Somerset Pharmaceuticals, Inc., a proprietary research and development pharmaceutical company. Mr. Lowenthal holds a B.S. in biochemistry and a M.S. in organic chemistry from Florida State University.

Mike A. Royal, M.D., J.D. has served as our Vice President, Clinical Development, Analgesics since April 2006. From December 2004 to March 2006, Dr. Royal served as Chief Medical Officer of Solstice Neurosciences, Inc., a specialty biopharmaceutical company. From May 2003 to December 2004, Dr. Royal served as Vice President, Strategic Brand Development and Global Medical Affairs of Alpharma Inc., a global specialty pharmaceutical company. From January 2002 to May 2003, he served as Senior Medical Director of Elan Pharmaceuticals, Inc., a neuroscience-based biotechnology company. From 1994 to January 2002, he owned and managed the largest private practice pain management clinic and research center in Oklahoma. Dr. Royal has also served as Director of the Acute Pain Service, Staff Anesthesiologist, and Assistant Professor of Anesthesiology and Critical Care Medicine at the University of Pittsburgh Medical Center. Dr. Royal is board certified in internal medicine, anesthesiology, pain management, and addiction medicine and has published extensively in the area of pain management. He holds a B.S. in chemistry from the Massachusetts Institute of Technology, an M.D. from the University of Massachusetts, a J.D. from the University of Maryland and an M.B.A. from New York University (TRIUM).

David A. Socks is one of our co-founders and has served as our Vice President, Business Development since our inception in May 2004. From May 2004 to June 2006, Mr. Socks also served as our Chief Financial Officer, Treasurer, and Secretary. From July 2000 to May 2004, Mr. Socks was a Venture Partner at Windamere Venture Partners, a venture capital firm investing in early stage life science companies. In this capacity, Mr. Socks held management positions at two portfolio companies of Windamere Venture Partners. These positions included Vice President of Business Development of Kanisa Pharmaceuticals, Inc., an oncology-focused specialty pharmaceutical company and Vice President of Finance of CelTor Biosystems, Inc., a drug discovery company. Mr. Socks co-founded several pharmaceutical companies including Avera Pharmaceuticals, Inc., Kanisa Pharmaceuticals, Inc., Somaxon Pharmaceuticals, Inc. and Verus Pharmaceuticals, Inc. and two medical technology companies including MiraMedica, Inc. and SpineWave, Inc. In 1999, Mr. Socks worked in business development at Neurocrine Biosciences, a biopharmaceutical company. In 1998, he worked in the venture capital arm of EFO Holdings, L.P., an investment firm. From 1995 to 1998, he worked at Kaiser Associates, Inc., a strategic management consulting firm, where he was most recently a Senior Manager. Mr. Socks holds a B.S. in business administration from Georgetown University and an M.B.A. from Stanford University.

Board of Directors

Cam L. Garner is one of our co-founders and has served as a member of our board of directors since our inception in May 2004, and as the chairman of our board of directors since July 2004. Mr. Garner co-founded Verus Pharmaceuticals, Inc., Somaxon Pharmaceuticals, Inc. and Xcel Pharmaceuticals, Inc., which are specialty pharmaceutical companies. Since July 2004, he has served as Chairman and Chief Executive Officer of Verus. He served as Chairman of Xcel Pharmaceuticals, Inc. from January 2001 until it was acquired in March 2005 by Valeant Pharmaceuticals International. From August 2001 to February 2002, he served as acting Chief Executive Officer of Favrille, Inc., a biotechnology company, and is currently the Chairman of its board of directors. From 1989 to 1995, he served as Chief Executive Officer of Dura Pharmaceuticals, Inc., a specialty respiratory pharmaceutical and pulmonary drug delivery company, and Chairman and Chief Executive Officer from 1995 to 2000 until it was sold to Elan in November 2000. Previously, he served as Chairman of DJ Pharma, a specialty pharmaceutical sales and marketing company, which was sold to Biovail Corporation in 2000. Mr. Garner also serves on the board of directors of two publicly-held companies — Somaxon Pharmaceuticals, Inc. and Pharmion Corporation — and other privately-held pharmaceutical companies. In addition, Mr. Garner participates on the boards of several charitable organizations. Mr. Garner holds a B.A. in biology and an M.B.A. from Baldwin-Wallace College and an honorary Doctor of Science from Virginia Wesleyan College.

Brian G. Atwood has served as a member of our board of directors since March 2006. Since 1999, Mr. Atwood has served as a Managing Director of Versant Ventures I, LLC, Versant Ventures II, LLC and Versant Ventures III, LLC (Versant Ventures), a venture capital firm focusing on healthcare that he

co-founded. Prior to founding Versant Ventures, Mr. Atwood served as a general partner of Brentwood Associates, a venture capital firm. Mr. Atwood also serves on the board of directors of Pharmion Corporation, ForteBio, FivePrime Therapeutics, Inc., Saegis Pharmaceuticals, Helicos Biosciences Corp. and Spaltudaq Corporation. Mr. Atwood holds a B.S. in biological sciences from the University of California, Irvine, an M.S. in ecology from the University of California, Davis and an M.B.A. from Harvard University.

Samuel L. Barker, Ph.D. has served as a member of our board of directors since August 2006. In March 2001, Dr. Barker co-founded Clearview Projects, Inc., a provider of partnering and transaction services to biopharmaceutical companies, and has served as a principal since that time. Dr. Barker also served as President and Chief Executive Officer of Clearview Projects from July 2003 to November 2004. Dr. Barker served in a series of leadership positions at Bristol-Myers Squibb Company until his retirement in 1999. His positions at Bristol-Myers Squibb included service as Executive Vice President, Worldwide Franchise Management and Strategy during 1998, President, United States Pharmaceuticals from 1992 to 1997, and President, Bristol-Myers Squibb Intercontinental Commercial Operations from 1990 to 1992. Prior to 1990, Dr. Barker held executive positions in research and development, manufacturing, finance, business development and sales and marketing at Squibb Pharmaceuticals. Dr. Barker also serves on the board of directors of AtheroGenics, Inc., a pharmaceutical company, and Lexicon Genetics Incorporated, a biopharmaceutical company, where he serves as chairman. Dr. Barker holds a B.S. from Henderson State College, an M.S. from the University of Arkansas and a Ph.D. from Purdue University.

Michael A. Berman, M.D. has served as a member of our board of directors since April 2006. Since January 2005, Dr. Berman has served as President and Chief Executive Officer of the Michael A. Berman Group, Inc., a consulting firm specializing in the healthcare industry. Since January 2005, Dr. Berman has also served as a consultant for Stockamp and Associates, Inc., a business process consulting firm specializing in the healthcare industry. From October 1999 to January 2005, Dr. Berman served as Executive Vice President and Director of New York Presbyterian Hospital, and from September 1997 to October 1999 as its Senior Vice President and Chief Medical Officer. From April 1984 to September 1997, he served as Professor and Chairman of the Department of Pediatrics at the University of Maryland School of Medicine. Dr. Berman holds a M.D. from the State University of New York, Syracuse.

James C. Blair, Ph.D. has served as a member of our board of directors since September 2005. Since 1985, Mr. Blair has been a partner of Domain Associates, L.L.C., a venture capital management company focused on life sciences. Mr. Blair also serves on the board of directors of Cell Biosciences, Inc., Five Prime Therapeutics, Inc., GenVault Corporation, NeuroPace, Inc., Novacea, Inc., NuVasive, Inc., Pharmion Corporation, Verus Pharmaceuticals, Inc. and Volcano Corporation. Mr. Blair has over 35 years experience with venture and emerging growth companies. In the course of this experience, he has been involved in the creation and successful development at the board level of over forty life science ventures, including Amgen Inc., Aurora Biosciences Corporation, Amylin Pharmaceuticals, Inc., Applied Biosystems Inc., Dura Pharmaceuticals, GeneOhm Sciences, Inc. and Molecular Dynamics Inc. A former managing director of Rothschild Inc., Mr. Blair was directly involved at a senior level with Rothschild/ New Court venture capital activities from 1978 to 1985. From 1969 to 1978, he was associated with F.S. Smithers and Co. and White, Weld and Co., two investment banking firms actively involved with new ventures and emerging growth companies. From 1961 to 1969, Mr. Blair was an engineering manager with RCA Corporation, during which time he received a David Sarnoff Fellowship. He currently serves on the board of directors of the Prostate Cancer Foundation, a philanthropic organization, and he is on the advisory boards of the Department of Molecular Biology at Princeton University and the Department of Biomedical Engineering at the University of Pennsylvania. Mr. Blair holds a B.S.E. from Princeton University and an M.S.E. and Ph.D. from the University of Pennsylvania.

Alan D. Frazier has served as a member of our board of directors since March 2006. In 1991, Mr. Frazier founded Frazier Healthcare Ventures, a venture capital firm, and has served as the managing partner since its inception. From 1983 to 1991, Mr. Frazier served as Executive Vice President, Chief Financial Officer and Treasurer of Immunex Corporation, a biopharmaceutical company. From 1980 to

1983, Mr. Frazier was a principal in the Audit Department of Arthur Young & Company, which is now Ernst & Young LLP. Mr. Frazier is a member of the board of directors of Alexza Pharmaceuticals, Inc. and Rigel Pharmaceuticals, Inc., both of which are pharmaceutical companies. Mr. Frazier received a B.A. in economics from the University of Washington.

Alain B. Schreiber, M.D. has served as a member of our board of directors since July 2004. Since 2000, Dr. Schreiber has been a General Partner of ProQuest Investments, a venture capital firm. From May 1992 to June 2000, Dr. Schreiber served as President, Chief Executive Officer and a director of Vical Incorporated, a biopharmaceutical company. From July 1985 to April 1992, he held various positions with Rhone-Poulenc Rorer Inc., which is now Sanofi-Aventis, most recently as Senior Vice President of Discovery Research. From October 1982 to June 1985, Dr. Schreiber served as Biochemistry Department Head at Syntex Research, which is now Roche Bioscience. Dr. Schreiber currently serves on the board of several privately held companies including BioRexis Pharmaceutical Corporation, Concentric Medical, Inc. and Optimer Pharmaceuticals, Inc. Dr. Schreiber holds a B.S. in chemistry and an M.D. from the Free University in Brussels, Belgium.

Christopher J. Twomey has served as a member of our board of directors since July 2006. Mr. Twomey joined Biosite Incorporated, a medical diagnostic company, in March 1990 and is currently its Senior Vice President, Finance and Chief Financial Officer. From 1981 to 1990, Mr. Twomey worked for Ernst & Young LLP, where he served as an Audit Manager. Mr. Twomey also serves on the board of directors of Senomyx, Inc., a biotechnology company, where he serves as Chair of the Audit Committee. Mr. Twomey holds a B.A. in business economics from the University of California at Santa Barbara.

Board Composition

Our board of directors is currently authorized to have eight members, and is currently composed of seven non-employee members and our current President and Chief Executive Officer, Theodore R. Schroeder. Upon completion of this offering, our amended and restated certificate of incorporation will provide for a classified board of directors consisting of three classes of directors, each serving staggered three-year terms. As a result, a portion of our board of directors will be elected each year. To implement the classified structure, prior to the consummation of this offering, two of the nominees to the board will be appointed to one-year terms, three will be appointed to two-year terms and three will be appointed to three-year terms. Thereafter, directors will be elected for three-year terms. Our Class I directors, whose terms will expire at the 2007 annual meeting of stockholders, will be Drs. Berman and Schreiber and Mr. Schroeder. Our Class II directors, whose terms will expire at the 2008 annual meeting of stockholders, will be Dr. Blair and Messrs. Frazier and Twomey. Our Class III directors, whose terms will expire at the 2009 annual meeting of stockholders, will be Dr. Barker and Messrs. Atwood and Garner.

Pursuant to a voting agreement originally entered into in July 2004 and most recently amended in August 2006 by and among us and certain of our stockholders, Drs. Barker, Berman, Blair and Schreiber and Messrs. Atwood, Frazier, Garner, Schroeder and Twomey were each elected to serve as members on our board of directors and, as of the date of this prospectus, continue to so serve. The voting agreement will terminate upon completion of this offering, and members previously elected to our board of directors pursuant to this agreement will continue to serve as directors until their successors are duly elected by holders of our common stock. For a more complete description of the voting agreement, see “Certain Relationships and Related Party Transactions — Voting Agreement.”

Board Committees

Our board of directors has established three committees: the audit committee, the compensation committee and the nominating/corporate governance committee. Our board of directors may establish other committees to facilitate the management of our business.

Audit Committee. Our audit committee consists of Messrs. Twomey (chair and audit committee financial expert) and Frazier and Dr. Berman, each of whom our board of directors has determined is

independent within the meaning of the independent director standards of the SEC and the Nasdaq Stock Market, Inc.

This committee's main function is to oversee our accounting and financial reporting processes, internal systems of control, independent registered public accounting firm relationships and the audits of our financial statements. This committee's responsibilities include:

- selecting and hiring our independent registered public accounting firm;
- evaluating the qualifications, independence and performance of our independent registered public accounting firm;
- approving the audit and non-audit services to be performed by our independent registered public accounting firm;
- reviewing the design, implementation, adequacy and effectiveness of our internal controls and our critical accounting policies;
- overseeing and monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to financial statements or accounting matters;
- reviewing with management and our auditors any earnings announcements and other public announcements regarding our results of operations;
- preparing the report that the SEC requires in our annual proxy statement; and
- reviewing and approving any related party transactions and reviewing and monitoring compliance with our code of conduct and ethics.

Compensation Committee. Our compensation committee consists of Messrs. Garner (chair) and Frazier and Dr. Blair, each of whom our board of directors has determined is independent within the meaning of the independent director standards of the Nasdaq Stock Market, Inc. This committee's purpose is to assist our board of directors in determining the development plans and compensation for our senior management and directors and recommend these plans to our board. This committee's responsibilities include:

- reviewing and recommending compensation and benefit plans for our executive officers and compensation policies for members of our board of directors and board committees;
- reviewing the terms of offer letters and employment agreements and arrangements with our officers;
- setting performance goals for our officers and reviewing their performance against these goals;
- evaluating the competitiveness of our executive compensation plans and periodically reviewing executive succession plans; and
- preparing the report that the SEC requires in our annual proxy statement.

Nominating/ Corporate Governance Committee. Our nominating/corporate governance committee consists of Mr. Atwood (chair) and Drs. Berman and Schreiber, each of whom our board of directors has determined is independent within the meaning of the independent director standards of the Nasdaq Stock Market, Inc. This committee's purpose is to assist our board by identifying individuals qualified to become members of our board of directors, consistent with criteria set by our board, and to develop our corporate governance principles. This committee's responsibilities include:

- evaluating the composition, size and governance of our board of directors and its committees and making recommendations regarding future planning and the appointment of directors to our committees;

- administering a policy for considering stockholder nominees for election to our board of directors;
- evaluating and recommending candidates for election to our board of directors;
- overseeing our board of directors' performance and self-evaluation process; and
- reviewing our corporate governance principles and providing recommendations to the board regarding possible changes.

Compensation Committee Interlocks and Insider Participation

Prior to establishing the compensation committee, our board of directors as a whole performed the functions delegated to the compensation committee. None of the members of our compensation committee has ever been one of our officers or employees. None of our executive officers currently serves, or has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

Director Compensation

From September 2004 through August 2005, we paid Mr. Garner $5,000 per month plus qualified business expenses for his services as chairman of our board of directors under the terms of a consulting agreement between us and a limited liability company affiliated with Mr. Garner. The agreement expired on August 31, 2005. From September 2005 to February 2006, we continued to pay Mr. Garner $5,000 per month for his services as chairman of our board of directors. In February 2006, Mr. Garner's monthly compensation for his services as chairman of our board of directors was increased to $8,333 per month.

Other than to Mr. Garner, we have historically not provided cash compensation to directors for their services as directors or members of committees of the board of directors. Following the completion of this offering, we intend to provide cash compensation in the form of an annual retainer of $25,000 for each non-employee director. We will also pay an additional annual retainer to the non-employee director serving as (i) the chairman of our Audit Committee equal to $10,000, and (ii) the chairman of our Compensation Committee or our Nominating/ Corporate Governance Committee equal to $4,000. We will pay an additional annual retainer to non-employee directors (other than the chairman) serving on the Audit Committee equal to $5,000 and to non-employee directors (other than the chairman) serving on the Compensation Committee or the Nominating/Corporate Governance Committee equal to $2,000. We will pay additional cash compensation to the non-employee director serving as the chairman of our board of directors equal to $100,000 per year. We have reimbursed and will continue to reimburse our non-employee directors for their reasonable expenses incurred in attending meetings of our board of directors and committees of the board of directors.

Following the completion of this offering, any non-employee director who is first elected to the board of directors will be granted a non-qualified option to purchase 25,000 shares of our common stock (subject to adjustment as provided in the 2006 plan described below) on the date of his or her initial election to the board of directors. Such options will have an exercise price per share equal to the fair market value of our common stock on the date of grant. In addition, on the date of each annual meeting of our stockholders following this offering, each non-employee director will be eligible to receive a non-qualified option to purchase 12,500 shares of common stock (subject to adjustment as provided in the 2006 plan described below).

The initial options granted to non-employee directors described above will vest in thirty-six (36) equal monthly installments on the first day of each calendar month subsequent to the date of grant, subject to the director's continuing service on our board of directors on those dates. The annual options granted to non-employee directors described above will vest in twelve equal monthly installments on the first day of each calendar month following the date of grant, subject to the director's continuing service on our board of directors on those dates. The term of each option granted to a non-employee director shall be

ten years. The terms of these options are described in more detail under "— Employee Benefit and Stock Plans."

Executive Compensation

The following table summarizes the compensation that we paid to our Chief Executive Officer and each of our four other most highly compensated executive officers during the year ended December 31, 2005. We refer to these officers in this prospectus as our named executive officers.

Summary Compensation Table

	Annual Compensation			Long-Term Compensation	
Name and Principal Position	Salary	Bonus	Other Annual Compensation	Securities Underlying Options	All Other Compensation
Named Executive Officers					
Theodore R. Schroeder *President and Chief Executive Officer*	$ 250,000	$ 30,000	—	250,000	—
Richard E. Lowenthal *Vice President, Regulatory Affairs and Quality Assurance*	220,000	25,430	—	564,000	—
William S. Craig, Ph.D. *Senior Vice President, Pharmaceutical Development and Manufacturing*	220,000	23,161	—	350,000	—
Kenneth R. Heilbrunn, M.D.(1) *Senior Vice President, Clinical Development*	206,250	6,000	—	350,000	—
David A. Socks *Vice President, Business Development*	175,000	10,000	—	—	—

(1) Dr. Heilbrunn joined us as our Senior Vice President, Clinical Development in April 2005 and, therefore, the amounts set forth above reflect less than a full year. Dr. Heilbrunn has provided us with notice of his resignation effective September 30, 2006.

In May 2006, Dr. Mike A. Royal, M.D., J.D. joined us as our Vice President, Clinical Development, Analgesics at an annual salary of $275,000. In June 2006, Mr. William R. LaRue joined us as our Senior Vice President, Chief Financial Officer, Treasurer and Secretary at an annual salary of $265,000. In August 2006, Dr. James B. Breitmeyer joined us as our Executive Vice President, Development and Chief Medical Officer at an annual salary of $330,000.

Option Grants in Last Fiscal Year

The following table sets forth certain information with respect to stock options granted to the individuals named in the Summary Compensation Table during the fiscal year ended December 31, 2005, including the potential realizable value over the ten-year term of the options, based on assumed rates of stock appreciation of 5% and 10%, compounded annually, minus the applicable per share exercise price.

These assumed rates of appreciation are mandated by the rules of the SEC and do not represent our estimate or projection of our future common stock price. We cannot assure you that any of the values in the table will be achieved. Actual gains, if any, on stock option exercises will be dependent on the future performance of our common stock and overall stock market conditions. The assumed 5% and 10% rates of stock appreciation are based on the assumed initial public offering price of $ per share (the

mid-point of the price range set forth on the cover page of this prospectus). The percentage of total options granted is based upon our granting of options to employees, directors and consultants in 2005 to purchase an aggregate of 3,077,000 shares of our common stock.

	Individual Grants				Potential Realizable Value at Assumed Annual Rates of Stock Price Appreciation for Option Term	
Name	Number of Shares Underlying Options Granted	% of Total Options Granted to Employees In Last Fiscal Year	Exercise Price Per Share	Expiration Date	5%	10%
Theodore R. Schroeder	250,000	8.12%	$ 0.10	12-29-2015	$	$
Richard E. Lowenthal	300,000	9.75%	0.10	2-15-2015		
	264,000	8.58%	0.10	12-29-2015		
William S. Craig, Ph.D.	350,000	11.37%	0.10	2-15-2015		
Kenneth R. Heilbrunn, M.D.	350,000	11.37%	0.10	5-19-2015		
David A. Socks	—	—	—	—		

Aggregate Option Exercises in Last Fiscal Year and Fiscal Year-End Option Values

The following table describes for the named executive officers the number and value of securities underlying exercisable and unexercisable options held by them as of December 31, 2005. The value realized and the value of unexercised in-the-money options at December 31, 2005 are based on the assumed initial public offering price of $ per share (the mid-point of the price range set forth on the cover page of this prospectus) less the per share exercise price, multiplied by the number of shares issued or issuable, as the case may be, upon exercise of the option. All options were granted under our 2004 equity incentive award plan.

			Number of Securities Underlying Unexercised Options at December 31, 2005		Value of Unexercised In-the-Money Options at December 31, 2005	
Name	Number of Shares Acquired on Exercise	Value Realized	Exercisable	Unexercisable	Exercisable	Unexercisable
Theodore R. Schroeder	1,000,000(1)	$	—	—	$	$
Richard E. Lowenthal	564,000(2)		—	—		
William S. Craig, Ph.D.	—		350,000(3)	—		
Kenneth R. Heilbrunn, M.D.	—		350,000(4)	—		
David A. Socks	—		100,000(5)	—		

(1) Of these 1,000,000 shares, 765,625 were unvested as of December 31, 2005.

(2) Of these 564,000 shares, 489,000 were unvested as of December 31, 2005.

(3) Of these 350,000 shares, 255,208 were unvested as of December 31, 2005.

(4) Of these 350,000 shares, 350,000 were unvested as of December 31, 2005.

(5) Of these 100,000 shares, 68,750 were unvested as of December 31, 2005.

Employment Agreements

We have entered into employment agreements with Theodore R. Schroeder, our President and Chief Executive Officer, James B. Breitmeyer, M.D., Ph.D., our Executive Vice President, Development and Chief Medical Officer, William S. Craig, Ph.D., our Senior Vice President, Pharmaceutical Development and Manufacturing, Kenneth R. Heilbrunn, M.D., our Senior Vice President, Clinical

Development, William R. LaRue, our Senior Vice President, Chief Financial Officer, Treasurer and Secretary, Richard E. Lowenthal, our Vice President, Regulatory Affairs and Quality Assurance, Mike A. Royal, M.D., J.D., our Vice President, Clinical Development, Analgesics, and David A. Socks, our Vice President, Business Development.

Pursuant to the employment agreements, each executive is required to faithfully, industriously and to the best of his or her ability, experience and talent perform all of the duties that may be assigned to such executive pursuant to his or her employment agreement, and shall devote substantially all of his or her productive time and efforts to the performance of such duties.

The base salaries of the executives are set forth in the employment agreements. The employment agreements do not provide for automatic annual increases in salary, but each employment agreement provides for annual salary reviews. The employment agreements provide that each executive shall participate in any bonus plan that our board of directors or its designee may approve for our senior executives (see "— Employee Benefit and Stock Plans — Annual Bonus Plan" below). Each executive's employment is at-will and may be terminated by us at any time, with or without notice. Similarly, each executive may terminate his or her employment with us at any time, with or without notice.

The employment agreements provide each executive with certain severance benefits in the event his or her employment is terminated as a result of his or her death or permanent disability. Specifically, in the event of such a termination, each executive will receive any accrued but unpaid base salary as of the date of termination, a lump sum cash payment equal to the executive's annual base salary, and a lump sum cash payment equal to the executive's prorated annual bonus. Additionally, in the event of an executive's death, his or her eligible dependents would receive 12 months healthcare benefits continuation coverage at our expense. In the event of an executive's permanent disability, he or she will receive 12 months healthcare and life insurance benefits continuation at our expense.

The employment agreements also provide each executive with certain severance benefits in the event his or her employment is terminated by us other than for "cause", as defined in the agreements and described below, or if the executive resigns with "good reason", as defined in the agreements and described below. Specifically, if such termination occurs within three months prior to or within 12 months following a change of control, each executive will receive any accrued but unpaid base salary as of the date of termination, a lump sum cash payment equal to the executive's annual base salary, a lump sum cash payment equal to the executive's prorated annual bonus, and 12 months healthcare and life insurance benefits continuation coverage at our expense, plus a maximum of $15,000 towards outplacement services. If such termination occurs more than three months prior to a change of control or more than 12 months following a change of control, each executive will receive the benefits described in the previous sentence, less the prorated annual bonus.

The employment agreements provide that, in the event an executive's employment is terminated by us other than for cause or as a result of the executive's death or permanent disability, or if the executive resigns for good reason, that portion of the executive's stock awards, and any unvested shares issued upon the exercise of such stock awards, which would have vested if the executive had remained employed for an additional 12 months following the date of termination will immediately vest on the date of termination. In addition, if an executive's employment is terminated by us other than for cause or if an executive resigns for good reason within three months prior to or twelve months following a change of control, all of the executive's remaining unvested stock awards, and any unvested shares issued upon the exercise of such stock awards, will immediately vest on the later of (1) the date of termination or (2) the date of the change of control. This accelerated vesting is in addition to any accelerated vesting provided under our stock option plans.

Provided that the relevant stock award agreements do not specify a longer exercise period, an executive may generally exercise his or her stock awards until three months after the date of the executive's termination of employment, except that the executive may also exercise his or her stock awards three months after the date of a change of control, if the executive's employment is terminated by us other than for cause or if the executive resigns for good reason within three months prior to a change of control,

and if such stock awards were granted on or after the effective date of the executive's employment agreement. In no event, however, may an executive exercise any stock award later than its original outside expiration date.

In addition, the employment agreements provide that, in connection with a change of control, 50% of the executive's unvested stock awards, and any unvested shares issued upon the exercise of stock awards, will immediately become vested. This accelerated vesting is in addition to any accelerated vesting provided under our stock option plans.

The employment agreements also include standard noncompetition, nonsolicitation and nondisclosure covenants on the part of the executives. During the term of each executive's employment with us, the employment agreements provide that he or she may not compete with our business in any manner, except that an executive may own insignificant equity positions in publicly traded companies so long as the executive does not control such company. During the term of each executive's employment with us and for any period during which he or she is receiving severance, the employment agreements provide that he or she may not solicit our employees or consultants. The employment agreements also reaffirm the executives' obligations under our standard employee proprietary information and inventions agreement to which each executive is a party.

For purposes of the employment agreements, "cause" means, generally, the executive's commission of an act of fraud, embezzlement or dishonesty that has a material adverse impact on us, the executive's conviction of, or plea of guilty or no contest to a felony, the executive's unauthorized use or disclosure of our confidential information or trade secrets that has a material adverse impact on us, the executive's gross negligence, insubordination, material violation of any duty of loyalty to us or any other material misconduct on the part of the executive, the executive's ongoing and repeated failure or refusal to perform or neglect of his or her duties (where such failure, refusal or neglect continues for 15 days following the executive's receipt of written notice from our board), or a breach by the executive of any material provision of his or her employment agreement. Prior to any determination by us that "cause" has occurred, we will provide the executive with written notice of the reasons for such determination, afford the executive a reasonable opportunity to remedy any such breach, and provide the executive an opportunity to be heard prior to the final decision to terminate the executive's employment.

For purposes of the employment agreements, "good reason" means, generally, a change by us in the executive's position or responsibilities, other than a change in the executive's reporting relationship, that, in the executive's reasonable judgment, represents a substantial and material reduction in the position or responsibilities as in effect immediately prior thereto, our assignment to the executive of any duties or responsibilities that, in the executive's reasonable judgment, are materially inconsistent with such position or responsibilities, any removal of the executive from or failure to reappoint or reelect the executive to any of such positions, except in connection with the termination of the executive's employment for cause, as a result of his or her permanent disability or death, or by the executive other than for good reason, a material reduction in the executive's annual base salary (other than in connection with a general reduction in wages for personnel with similar status and responsibilities), our requiring the executive (without the executive's consent) to be based at any place outside a 50-mile radius of his or her initial place of employment with us, except for reasonably required travel on behalf of our business, our failure to provide the executive with compensation and benefits substantially equivalent (in terms of benefit levels and/or reward opportunities) to those provided for under each of our material employee benefit plans, programs and practices as in effect immediately prior to the date of the employment agreement, or any material breach by us of our obligations to the executive under the employment agreement.

Proprietary Information and Inventions Agreement

Each of our named executive officers has also entered into a standard form agreement with respect to proprietary information and inventions. Among other things, this agreement obligates each named executive officer to refrain from disclosing any of our proprietary information received during the

course of employment and, with some exceptions, to assign to us any inventions conceived or developed during the course of employment.

Employee Benefit and Stock Plans

Annual Bonus Plan

In August 2006, our board of directors approved our 2006 corporate bonus plan. Pursuant to the 2006 corporate bonus plan, our board of directors designated for each executive officer a target bonus amount, expressed as a percentage of his or her base salary (40% for our chief executive officer, 30% for our executive vice presidents and senior vice presidents and 25% for our other executive officers). Our executive officers are eligible to receive bonuses if certain individual and corporate performance criteria are achieved during the 2006 fiscal year, and such bonuses are payable as cash, stock, options, or a combination of the foregoing. Bonus payments will be based on the compensation committee's evaluation of our achievement of corporate performance goals for 2006, which were determined by the compensation committee prior to the inception of the 2006 incentive plan. The use of corporate performance goals is intended to establish a link between the executive's pay and our business performance. The individual performance of each of the executive officers during 2006 will be evaluated according to the achievement of individual performance goals, which were approved by the president and chief executive officer and the relevant vice presidents prior to the inception of the 2006 incentive plan. Our president and chief executive officer will receive a bonus determined solely by reference to the achievement of corporate performance goals. The compensation committee is responsible for approving any bonuses to our executive officers pursuant to the 2006 incentive plan.

2006 Equity Incentive Award Plan

In August 2006, our board of directors approved our 2006 Equity Incentive Award Plan, or the 2006 plan, which was approved by our stockholders in August 2006. The 2006 plan will become effective on the day prior to the day of this offering.

We have initially reserved shares of our common stock for issuance under the 2006 plan. In addition, the number of shares initially reserved under the 2006 plan will be increased by (i) the number of shares of common stock available for issuance and not subject to options granted under our 2004 equity incentive award plan as of the effective date of the 2006 plan, and (ii) the number of shares of common stock related to options granted under our 2004 equity incentive award plan that are repurchased, forfeited, expired or are cancelled on or after the effective date of the 2006 plan. The total number of shares described in clauses (i) and (ii) of the preceding sentence shall not exceed shares of our common stock. The 2006 plan contains an "evergreen provision" that allows for an annual increase in the number of shares available for issuance under the 2006 plan on January 1 of each year during the ten-year term of the 2006 plan, beginning on January 1, 2008. The annual increase in the number of shares shall be equal to the lesser of:

- 4% of our outstanding common stock on the applicable January 1; and
- a lesser amount determined by our board of directors.

Notwithstanding the "evergreen provision", the 2006 plan also provides for an aggregate limit of 20,000,000 shares of common stock which may be issued under the 2006 plan over the course of its ten-year term. The material terms of the 2006 plan are summarized below. The 2006 plan is filed as an exhibit to the registration statement of which this prospectus is a part.

Administration. The compensation committee of our board of directors will administer the 2006 plan (except with respect to any award granted to "independent directors" (as defined in the 2006 plan), which must be administered by our full board of directors). To administer the 2006 plan, our compensation committee must consist of at least two members of our board of directors, each of whom is a "non-employee director" for purposes of Rule 16b-3 under the Securities Exchange Act of 1934, as amended, and, with respect to awards that are intended to constitute performance-based compensation

under Section 162(m) of the Internal Revenue Code of 1986, as amended, an "outside director" for purposes of Section 162(m). Subject to the terms and conditions of the 2006 plan, our compensation committee has the authority to select the persons to whom awards are to be made, to determine the type or types of awards to be granted to each person, the number of awards to grant, the number of shares to be subject to such awards, and the terms and conditions of such awards, and to make all other determinations and decisions and to take all other actions necessary or advisable for the administration of the 2006 plan. Our compensation committee is also authorized to adopt, amend or rescind rules relating to administration of the 2006 plan. Our board of directors may at any time abolish the compensation committee and revest in itself the authority to administer the 2006 plan. The full board of directors will administer the 2006 plan with respect to awards to non-employee directors.

Eligibility. Options, stock appreciation rights, or SARs, restricted stock and other awards under the 2006 plan may be granted to individuals who are then our officers or employees or are the officers or employees of any of our subsidiaries. Such awards may also be granted to our non-employee directors and consultants but only employees may be granted incentive stock options, or ISOs. The maximum number of shares that may be subject to awards granted under the 2006 plan to any individual in any calendar year cannot exceed 1,000,000.

Awards. The 2006 plan provides that our compensation committee (or the board of directors, in the case of awards to non-employee directors) may grant or issue stock options, SARs, restricted stock, restricted stock units, dividend equivalents, performance share awards, performance stock units, stock payments, deferred stock, performance bonus awards, performance-based awards, and other stock-based awards, or any combination thereof. The compensation committee (or the board of directors, in the case of awards to non-employee directors) will consider each award grant subjectively, considering factors such as the individual performance of the recipient and the anticipated contribution of the recipient to the attainment of the company's long-term goals. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms and conditions of the award.

- Nonqualified stock options, or NQSOs, will provide for the right to purchase shares of our common stock at a specified price which may not be less than par value of a share of common stock on the date of grant, and usually will become exercisable (at the discretion of our compensation committee or the board of directors, in the case of awards to non-employee directors) in one or more installments after the grant date, subject to the participant's continued employment or service with us and/or subject to the satisfaction of performance targets established by our compensation committee (or the board of directors, in the case of awards to non-employee directors). NQSOs may be granted for any term specified by our compensation committee (or the board of directors, in the case of awards to non-employee directors), but the term may not exceed ten years.
- ISOs will be designed to comply with the provisions of the Internal Revenue Code and will be subject to specified restrictions contained in the Internal Revenue Code. Among such restrictions, ISOs must have an exercise price of not less than the fair market value of a share of common stock on the date of grant, may only be granted to employees, must expire within a specified period of time following the optionee's termination of employment, and must be exercised within the ten years after the date of grant. In the case of an ISO granted to an individual who owns (or is deemed to own) more than 10% of the total combined voting power of all classes of our capital stock, the 2006 plan provides that the exercise price must be more than 110% of the fair market value of a share of common stock on the date of grant and the ISO must expire upon the fifth anniversary of the date of its grant.
- Restricted stock may be granted to participants and made subject to such restrictions as may be determined by our compensation committee (or the board of directors, in the case of awards to non-employee directors). Typically, restricted stock may be forfeited for no consideration if the conditions or restrictions are not met, and they may not be sold or otherwise transferred to third parties until restrictions are removed or expire. Recipients of

restricted stock, unlike recipients of options, may have voting rights and may receive dividends, if any, prior to the time when the restrictions lapse.

- Restricted stock units may be awarded to participants, typically without payment of consideration or for a nominal purchase price, but subject to vesting conditions including continued employment or on performance criteria established by our compensation committee (or the board of directors, in the case of awards to non-employee directors). Like restricted stock, restricted stock units may not be sold or otherwise transferred or hypothecated until vesting conditions are removed or expire. Unlike restricted stock, stock underlying restricted stock units will not be issued until the restricted stock units have vested, and recipients of restricted stock units generally will have no voting or dividend rights prior to the time when vesting conditions are satisfied.
- SARs may be granted in connection with stock options or other awards, or separately. SARs granted under the 2006 plan in connection with stock options or other awards typically will provide for payments to the holder based upon increases in the price of our common stock over the exercise price of the related option or other awards. Except as required by Section 162(m) of the Internal Revenue Code with respect to an SAR intended to qualify as performance-based compensation as described in Section 162(m) of the Internal Revenue Code, there are no restrictions specified in the 2006 plan on the exercise of SARs or the amount of gain realizable therefrom. Our compensation committee (or the board of directors, in the case of awards to non-employee directors) may elect to pay SARs in cash or in common stock or in a combination of both.
- Dividend equivalents represent the value of the dividends, if any, per share paid by us, calculated with reference to the number of shares covered by the stock options, SARs or other awards held by the participant.
- Performance awards (*i.e.*, performance share awards, performance stock units, performance bonus awards, performance-based awards and deferred stock) may be granted by our compensation committee (or the board of directors, in the case of awards to non-employee directors) on an individual or group basis. Generally, these awards will be based upon specific performance targets and may be paid in cash or in common stock or in a combination of both. Performance awards may include “phantom” stock awards that provide for payments based upon increases in the price of our common stock over a predetermined period. Performance awards may also include bonuses that may be granted by our compensation committee (or the board of directors, in the case of awards to non- employee directors) on an individual or group basis, which may be paid on a current or deferred basis and may be payable in cash or in common stock or in a combination of both. The maximum amount of any such bonuses to a “covered employee” within the meaning of Section 162(m) of the Code shall not exceed $1,000,000 for any fiscal year during the term of the 2006 plan.
- Stock payments may be authorized by our compensation committee (or the board of directors, in the case of awards to non-employee directors) in the form of common stock or an option or other right to purchase common stock as part of a deferred compensation arrangement, made in lieu of all or any part of compensation, including bonuses, that would otherwise be payable to employees or consultants or members of our board of directors.

Corporate Transactions. In the event of a change of control where the acquiror does not assume awards granted under the plan, awards issued under the 2006 plan will be subject to accelerated vesting such that 100% of the awards will become vested and exercisable or payable, as applicable. Under the 2006 plan, a change of control is generally defined as:

- the direct or indirect sale or exchange in a single or series of related transactions (other than an offering of our stock to the general public through a registration statement filed with the

SEC) whereby any person or entity or related group of persons or entities (other than us, our subsidiaries, an employee benefit plan maintained by us or any of our subsidiaries or a person or entity that, prior to such transaction, directly or indirectly controls, is controlled by, or is under common control with, us) directly or indirectly acquires beneficial ownership (within the meaning of Rule 13d-3 under the Exchange Act) of more than 50% of the total combined voting power of our securities outstanding immediately after such acquisition;

- during any two-year period, individuals who, at the beginning of such period, constitute our board of directors together with any new director(s) whose election by our board of directors or nomination for election by our stockholders was approved by a vote of at least two-thirds of the directors then still in office who either were directors at the beginning of the two-year period or whose election or nomination for election was previously so approved, cease for any reason to constitute a majority of our board of directors;
- the merger, consolidation, reorganization, or business combination in which the company is a party (whether directly involving the company or indirectly involving the company through one or more intermediaries, other than a merger, consolidation, reorganization, or business combination that results in our outstanding voting securities immediately before the transaction continuing to represent a majority of the voting power of the acquiring company's outstanding voting securities or a merger, consolidation, reorganization, or business combination after which no person or entity owns 50% of the successor company's voting power); and
- the sale, exchange or transfer of all or substantially all of our assets.

Amendment and Termination of the 2006 Plan. Our board of directors may terminate, amend or modify the 2006 plan. However, stockholder approval of any amendment to the 2006 plan will be obtained to the extent necessary and desirable to comply with any applicable law, regulation or stock exchange rule, or for any amendment to the 2006 plan that increases the number of shares available under the 2006 plan. If not terminated earlier by the compensation committee or the board of directors, the 2006 plan will terminate on the tenth anniversary of the date of its initial approval by our board of directors.

Securities Laws and Federal Income Taxes. The 2006 plan is designed to comply with various securities and federal tax laws as follows:

- *Securities Laws.* The 2006 plan is intended to conform to all provisions of the Securities Act and the Exchange Act and any and all regulations and rules promulgated by the SEC thereunder, including without limitation, Rule 16b-3. The 2006 plan will be administered, and awards will be granted and may be exercised, only in such a manner as to conform to such laws, rules and regulations.
- *General Federal Tax Consequences.* Under current federal laws, in general, recipients of awards and grants of NQSOs, SARs, restricted stock, restricted stock units, dividend equivalents, performance awards and stock payments under the plan are taxable under Section 83 of the Internal Revenue Code upon their receipt of common stock or cash with respect to such awards or grants and, subject to Section 162(m) of the Internal Revenue Code, we will be entitled to an income tax deduction with respect to the amounts taxable to such recipients. However, Section 409A of the Internal Revenue Code provides certain new requirements on non-qualified deferred compensation arrangements. Certain awards under the 2006 plan are subject to the requirements of Section 409A, in form and in operation, such as restricted stock unit awards. We intend that all plan awards that are subject to Section 409A will satisfy the requirements of Section 409A. However, if a plan award is subject to and fails to satisfy the requirements of Section 409A, the recipient of that award may recognize ordinary income on the amounts deferred under the award, to the extent vested, which may be prior to when the compensation is actually or constructively received. Also, if an award that is subject to Section 409A fails to comply, Section 409A imposes an

additional 20% federal income tax on compensation recognized as ordinary income, as well as interest on such deferred compensation.

Under Sections 421 and 422 of the Internal Revenue Code, recipients of ISOs are generally not taxed on their receipt of common stock upon their exercises of ISOs if the ISOs and option stock are held for specified minimum holding periods and, in such event, we are not entitled to income tax deductions with respect to such exercises. Participants in the 2006 plan will be provided with detailed information regarding the tax consequences relating to the various types of awards and grants under the 2006 plan.

- *Section 162(m) Limitation.* In general, under Section 162(m) of the Internal Revenue Code, income tax deductions of publicly-held corporations may be limited to the extent total compensation (including base salary, annual bonus, stock option exercises and non-qualified benefits paid) for certain executive officers exceeds $1 million (less the amount of any "excess parachute payments" as defined in Section 280G of the Internal Revenue Code) in any one year. However, under Section 162(m), the deduction limit does not apply to certain "performance-based compensation" if an independent compensation committee determines performance goals, and if the material terms of the performance-based compensation are disclosed to and approved by our stockholders. In particular, stock options and SARs will satisfy the "performance-based compensation" exception if the awards are made by a qualifying compensation committee, the 2006 plan sets the maximum number of shares that can be granted to any person within a specified period and the compensation is based solely on an increase in the stock price after the grant date. Specifically, the option exercise price must be equal to or greater than the fair market value of the stock subject to the award on the grant date. Under a Section 162(m) transition rule for compensation plans of corporations which are privately held and which become publicly held in an initial public offering, the 2006 plan will not be subject to Section 162(m) until a specified transition date, which is the earlier of (i) the material modification of the 2006 plan, (ii) the issuance of all employer stock and other compensation that has been allocated under the 2006 plan, or (iii) the first annual meeting of stockholders at which directors are to be elected that occurs after the close of the third calendar year following the calendar year in which the initial public offering occurs. After the transition date, rights or awards granted under the 2006 plan, other than options and SARs, will not qualify as "performance-based compensation" for purposes of Section 162(m) unless such rights or awards are granted or vest upon pre-established objective performance goals, the material terms of which are disclosed to and approved by our stockholders.

We have attempted to structure the 2006 plan in such a manner that, after the transition date, the compensation attributable to stock options and SARs which meet the other requirements of Section 162(m) will not be subject to the $1 million limitation. We have not, however, requested a ruling from the Internal Revenue Service, or IRS, or an opinion of counsel regarding this issue.

2004 Equity Incentive Award Plan

Our 2004 equity incentive award plan, or 2004 plan, was initially adopted by our board of directors and approved by our stockholders in November 2004. As amended to date, we have reserved a total of 11,500,000 shares of common stock for issuance under the 2004 plan. As of June 30, 2006, options to purchase 4,081,740 shares of common stock had been exercised (30,000 shares of which were repurchased by us), options to purchase 5,769,471 shares of common stock were outstanding and 1,678,789 shares of common stock remained available for grant. As of June 30, 2006, the outstanding options were exercisable at a weighted average exercise price of approximately $0.38 per share. The material terms of the 2004 plan are summarized below. The 2004 plan is filed as an exhibit to the registration statement of which this prospectus is a part.

No Further Grants. After the effective date of the 2006 Plan, no additional awards will be granted under the 2004 plan.

Administration. The compensation committee of our board of directors administers the 2004 plan. Following the completion of this offering, to administer the 2004 plan, our compensation committee must be constituted as described above in our description of the 2006 Plan. Subject to the terms and conditions of the 2004 plan, our compensation committee has the authority to select the persons to whom awards are to be made, to determine the number of shares to be subject thereto and the terms and conditions thereof, and to make all other determinations and to take all other actions necessary or advisable for the administration of the 2004 plan. Our compensation committee is also authorized to establish, adopt, amend or rescind rules relating to administration of the 2004 plan. Our board of directors may at any time abolish the compensation committee and revest in itself the authority to administer the 2004 plan. The full board of directors administers the 2004 plan with respect to awards to non-employee directors.

Eligibility. Options and restricted stock under the 2004 plan may be granted to individuals who are then our officers or employees or are the officers or employees of any of our subsidiaries. Such awards may also be granted to our non-employee directors or consultants, but only employees may be granted ISOs.

Awards. The 2004 plan provides that our compensation committee may grant or issue stock options and restricted stock, stock appreciation rights, performance share awards, restricted stock units, dividend equivalents, stock payments or performance-based awards or any combination thereof. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms and conditions of the award.

- NQSOs provide for the right to purchase shares of our common stock at a specified price, which for purposes of the 2004 plan prior to the date of this offering, may be no less than 85% of the fair market value on the date of grant, and usually will become exercisable (at the discretion of our compensation committee (or the board of directors, in the case of awards to non-employee directors), in one or more installments after the grant date, subject to the participant's continued employment or service with us and/or subject to the satisfaction of performance targets established by our compensation committee (or the board of directors, in the case of awards to non-employee directors). NQSOs may be granted for a maximum 10-year term.
- ISOs are designed to comply with the provisions of the Internal Revenue Code and will be subject to specified restrictions contained in the Internal Revenue Code and as further described above in connection with the 2006 Equity Incentive Award Plan.

To date, we have only granted stock options under the 2004 plan.

Corporate Transactions. In the event of a change of control where the acquiror does not assume awards granted under the plan and does not substitute substantially similar awards for those outstanding under the plan, awards issued under the plan will be subject to accelerated vesting such that 100% of the awards will become vested and exercisable or payable, as applicable. Under the 2004 plan, a change of control is generally defined as:

- a merger or consolidation of us with or into any other corporation or other entity or person; or
- a sale, lease, exchange or other transfer in one transaction or a series of related transactions of all or substantially all of our outstanding securities or all or substantially all of our assets.

Amendment and Termination of the 2004 plan. The compensation committee, with the approval of the board of directors, may terminate, amend or modify the 2004 plan. However, stockholder approval of any amendment to the 2004 plan will be obtained to the extent necessary and desirable to comply with any applicable law, regulation, or stock exchange rule. If not terminated earlier by the compensation committee, with the approval of the board of directors, the 2004 plan will terminate on the tenth anniversary of the date of its initial adoption by our board of directors.

401(k) Plan

We provide a basic savings plan, or 401(k) plan, which is intended to qualify under Section 401(k) of the Internal Revenue Code so that contributions to our 401(k) plan by employees or by us, and the investment earnings thereon, are not taxable to employees until withdrawn from our 401(k) plan. If our 401(k) plan qualifies under Section 401(k) of the Internal Revenue Code, contributions by us, if any, will be deductible by us when made.

All of our employees are eligible to participate in our 401(k) plan. Pursuant to our 401(k) plan, employees may elect to reduce their current compensation by up to the statutorily-prescribed annual limit of $15,000 in 2006 and to have the amount of this reduction contributed to our 401(k) plan. Our 401(k) plan permits, but does not require, additional matching or non-elective contributions to our 401(k) plan by us on behalf of all participants in our 401(k) plan. To date, we have not made any matching or non-elective contributions to our 401(k) plan.

Limitations of Liability and Indemnification Matters

We will adopt provisions in our amended and restated certificate of incorporation that limit the liability of our directors for monetary damages for breach of their fiduciary duties, except for liability that cannot be eliminated under the Delaware General Corporation Law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors, except liability for any of the following:

- any breach of their duty of loyalty to the corporation or its stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

This limitation of liability does not apply to liabilities arising under the federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated certificate of incorporation and our amended and restated bylaws also will provide that we shall indemnify our directors and executive officers and may indemnify our other officers and employees and other agents to the fullest extent permitted by law. We believe that indemnification under our amended and restated bylaws covers at least negligence and gross negligence on the part of indemnified parties. Our amended and restated bylaws also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in this capacity, regardless of whether our amended and restated bylaws would permit indemnification.

We have entered into separate indemnification agreements with our directors and executive officers, in addition to indemnification provided for in our charter documents. These agreements, among other things, provide for indemnification of our directors and executive officers for expenses, judgments, fines and settlement amounts incurred by this person in any action or proceeding arising out of this person’s services as a director or executive officer or at our request. We believe that these provisions and agreements are necessary to attract and retain qualified persons as directors and executive officers.

PRINCIPAL STOCKHOLDERS

The following table sets forth information about the beneficial ownership of our common stock at August 28, 2006, and as adjusted to reflect the sale of the shares of common stock in this offering, for:

- each person known to us to be the beneficial owner of more than 5% of our common stock;
- each named executive officer and two additional executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

Unless otherwise noted below, the address of each beneficial owner listed on the table is c/o Cadence Pharmaceuticals, Inc., 12481 High Bluff Drive, Suite 200, San Diego, CA 92130. We have determined beneficial ownership in accordance with the rules of the SEC. Except as indicated by the footnotes below, we believe, based on the information furnished to us by the stockholders, that the persons and entities named in the tables below have sole voting and investment power with respect to all shares of common stock that they beneficially own, subject to applicable community property laws. We have based our calculation of the percentage of beneficial ownership on 88,342,195 shares of common stock outstanding on August 28, 2006, which assumes the conversion of all outstanding shares of preferred stock into common stock and shares of common stock outstanding upon completion of this offering.

In computing the number of shares of common stock beneficially owned by a person and the percentage ownership of that person, we deemed outstanding shares of common stock subject to options or warrants held by that person that are currently exercisable or exercisable within 60 days of August 28, 2006. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Common Stock Beneficially Owned	
		Prior to Offering	After Offering
5% or Greater Stockholders:			
Funds affiliated with Domain Associates, L.L.C.(1) One Palmer Square, Suite 515 Princeton, NJ 08542	22,964,492	26.0%	
ProQuest Investments III, L.P.(2) 90 Nassau Street, 5th Floor Princeton, NJ 08542	12,322,698	13.9	
Frazier Healthcare V, LP(3) 601 Union Street, Suite 3200 Seattle, WA 98101	10,100,000	11.4	
Funds affiliated with Versant Ventures II, L.L.C.(4) 3000 Sand Hill Road Building 4, Suite 210 Menlo Park, CA 94025	8,100,000	9.2	
Funds affiliated with Technology Partners(5) 100 Shoreline Highway Suite 282, Building B Mill Valley, CA 94941	8,000,000	9.1	
BB Biotech Ventures II, L.P.(6) Trafalgar Court, Les Banques St Peter Port, Guernsey, Channel Islands GY1 3QL	7,000,000	7.9	

Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Common Stock Beneficially Owned	
		Prior to Offering	After Offering
Directors and Executive Officers:			
Theodore R. Schroeder(7)	4,043,740	4.5	
James B. Breitmeyer, M.D., Ph.D.(8)	705,000	*	
William S. Craig, Ph.D.(9)	705,303	*	
Kenneth R. Heilbrunn, M.D.(10)	650,000	*	
William R. LaRue(11)	899,000	1.0	
Richard E. Lowenthal(12)	564,000	*	
Mike A. Royal, M.D., J.D.(13)	375,000	*	
David A. Socks(14)	1,692,728	1.9	
Cam L. Garner(15)	4,250,123	4.8	
Brian G. Atwood(4)	8,100,000	9.2	
Samuel L. Barker, Ph.D.(16)	100,000	*	
Michael A. Berman, M.D.(17)	100,000	*	
James C. Blair, Ph.D.(1)	22,964,492	26.0	
Alan D. Frazier(3)	10,100,000	11.4	
Alain B. Schreiber, M.D.(2)	12,322,698	13.9	
Christopher J. Twomey(18)	100,000	*	
Executive officers and directors as a group (16 persons)(19)	67,672,084	71.2	

* Represents beneficial ownership of less than one percent of our outstanding common stock.

(1) Includes 22,612,155 shares of common stock owned by Domain Partners VI, L.P., 242,337 shares of common stock owned by DP VI Associates, L.P. and 110,000 shares of common stock owned by Domain Associates, L.L.C. Of the 110,000 shares owned by Domain Associates, 86,875 will be subject to our right of repurchase within 60 days of August 28, 2006. Dr. Blair is a member of our board of directors and a managing member of Domain Associates, L.L.C. and a managing member of One Palmer Square Associates VI, L.L.C., which is the general partner of Domain Partners VI, L.P. and DP VI Associates, L.P. Dr. Blair disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.

(2) Includes 12,212,698 shares of common stock owned by ProQuest Investments III, L.P. and 50,000 shares of common stock owned by ProQuest Management LLC. Of the 50,000 shares owned by ProQuest Management, 17,500 will be subject to our right of repurchase within 60 days of August 28, 2006. Also includes 60,000 shares Dr. Schreiber has the right to acquire pursuant to outstanding options which are immediately exercisable, 55,000 of which would be subject to our right of repurchase within 60 days of August 28, 2006. Dr. Schreiber is a member of our board of directors and a managing member of ProQuest Management LLC and a managing member of ProQuest Associates III LLC, the ultimate general partner of ProQuest Investments III, L.P.

(3) Includes 100,000 shares Mr. Frazier has the right to acquire pursuant to outstanding options which are immediately exercisable, 87,500 of which would be subject to our right of repurchase within 60 days of August 28, 2006. The voting and disposition of the shares held by Frazier Healthcare V, LP is determined by FHM V, LLC, which is the general partner of FHM V, LP, which is the general partner of Frazier Healthcare V, LP. Mr. Frazier is a member of our board of directors and a managing member of FHM V, LLC. Mr. Frazier disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.

footnotes continued on the following page

(4) Includes 7,782,747 shares of common stock owned by Versant Venture Capital II, L.P., 147,695 shares of common stock owned by Versant Affiliates Fund II-A, L.P. and 69,558 shares of common stock owned by Versant Side Fund II, L.P. Also includes 100,000 shares Mr. Atwood has the right to acquire pursuant to outstanding options which are immediately exercisable, 87,500 of which would be subject to our right of repurchase within 60 days of August 28, 2006. Mr. Atwood is a member of our board of directors and a managing member of Versant Ventures II, L.L.C., which is the general partner of each of these Versant funds. Mr. Atwood disclaims beneficial ownership of shares owned by these Versant funds except to the extent of his pecuniary interest therein.

(5) Includes 7,520,000 shares of common stock owned by Technology Partners Fund VII, L.P. and 480,000 shares of common stock owned by Technology Partners Affiliates VII, L.P. The voting and disposition of the shares held by Technology Partners Fund VII, L.P. and Technology Partners Affiliates VII is determined by TP Management VII, L.L.C., which is the general partner of each of these Technology Partners funds. John E. Ardell III, Ira Ehrenpreis, James Glasheen, Sheila Mutter and Roger J. Quy share voting and dispositive authority over the shares held by Technology Partners.

(6) The voting and disposition of the shares held by BB Biotech Ventures II, L.P. is determined by its general partner, BB Biotech Ventures GP (Guernsey) Limited. Christopher Wilfred Cochrane, Benedict Peter Goronwy Morgan and Hans Jorg Graf, in their capacities as directors of the general partner, share voting and dispositive authority over the shares held by BB Biotech Ventures.

(7) Includes 2,043,740 shares Mr. Schroeder has the right to acquire pursuant to outstanding options which are immediately exercisable, all of which would be subject to our right of repurchase within 60 days of August 28, 2006. Also includes 1,000,000 unvested shares acquired by Mr. Schroeder upon the early exercise of stock options, 609,375 of which will be subject to our right of repurchase within 60 days of August 28, 2006.

(8) Includes 705,000 shares Dr. Breitmeyer has the right to acquire pursuant to outstanding options that are immediately exercisable, all of which would be subject to our right of repurchase within 60 days of August 28, 2006.

(9) Includes 705,303 shares Dr. Craig has the right to acquire pursuant to outstanding options which are immediately exercisable, 537,595 of which would be subject to our right of repurchase within 60 days of August 28, 2006.

(10) Includes 650,000 shares Dr. Heilbrunn has the right to acquire pursuant to outstanding options that are immediately exercisable, 518,750 of which would be subject to our right of repurchase within 60 days of August 28, 2006.

(11) Includes 44,000 shares acquired by Mr. LaRue upon exercise of stock options, 30,250 of which will be subject to our right of repurchase within 60 days of August 28, 2006. These 44,000 shares are held by a trust for the benefit of Mr. LaRue's family. Also includes 855,000 shares of common stock Mr. LaRue has the right to acquire pursuant to outstanding options that are immediately exercisable, all of which would be subject to our right of repurchase within 60 days of August 28, 2006.

(12) Includes 564,000 shares acquired by Mr. Lowenthal upon the exercise of stock options, 426,500 of which will be subject to our right of repurchase within 60 days of August 28, 2006. These 564,000 shares are held of record by a trust for the benefit of Mr. Lowenthal's family.

(13) Includes 375,000 shares Dr. Royal has the right to acquire pursuant to outstanding options which are immediately exercisable, all of which would be subject to our right of repurchase within 60 days of August 28, 2006.

(14) Includes 842,728 shares Mr. Socks has the right to acquire pursuant to outstanding options which are immediately exercisable, 790,645 of which would be subject to our right of repurchase within 60 days of August 28, 2006.

footnotes continued on the following page

(15) Includes 2,293,740 shares acquired by Mr. Garner upon the exercise of stock options, 2,058,414 of which will be subject to our right of repurchase within 60 days of August 28, 2006. Of these 2,293,740 shares, 2,153,740 shares are held of record by a trust for which Mr. Garner serves as trustee and 140,000 shares are held by a limited liability company for which Mr. Garner is the sole member. Also includes 1,750,000 shares acquired by Mr. Garner as one of our co-founders. Of these 1,750,000 shares, 1,600,000 shares are held by a limited liability company for which Mr. Garner is the sole member and 150,000 shares are held by siblings of Mr. Garner. Also includes 206,383 shares acquired by a limited liability company for which Mr. Garner is the sole member.

(16) Includes 100,000 shares Dr. Barker has the right to acquire pursuant to outstanding options which are immediately exercisable, 91,667 of which would be subject to our right of repurchase within 60 days of August 28, 2006.

(17) Includes 100,000 shares Dr. Berman has the right to acquire pursuant to outstanding options which are immediately exercisable, 90,000 of which would be subject to our right of repurchase within 60 days of August 28, 2006.

(18) Includes 100,000 shares acquired by Mr. Twomey upon exercise of stock options, 91,667 of which would be subject to our right of repurchase within 60 days of August 28, 2006. These 100,000 shares are held of record by a trust for the benefit of Mr. Twomey's family.

(19) Includes 6,636,771 shares of common stock subject to outstanding options which are immediately exercisable, 6,237,397 of which would be subject to our right of repurchase within 60 days of August 28, 2006. Includes 4,161,740 shares of common stock acquired upon the exercise of options, 3,320,581 of which will be subject to our right of repurchase within 60 days of August 28, 2006.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

We describe below transactions and series of similar transactions, since our inception, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed $60,000; and
- a director, executive officer, holder of more than 5% of our common stock or any member of their immediate family had or will have a direct or indirect material interest.

We also describe below certain other transactions with our directors, executive officers and stockholders.

Preferred Stock Issuances

In July and August 2004, we issued in a private placement an aggregate of 8,085,108 shares of Series A-1 preferred stock at a per share price of $0.94, for aggregate consideration of $7,600,002. In June and September 2005, we issued in a private placement an aggregate of 17,675,347 shares of Series A-2 preferred stock at a per share price of $1.00, for aggregate consideration of $17,675,347. In March 2006, we issued in a private placement 53,870,000 shares of Series A-3 preferred stock at a per share price of $1.00, for aggregate consideration of $53,870,000.

The following table sets forth the aggregate number of these securities acquired by the listed directors, executive officers or holders of more than 5% of our common stock, or their affiliates:

	Shares of Preferred Stock		
Investor	**Series A-1**	**Series A-2**	**Series A-3**
Funds affiliated with Domain Associates, L.L.C.(1)	3,989,362	6,365,130	12,500,000
ProQuest Investments III, L.P.(2)	2,393,618	3,819,080	6,000,000
Frazier Healthcare V, LP(3)	—	—	10,000,000
Funds affiliated with Versant Ventures II, L.L.C.(4)	—	—	8,000,000
Funds affiliated with Technology Partners(5)	—	—	8,000,000
BB Biotech Ventures II, L.P.(6)	—	3,000,000	4,000,000
Cam L. Garner(7)	106,383	—	100,000

(1) Includes 3,947,061 shares of Series A-1 preferred stock, 6,297,638 shares of Series A-2 preferred stock and 12,367,456 shares of Series A-3 preferred stock owned by Domain Partners VI, L.P., and 42,301 shares of Series A-1 preferred stock, 67,492 shares of Series A-2 preferred stock, and 132,544 shares of Series A-3 preferred stock owned by DP VI Associates, L.P. Dr. Blair, a member of our board of directors, is a managing member of Domain Associates, L.L.C. and a managing member of One Palmer Square Associates VI, L.L.C., which is the general partner of Domain Partners VI, L.P. and DP VI Associates, L.P.

(2) The voting and disposition of the shares held by ProQuest Investments III, L.P. is determined by ProQuest Associates III LLC, the ultimate general partner of ProQuest Investments III, L.P. Dr. Schreiber, a member of our board of directors, is a managing member of ProQuest Associates III LLC.

(3) The voting and disposition of the shares held by Frazier Healthcare V, LP is determined by FHM V, LLC, which is the general partner of FHM V, LP, which is the general partner of Frazier Healthcare V, LP. Mr. Frazier, a member of our board of directors, is a managing member of FHM V, LLC.

footnotes continued on the following page

(4) Includes 7,782,747 shares of Series A-3 preferred stock owned by Versant Venture Capital II, L.P., 147,695 shares of Series A-3 preferred stock owned by Versant Affiliates Fund II-A, L.P., and 69,558 shares of Series A-3 preferred stock owned by Versant Side Fund II, L.P. Mr. Atwood, a member of our board of directors, is a managing member of Versant Ventures II, L.L.C., which is the general partner of each of these Versant funds.

(5) Includes 7,520,000 shares of Series A-3 preferred stock owned by Technology Partners Fund VII, L.P. and 480,000 shares of Series A-3 preferred stock owned by Technology Partners Affiliates VII, L.P. The voting and disposition of the shares held by Technology Partners Fund VII, L.P. and Technology Partners Affiliates VII is determined by TP Management VII, L.L.C., which is the general partner of each of these Technology Partners funds. John E. Ardell III, Ira Ehrenpreis, James Glasheen, Sheila Mutter and Roger J. Quy share voting and dispositive authority over the shares held by Technology Partners.

(6) The voting and disposition of the shares held by BB Biotech Ventures II, L.P. is determined by its general partner, BB Biotech Ventures GP (Guernsey) Limited. Christopher Wilfred Cochrane, Benedict Peter Goronwy Morgan and Hans Jorg Graf, in their capacities as directors of the general partner, share voting and dispositive authority over the shares held by BB Biotech Ventures.

(7) Shares held by a limited liability company for which Mr. Garner is the sole member.

Common Stock Issuances

In July 2004, in connection with the inception of our company, we issued and sold a total of 4,500,000 shares of common stock for an aggregate consideration of $4,500. The price for the common stock was determined through negotiations between our board of directors and the purchasers based primarily on the early stage of our development at the time of the transaction. The following table sets forth the aggregate number of these securities acquired by the listed directors and executive officers or their affiliates:

Investor	Common Stock
Cam L. Garner(1)	1,750,000
Theodore R. Schroeder(2)	1,000,000
David A. Socks	850,000

(1) Of these 1,750,000 shares, 1,600,000 shares are held by a limited liability company for which Mr. Garner is the sole member and 150,000 shares are held by siblings of Mr. Garner.

(2) Shares held by a trust for the benefit of Mr. Schroeder’s family.

Investor Rights Agreement

We have entered into an agreement with purchasers of our preferred stock that provides for certain rights relating to the registration of their shares of common stock issuable upon conversion of their preferred stock. The agreement also provides these rights to shares of common stock held by Messrs. Schroeder and Socks. These rights will continue following this offering and will terminate seven years following the completion of this offering, or for any particular holder with registration rights, at such time following this offering when all securities held by that stockholder subject to registration rights may be sold pursuant to Rule 144 under the Securities Act. All holders of our preferred stock are parties to this agreement. See “Description of Capital Stock — Registration Rights” for additional information.

Voting Agreement

Pursuant to a voting agreement originally entered into in July 2004 and most recently amended in March 2006 by and among us and certain of our stockholders, the following directors were each elected to serve as members on our board of directors and, as of the date of this prospectus, continue to so serve: Drs. Barker, Berman, Blair and Schreiber and Messrs. Atwood, Frazier, Garner and Schroeder. Pursuant

to the voting agreement, Mr. Schroeder, as our president and chief executive officer, and Mr. Garner were initially selected to serve on our board of directors as representatives of our common stock, as designated by a majority of our common stockholders. Dr. Schreiber and Messrs. Atwood, Blair and Frazier were initially selected to serve on our board of directors as representatives of our preferred stock, as designated by ProQuest Investments III, L.P., Versant Venture Capital II, L.P., Domain Partners VI, L.P. and Frazier Healthcare V, LP, respectively. Drs. Barker and Berman and Mr. Twomey were selected to serve on our board of directors as representatives of our common stock and preferred stock, as designated by a majority of our common and preferred stockholders.

The voting agreement will terminate upon completion of this offering, and members previously elected to our board of directors pursuant to this agreement will continue to serve as directors until their successors are duly elected by holders of our common stock.

Stock Option Grants

Certain stock option grants to our directors and executive officers and related option grant policies are described in this prospectus under the captions "Management — Director Compensation" and "Management — Option Grants in Last Fiscal Year." Prior to this offering, we granted the following options to certain non-employee directors:

- In November 2004, we granted to Dr. Schreiber an option to purchase 40,000 shares of our common stock at an exercise price of $0.10 per share, vesting over 16 calendar quarters from September 2004.
- In November 2005, we granted to Dr. Blair an option to purchase 40,000 shares of our common stock at an exercise price of $0.10 per share, vesting over 16 calendar quarters from September 2005.
- In November 2005, we granted to each of Dr. Schreiber and Mr. Garner an option to purchase 10,000 shares of our common stock at an exercise price of $0.10 per share, vesting over four calendar quarters from September 2005.
- In December 2005, we granted to Mr. Garner an option to purchase 1,362,000 shares of our common stock at an exercise price of $0.10 per share, vesting over four years from December 2005.
- In May 2006, we granted to Mr. Garner an option to purchase 781,740 shares of our common stock at an exercise price of $0.34 per share, vesting over four years from February 2006.
- In May 2006, we granted to Dr. Berman an option to purchase 40,000 shares of our common stock at an exercise price of $0.34 per share, vesting over 16 calendar quarters from April 2006.
- In May 2006, we granted to each of Messrs. Atwood and Frazier an option to purchase 40,000 shares of our common stock at an exercise price of $0.34 per share, vesting over 16 calendar quarters from March 2006.
- In July 2006, we granted to Mr. Twomey an option to purchase 100,000 shares of our common stock at an exercise price of $0.80 per share, vesting over 12 calendar quarters from July 2006.
- In July 2006, we granted to each of Mr. Atwood, Drs. Berman and Blair, Mr. Frazier and Dr. Schreiber an option to purchase 60,000 shares of our common stock at an exercise price of $0.80 per share, vesting over 12 calendar quarters from July 2006.
- In August 2006, we granted to Dr. Barker an option to purchase 100,000 shares of our common stock at an exercise price of $0.80 per share, vesting over 12 calendar quarters from August 2006.

In addition, we granted to each of Messrs. Craig, Heilbrunn and Socks an option in May 2006 to purchase 355,303, 300,000 and 742,728, respectively, shares of our common stock at an exercise price of $0.34 per share. In June 2006, we granted to each of Mr. LaRue and Dr. Royal an option to purchase 705,000 and 300,000, respectively, shares of our common stock at an exercise price of $0.80 per share. In August 2006, we granted to Dr. Breitmeyer an option to purchase 705,000 shares of our common stock at an exercise price of $0.80 per share. Also in August 2006, we granted to each of Mr. LaRue and Dr. Royal an option to purchase 150,000 and 75,000 shares of our common stock at an exercise price of $.80 per share. Each of these options vests with respect to 25% of the shares subject to the option one year after the applicable vesting commencement date and monthly thereafter over the following three years.

Employment Agreements

We have entered into employment agreements with Theodore R. Schroeder, our President and Chief Executive Officer, James B. Breitmeyer, M.D., Ph.D., our Executive Vice President, Development and Chief Medical Officer, William S. Craig, Ph.D., our Senior Vice President, Pharmaceutical Development and Manufacturing, Kenneth R. Heilbrunn, M.D., our Senior Vice President, Clinical Development, William R. LaRue, our Senior Vice President, Chief Financial Officer, Treasurer and Secretary, Richard E. Lowenthal, our Vice President, Regulatory Affairs and Quality Assurance, Mike A. Royal, M.D., J.D. our Vice President, Clinical Development, Analgesics, and David A. Socks, our Vice President, Business Development. For further information, see “Management — Employment Agreements.”

Indemnification of Officers and Directors

Our restated certificate of incorporation and our amended and restated bylaws provide that we will indemnify each of our directors and officers to the fullest extent permitted by the Delaware General Corporation Law. Further, we have entered into indemnification agreements with each of our directors and officers, and we have purchased a policy of directors’ and officers’ liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment under certain circumstances. For further information, see “Management — Limitations of Liability and Indemnification Matters.”

Consulting Agreement with Mr. Cam L. Garner

From September 2004 through August 2005, we paid Mr. Garner $5,000 per month plus qualified business expenses for his services as chairman of our board of directors under the terms of a consulting agreement between us and a limited liability company affiliated with Mr. Garner. The agreement expired on August 31, 2005.

Other Transactions

During 2004, Windamere III, LLC, a limited liability company affiliated with our former director, Scott L. Glenn, advanced $500,000 for pre-operating expenses and an exclusivity fee due in connection with the Collaboration and License Agreement between us and Migenix. The advance was settled with 531,915 shares of our Series A-1 preferred stock.

In May 2005, we executed an engagement letter with Clearview Projects, Inc., or Clearview, a provider of partnering and transaction services to biopharmaceutical companies. Dr. Barker is a founder of Clearview and served as its President and Chief Executive Officer from July 2003 until November 2004. Under the terms of the engagement letter, we made retainer payments and reimbursed expenses to Clearview totaling $205,341 in 2005 and made retainer and success fee payments totaling $375,000 from January 2006 through the conclusion of Clearview’s engagement in March 2006. The success fee was related to our in-license of rights to IV APAP from BMS in March 2006.

DESCRIPTION OF CAPITAL STOCK

Upon completion of this offering and filing of our amended and restated certificate of incorporation, our authorized capital stock will consist of 100,000,000 shares of common stock, $0.0001 par value per share, and 10,000,000 shares of preferred stock, $0.0001 par value per share. The following description summarizes some of the terms of our capital stock. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description you should refer to our amended and restated certificate of incorporation and amended and restated bylaws, copies of which have been filed as exhibits to the registration statement of which the prospectus is a part.

Common Stock

On June 30, 2006, there were 8,551,740 shares of common stock outstanding, held of record by 15 stockholders. This amount excludes our outstanding shares of preferred stock as of June 30, 2006 which will convert into 79,630,455 shares of common stock upon completion of the offering. After this offering, there will be shares of our common stock outstanding, or shares if the underwriters exercise their over-allotment option in full.

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared by the board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities of our company, subject to the prior rights of any preferred stock then outstanding. Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking funds provisions applicable to the common stock. All outstanding shares of common stock are, and the common stock to be outstanding upon completion of this offering will be, fully paid and nonassessable.

Preferred Stock

On June 30, 2006, there were 79,630,455 shares of preferred stock outstanding, held of record by 32 stockholders. Our stockholders have agreed to convert their shares of preferred stock to common stock in connection with the completion of this offering. Accordingly, upon the completion of this offering, all outstanding shares of preferred stock as of June 30, 2006 will automatically convert into 79,630,455 shares of our common stock.

Following the offering, our board of directors will have the authority, without any action by the stockholders, to issue from time to time preferred stock in one or more series and to fix the number of shares, designations, preferences, powers, and relative, participating, optional or other special rights and the qualifications or restrictions thereof. The preferences, powers, rights and restrictions of different series of preferred stock may differ with respect to dividend rates, amounts payable on liquidation, voting rights, conversion rights, redemption provisions, sinking fund provisions, and purchase funds and other matters. The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to holders of common stock or adversely affect the rights and powers, including voting rights, of the holders of common stock, and may have the effect of delaying, deferring or preventing a change in control of our company. The existence of authorized but unissued preferred stock may enable the board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, the board of directors were to determine that a takeover proposal is not in our best interests, the board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more

private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group.

Warrants

In February 2006, in connection with our loan and security agreement, we issued a warrant to purchase up to an aggregate of 192,500 shares of our Series A-2 preferred stock to each of Silicon Valley Bank and Oxford Finance Corporation. These warrants are immediately exercisable at an exercise price of $1.00 per share and, excluding certain mergers or acquisitions, expire upon the later of ten years from the date of grant, which is February 17, 2016, or five years after the closing of this offering. These warrants will become exercisable for an aggregate of 385,000 shares of our common stock, at an exercise price of $1.00 per share, upon completion of this offering.

Each of these warrants has a net exercise provision under which its holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive, after this offering, a net amount of shares of our common stock based on the fair market value of our common stock at the time of exercise of the warrant after deduction of the aggregate exercise price. Each of these warrants for common stock also contains provisions for the adjustment of the exercise price and the aggregate number of shares issuable upon the exercise of the warrant in the event of stock dividends, stock splits, reorganizations and reclassifications and consolidations.

Registration Rights

After this offering, the holders of approximately 83,555,455 shares of common stock and the holders of warrants to purchase 385,000 shares of common stock will be entitled to rights with respect to the registration of these shares under the Securities Act. These shares are referred to as registrable securities. Under the terms of the agreement between us and the holders of the registrable securities, if we propose to register any of our securities under the Securities Act, these holders are entitled to notice of such registration and are entitled to include their shares of registrable securities in our registration. Certain of these holders are also entitled to demand registration, pursuant to which they may require us to use our best efforts to register their registrable securities under the Securities Act at our expense, up to a maximum of two such registrations. Holders of registrable securities may also require us to file an unlimited number of additional registration statements on Form S-3 at our expense so long as the holders propose to sell registrable securities of at least $1.0 million and we have not already filed two such registration statements on Form S-3 in the previous twelve months.

All of these registration rights are subject to certain conditions and limitations, among them the right of the underwriters of an offering to limit the number of shares included in such registration and our right not to effect a requested registration 60 days prior to or 180 days after an offering of our securities, including this offering. These registration rights have been waived by all of the holders thereof with respect to this offering.

Anti-Takeover Effects of Provisions of Our Amended and Restated Certificate of Incorporation, Our Amended and Restated Bylaws and Delaware Law

Some provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: acquisition of us by means of a tender offer; acquisition of us by means of a proxy contest or otherwise; or removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions that might result in a premium over the market price for our shares.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased

protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings

Our charter documents provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Election and Removal of Directors

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. For more information on the classified board, see “Management — Board of Directors.” This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed “interested stockholders” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation’s voting stock. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least 66²/₃% of our then outstanding common stock.

The provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile

takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is , located at .

Nasdaq Global Market Listing

We have applied to have our common stock approved for quotation on the Nasdaq Global Market under the symbol “CADX.”

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Sales of Restricted Shares

Upon the closing of this offering, we will have outstanding an aggregate of approximately shares of common stock. Of these shares, the shares of common stock to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders were issued and sold by us in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under Rule 144, Rule 144(k) or Rule 701 under the Securities Act, which rules are summarized below.

As a result of the lock-up agreements described below and the provisions of Rule 144, Rule 144(k) and Rule 701 under the Securities Act, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

- shares will be eligible for sale on the date of this prospectus;
- shares will be eligible for sale upon the expiration of the lock-up agreements, as more particularly and except as described below, beginning 180 days after the date of this prospectus;
- shares will be eligible for sale, upon exercise of vested options, upon the expiration of the lock-up agreements, as more particularly and except as described below, beginning 180 days after the date of this prospectus;
- shares will be eligible for sale, upon exercise of outstanding warrants, upon the expiration of the lock-up agreements, as more particularly and except as described below, beginning 180 days after the date of this prospectus; and
- the remaining restricted shares will be eligible for sale from time to time thereafter upon expiration of their respective one-year holding periods.

Lock-up Agreements

We, each of our directors and executive officers, and all of the holders of our common stock and holders of securities exercisable for or convertible into shares of our common stock have each agreed not to sell or otherwise dispose of, directly or indirectly any shares of our common stock or any securities convertible into or exercisable or exchangeable for shares of our common stock for a period of not less than 180 days from the date of this prospectus without the prior written consent of Merrill Lynch & Co.

Merrill Lynch, in its sole discretion, at any time or from time to time and without notice, may release for sale in the public market all or any portion of the shares restricted by the terms of the lock-up agreements. The lock-up restrictions will not apply to transactions relating to common shares acquired in open market transactions after the closing of this offering provided that no filing by the transferor under Rule 144 of the Securities Act or Section 16 of the Exchange Act is required or will be voluntarily made in connection with such transactions. The lock-up restrictions also will not apply to certain transfers not involving a disposition for value, provided that the recipient agrees to be bound by these lock-up

restrictions and provided that no filing by the transferor under Rule 144 of the Securities Act or Section 16 of the Exchange Act is required or will be voluntarily made in connection with such transfers.

Rule 144

In general, under Rule 144 as currently in effect, beginning 90 days after the effective date of this offering, a person (or persons whose shares are required to be aggregated) who has beneficially owned restricted securities for at least one year, including the holding period of any prior owner other than one of our affiliates, is entitled to sell a number of restricted shares within any three-month period that does not exceed the greater of:

- one percent of the number of common shares then outstanding, which will equal shares immediately after this offering (assuming no exercise of the underwriters' over-allotment option and no exercise of outstanding options or warrants); or
- the average weekly trading volume of our common shares on the Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Sales of restricted shares under Rule 144 are also subject to requirements regarding the manner of sale, notice and the availability of current public information about us. Rule 144 also provides that affiliates that sell our common shares that are not restricted shares must nonetheless comply with the same restrictions applicable to restricted shares, other than the holding period requirement.

Rule 144(k)

Under Rule 144(k), a person who is not deemed to have been our affiliate at any time during the 90 days preceding a sale and who has beneficially owned the shares proposed to be sold for at least two years, including the holding period of any prior owner other than an affiliate, may sell those shares without complying with the manner of sale, public information, volume limitation or notice provisions of Rule 144.

Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquires common stock from us in connection with a compensatory stock or option plan or other written agreement before the effective date of this offering (to the extent such common stock is not subject to a lock-up agreement) is entitled to resell such shares 90 days after the effective date of this offering in reliance on Rule 144. The SEC has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after the date of this prospectus. Securities issued in reliance on Rule 701 are restricted securities and, subject to the lock-up agreements described above, beginning 90 days after the date of this prospectus, may be sold by persons other than affiliates, as defined in Rule 144, subject only to the manner of sale provisions of Rule 144 and by affiliates under Rule 144 without compliance with its one-year minimum holding period requirement.

Stock Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register shares of our common stock issued or reserved for issuance under our 2006 Equity Incentive Award Plan. The first such registration statement is expected to be filed soon after the date of this prospectus and will automatically become effective upon filing with the SEC. Accordingly, shares registered under such registration statement will be available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above.

Warrants

As of June 30, 2006, warrants to purchase a total of 385,000 shares of our Series A-2 preferred stock at a price of $1.00 per share were outstanding. Upon completion of this offering, these warrants will become exercisable for a total of 385,000 shares of our common stock at a price of $1.00 per share. See "Description of Capital Stock — Warrants." All of these common shares are subject to the terms of the lock-up agreements with the underwriters.

Stock Options

As of June 30, 2006, options to purchase a total of 5,769,471 shares of our common stock were outstanding, of which 5,419,165 were exercisable. All of the shares subject to options are subject to the terms of the lock-up agreements with the underwriters. An additional 1,678,789 shares of common stock were available for future option grants under our stock plan.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS TO NON-U.S. HOLDERS

This section summarizes material U.S. federal income tax considerations relating to the ownership and disposition of common stock to non-U.S. holders. This summary does not provide a complete analysis of all potential tax considerations. The information provided below is based on existing authorities. These authorities may change, or the IRS might interpret the existing authorities differently. In either case, the tax considerations of owning or disposing of common stock could differ from those described below. For purposes of this summary, a "non-U.S. holder" is any beneficial owner of our common stock other than a citizen or resident of the United States, a corporation or a partnership organized under the laws of the United States or any state, a trust that is (i) subject to the primary supervision of a U.S. court and the control of one of more U.S. persons or (ii) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person, or an estate whose income is subject to U.S. income tax regardless of source. If a partnership or other flow-through entity is a beneficial owner of common stock, the tax treatment of a partner in the partnership or an owner of the entity will depend upon the status of the partner or other owner and the activities of the partnership or other entity. Accordingly, partnerships and flow-through entities that hold our common stock and partners or owners of such partnerships or entities, as applicable, should consult their own tax advisors. The summary generally does not address tax considerations that may be relevant to particular investors because of their specific circumstances, or because they are subject to special rules, including, without limitation, banks, insurance companies, or other financial institutions; persons subject to the alternative minimum tax; tax exempt organizations; dealers in securities or currencies; traders in securities that elect to use a mark to market method of accounting for their securities holdings; persons that own, or are deemed to own, more than five percent of our company (except to the extent specifically set forth below); certain former citizens or long term residents of the United States; persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction; or persons deemed to sell our common stock under the constructive sale provisions of the Internal Revenue Code. Finally, the summary does not describe the effects of any applicable foreign, state or local laws.

INVESTORS CONSIDERING THE PURCHASE OF COMMON STOCK ARE URGED TO CONSULT THEIR OWN TAX ADVISORS REGARDING THE APPLICATION OF THE U.S. FEDERAL INCOME AND ESTATE TAX LAWS TO THEIR PARTICULAR SITUATIONS AND THE CONSEQUENCES OF FOREIGN, STATE, OR LOCAL LAWS, AND TAX TREATIES.

Dividends

We have not made any distributions on our common stock, and we do not plan to make any distributions for the foreseeable future. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. tax purposes to the extent paid from our current and accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed our current and accumulated earnings and profits, they will constitute a return of capital and will first reduce a non-U.S. holder's basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock. Any dividend paid to a non-U.S. holder on our common stock will generally be subject to U.S. withholding tax at a 30 percent rate. The withholding tax might not apply, however, or might apply at a reduced rate, under the terms of an applicable income tax treaty between the United States and the non-U.S. holder's country of residence. A non-U.S. holder must demonstrate its entitlement to treaty benefits by certifying its nonresident status. A non-U.S. holder can meet this certification requirement by providing a Form W-8BEN or appropriate substitute form to us or our paying agent. If the holder holds the stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to such financial institution or the agent. The financial institution or the agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. For payments made to a foreign partnership or other flow-through entity, the certification requirements generally apply to the partners or other owners rather than to the partnership or other entity, and the partnership or other entity must provide the partners' or other owners' documentation to us or our paying agent. Special rules, described

below, apply if a dividend is effectively connected with a U.S. trade or business conducted by the non-U.S. holder.

Sale of Common Stock

Non-U.S. holders will generally not be subject to U.S. federal income tax on any gains realized on the sale, exchange, or other disposition of common stock. This general rule, however, is subject to several exceptions. For example, the gain would be subject to U.S. federal income tax if:

- the gain is effectively connected with the conduct by the non-U.S. holder of a U.S. trade or business (in which case the special rules described below apply);
- the non-U.S. holder is an individual who holds our common stock as a capital asset (generally, an asset held for investment purposes) and who is present in the U.S. for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met;
- the non-U.S. holder was a citizen or resident of the United States and thus is subject to special rules that apply to expatriates; or
- the rules of the Foreign Investment in Real Property Tax Act, or FIRPTA (described below) treat the gain as effectively connected with a U.S. trade or business.

An individual non-U.S. holder described in the second bullet point immediately above will be subject to a flat 30% tax on the gain derived from the sale, which may be offset by U.S. source capital losses, even though the individual is not considered a resident of the U.S. If a non-U.S. holder is described in the third bullet point above, the non-U.S. holder should consult its own tax advisor to determine the U.S. federal, state, local and other tax consequences that may be relevant to such holder.

The FIRPTA rules may apply to a sale, exchange or other disposition of common stock if we are, or were within five years before the transaction, a "U.S. real property holding corporation," or a USRPHC. In general, we would be a USRPHC if interests in U.S. real estate comprised most of our assets. We do not believe that we are a USRPHC or that we will become one in the future. If we are or become a USRPHC, so long as our common stock is regularly traded on an established securities market, only a non-U.S. holder who, actually or constructively, holds or held (at any time during the shorter of the five year period preceding the date of disposition or the holder's holding period) more than 5% of our common stock will be subject to U.S. federal income tax on the disposition of our common stock.

Dividends or Gain Effectively Connected With a U.S. Trade or Business

If any dividend on common stock, or gain from the sale, exchange or other disposition of common stock, is effectively connected with a U.S. trade or business conducted by the non-U.S. holder, then the dividend or gain will be subject to U.S. federal income tax at the regular graduated rates. If the non-U.S. holder is eligible for the benefits of a tax treaty between the United States and the holder's country of residence, any "effectively connected" dividend or gain would generally be subject to U.S. federal income tax only if it is also attributable to a permanent establishment or fixed base maintained by the holder in the United States. Payments of dividends that are effectively connected with a U.S. trade or business, and therefore included in the gross income of a non-U.S. holder, will not be subject to the 30 percent withholding tax. To claim exemption from withholding, the holder must certify its qualification, which can be done by filing a Form W-8ECI. If the non-U.S. holder is a corporation, that portion of its earnings and profits that is effectively connected with its U.S. trade or business would generally be subject to a "branch profits tax." The branch profits tax rate is generally 30 percent, although an applicable income tax treaty might provide for a lower rate.

Backup Withholding and Information Reporting

The Internal Revenue Code and the Treasury regulations require those who make specified payments to report the payments to the IRS. Among the specified payments are dividends and proceeds paid by brokers to their customers. The required information returns enable the IRS to determine whether the recipient properly included the payments in income. This reporting regime is reinforced by "backup withholding" rules. These rules require the payors to withhold tax from payments subject to information reporting if the recipient fails to cooperate with the reporting regime by failing to provide his taxpayer identification number to the payor, furnishing an incorrect identification number, or repeatedly failing to report interest or dividends on his returns. The withholding tax rate is currently 28 percent. The backup withholding rules do not apply to payments to certain exempt holders, including corporations, whether domestic or foreign, who establish their exempt status.

Payments to non-U.S. holders of dividends on common stock will generally not be subject to backup withholding, and payments of proceeds made to non-U.S. holders by a broker upon a sale of common stock will not be subject to information reporting or backup withholding, in each case so long as the non-U.S. holder certifies its nonresident status. Some of the common means of certifying nonresident status are described under "— Dividends." We must report annually to the IRS any dividends paid to each non-U.S. holder and the tax withheld, if any, with respect to such dividends. Copies of these reports may be made available to tax authorities in the country where the non-U.S. holder resides.

Any amounts withheld from a payment to a holder of common stock under the backup withholding rules can be credited against any U.S. federal income tax liability of the holder.

EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR REGARDING THE PARTICULAR U.S. FEDERAL, STATE, LOCAL, AND FOREIGN TAX CONSEQUENCES OF PURCHASING, HOLDING, AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAWS.

UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated, Deutsche Bank Securities Inc., Pacific Growth Equities, LLC and JMP Securities LLC are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in a purchase agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Deutsche Bank Securities Inc.	
Pacific Growth Equities, LLC	
JMP Securities LLC	
Total	

Subject to the terms and conditions set forth in the purchase agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the purchase agreement if any of these shares are purchased. If an underwriter defaults, the purchase agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the purchase agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the purchase agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the initial public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of $ per share. The underwriters may allow, and the dealers may reallow, a discount not in excess of $ per share to other dealers. After the initial public offering, the public offering price, concession and discount may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their overallotment option.

	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

The expenses of the offering, not including the underwriting discount, are estimated at $ and are payable by us.

Overallotment Option

We have granted an option to the underwriters to purchase up to additional shares at the public offering price, less the underwriting discount. The underwriters may exercise this option for 30 days from the date of this prospectus solely to cover any overallotments. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the purchase agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We and our officers, directors, stockholders, warrant holders and option holders, who hold all of our shares of common stock, on a fully diluted basis, have agreed, subject to certain exceptions, not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 180 days after the date of this prospectus without first obtaining the written consent of Merrill Lynch. Specifically, we and these other individuals have agreed not to directly or indirectly

- offer, pledge, sell or contract to sell any common stock,
- sell any option or contract to purchase any common stock,
- purchase any option or contract to sell any common stock,
- grant any option, right or warrant for the sale of any common stock,
- lend or otherwise dispose of or transfer any common stock,
- request or demand that we file a registration statement related to the common stock, or
- enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any common stock, whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lockup provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

Quotation on the Nasdaq Global Market

We expect the shares to be approved for quotation on the Nasdaq Global Market, subject to notice of issuance, under the symbol "CADX."

Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations among us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us,
- our financial information,
- the history of, and the prospects for, our company and the industry in which we compete,
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues,
- the present state of our development, and

- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares in the offering. The underwriters may close out any covered short position by either exercising their overallotment option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the overallotment option. “Naked” short sales are sales in excess of the overallotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Offer, Sale and Distribution of Shares

A prospectus in electronic format will be made available on the websites maintained by one or more of the underwriters of this offering. Other than the electronic prospectus, the information on the websites of the underwriters is not part of this prospectus. The underwriters may agree to allocate a number of shares to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated to underwriters that may make Internet distributions on the same basis as other allocations.

Other Relationships

Some of the underwriters and their affiliates have provided from time to time, and may provide in the future, investment and commercial banking and financial advisory services to us in the ordinary course of business, for which they have received and may continue to receive customary fees and commissions.

LEGAL MATTERS

The validity of our common stock offered by this prospectus will be passed upon for us by Latham & Watkins LLP, San Diego, California. Latham & Watkins LLP and certain attorneys and investment funds affiliated with the firm collectively own an aggregate of 90,000 shares of our preferred stock, which will convert into an aggregate of 90,000 shares of our common stock upon the completion of this offering. Certain legal matters in connection with this offering will be passed upon for the underwriters by Heller Ehrman LLP, San Diego, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements as of December 31, 2004 and 2005 and for the period from May 26, 2004 (inception) through December 31, 2004 and for the year ended December 31, 2005 as set forth in their report. We have included our financial statements in this prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act of 1933, as amended, with respect to the shares of our common stock offered hereby. This prospectus does not contain all of the information set forth in the registration statement and the exhibits and schedules thereto. Some items are omitted in accordance with the rules and regulations of the SEC. For further information with respect to us and the common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus as to the contents of any contract, agreement or any other document are summaries of the material terms of this contract, agreement or other document. With respect to each of these contracts, agreements or other documents filed as an exhibit to the registration statement, reference is made to the exhibits for a more complete description of the matter involved. A copy of the registration statement, and the exhibits and schedules thereto, may be inspected without charge at the public reference facilities maintained by the SEC at 100 F Street NE, Washington, D.C. 20549. Copies of these materials may be obtained from the Public Reference Section of the SEC at 100 F Street NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facility. The SEC maintains a web site that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address of the SEC's website is http://www.sec.gov.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
Cadence Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of Cadence Pharmaceuticals, Inc. (a development stage company) as of December 31, 2004 and 2005 and the related statements of operations, stockholders' equity and cash flows for the period from May 26, 2004 (inception) through December 31, 2004 and for the year ended December 31, 2005. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Cadence Pharmaceuticals, Inc. (a development stage company) at December 31, 2004 and 2005 and the results of its operations and its cash flows for the period from May 26, 2004 (inception) through December 31, 2004 and for the year ended December 31, 2005 in conformity with generally accepted accounting principles in the United States.

/s/ Ernst & Young LLP

San Diego, California
April 21, 2006

Cadence Pharmaceuticals, Inc.
(a development stage company)

BALANCE SHEETS

	December 31, 2004	December 31, 2005	June 30, 2006 (Unaudited)	Pro Forma Stockholders' Equity at June 30, 2006 (Unaudited)
ASSETS				
Current assets:				
Cash and cash equivalents	$ 4,271,229	$ 8,025,285	$ 42,881,305	
Securities available-for-sale	—	7,000,000	—	
Prepaid expenses and other current assets	3,854	526,173	438,274	
Total current assets	4,275,083	15,551,458	43,319,579	
Property and equipment, net	108,735	117,740	770,693	
Restricted cash	—	—	1,581,130	
Other assets	152,159	100,000	683,405	
Total assets	$ 4,535,977	$ 15,769,198	$ 46,354,807	
LIABILITIES AND STOCKHOLDERS' EQUITY				
Current liabilities:				
Accounts payable	$ 68,509	$ 715,781	$ 1,860,993	
Accrued liabilities	45,965	430,220	2,949,955	
Current portion of long-term debt	—	—	1,032,457	
Total current liabilities	114,474	1,146,001	5,843,405	
Deferred rent	—	—	116,309	
Long-term debt, less current portion	—	—	5,967,543	
Commitments				
Stockholders' equity:				
Preferred stock, $0.0001 par value:				
Series A-1 convertible preferred stock, 8,085,108 shares authorized, issued and outstanding at December 31, 2004 and 2005 and June 30, 2006 (unaudited); aggregate liquidation preference of $7,600,002; no shares issued and outstanding pro forma (unaudited)	809	809	809	$ —
Series A-2 convertible preferred stock, 12,900,001 shares, 17,675,347 shares and 18,060,347 shares authorized at December 31, 2004 and 2005 and June 30, 2006 (unaudited), respectively; no shares, 17,675,347 shares and 17,675,347 shares issued and outstanding at December 31, 2004 and 2005 and June 30, 2006 (unaudited), respectively; aggregate liquidation preference of $17,675,347; no shares issued and outstanding pro forma (unaudited)	—	1,767	1,767	—
Series A-3 convertible preferred stock, 53,870,000 shares authorized at June 30, 2006 (unaudited); 53,870,000 shares issued and outstanding at June 30, 2006 (unaudited); aggregate liquidation preference of $53,870,000; no shares issued and outstanding pro forma (unaudited)	—	—	5,387	—
Common stock, $0.0001 par value; 33,000,000 shares, 40,000,000 shares and 100,000,000 shares authorized at December 31, 2004 and 2005 and June 30, 2006 (unaudited), respectively; 4,680,000 shares, 7,616,000 shares and 8,551,740 shares issued and outstanding at December 31, 2004 and 2005 and June 30, 2006 (unaudited), respectively; 88,182,195 shares issued and outstanding pro forma (unaudited)	468	762	855	8,818
Additional paid-in capital	7,562,463	25,472,308	79,953,466	79,953,466
Stock subscription receivable	—	(187,600)	—	—
Deficit accumulated during the development stage	(3,142,237)	(10,664,849)	(45,534,734)	(45,534,734)
Total stockholders' equity	4,421,503	14,623,197	34,427,550	$ 34,427,550
Total liabilities and stockholders' equity	$ 4,535,977	$ 15,769,198	$ 46,354,807	

See accompanying notes.

Cadence Pharmaceuticals, Inc.
(a development stage company)

STATEMENTS OF OPERATIONS

	Period from May 26, 2004 (Inception) Through December 31, 2004	Year Ended December 31, 2005	Six Months Ended June 30,		Period from May 26, 2004 (Inception) Through June 30, 2006
			2005 (Unaudited)	2006 (Unaudited)	(Unaudited)
Operating expenses:					
Research and development	$ 2,233,357	$ 6,126,226	$ 2,401,589	$ 33,573,970	$ 41,933,553
Marketing	41,114	240,361	142,501	316,541	598,016
General and administrative	877,146	1,411,810	539,914	1,487,980	3,776,936
Total operating expenses	3,151,617	7,778,397	3,084,004	35,378,491	46,308,505
Loss from operations	(3,151,617)	(7,778,397)	(3,084,004)	(35,378,491)	(46,308,505)
Other income (expense):					
Interest income	9,380	255,785	13,996	552,501	817,666
Interest expense	—	—	—	(43,895)	(43,895)
Total other income	9,380	255,785	13,996	508,606	773,771
Net loss	$ (3,142,237)	$ (7,522,612)	$ (3,070,008)	$ (34,869,885)	$ (45,534,734)
Basic and diluted net loss per share	$ (0.86)	$ (1.63)	$ (0.68)	$ (7.01)	
Shares used to compute basic and diluted net loss per share	3,658,356	4,623,517	4,526,865	4,974,000	
Pro forma basic and diluted net loss per share		$ (0.36)		$ (0.59)	
Shares used to compute pro forma basic and diluted net loss per share		20,648,526		58,711,140	

See accompanying notes.

Cadence Pharmaceuticals, Inc.
(a development stage company)

STATEMENTS OF STOCKHOLDERS' EQUITY
For the Period from May 26, 2004 (inception) through June 30, 2006

	Series A-1 Convertible Preferred Stock		Series A-2 Convertible Preferred Stock		Series A-3 Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Stock Subscription Receivable	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Issuance of common stock to founders for cash at $0.001 per share in July	—	$ —	—	$ —	—	$ —	4,500,000	$ 450	$ 4,050	$ —	$ —	$ 4,500
Exercise of common stock options for cash at $0.10 per share in December	—	—	—	—	—	—	180,000	18	17,982	—	—	18,000
Issuance of Series A-1 preferred stock for cash at $0.94 per share, net of $59,573 of offering costs, in July and August	8,085,108	809	—	—	—	—	—	—	7,539,620	—	—	7,540,429
Issuance of common stock options for consulting services in November	—	—	—	—	—	—	—	—	811	—	—	811
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	(3,142,237)	(3,142,237)
Balance at December 31, 2004	8,085,108	809	—	—	—	—	4,680,000	468	7,562,463	—	(3,142,237)	4,421,503
Exercise of common stock options at $0.10 per share in February, June and December, net of the repurchase of 30,000 shares at $0.10 per share	—	—	—	—	—	—	2,936,000	294	293,306	(187,600)	—	106,000
Issuance of Series A-2 preferred stock for cash at $1.00 per share, net of $57,041 of offering costs, in June and September	—	—	17,675,347	1,767	—	—	—	—	17,616,539	—	—	17,618,306
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	(7,522,612)	(7,522,612)
Balance at December 31, 2005	8,085,108	809	17,675,347	1,767	—	—	7,616,000	762	25,472,308	(187,600)	(10,664,849)	14,623,197
Exercise of common stock options for cash between $0.10 and $0.34 per share in January through June (unaudited)	—	—	—	—	—	—	935,740	93	281,099	—	—	281,192
Collection of stock subscription receivable (unaudited)	—	—	—	—	—	—	—	—	—	187,600	—	187,600
Issuance of Series A-3	—	—	—	—	53,870,000	5,387	—	—	53,769,626	—	—	53,775,013

preferred stock for cash at $1.00 per share, net of $94,987 of offering costs, in March (unaudited)												
Issuance of warrants in connection with loan and security agreement in February (unaudited)	—	—	—	—	—	—	—	—	313,572	—	—	313,572
Employee stock-based compensation recognized under SFAS No. 123(R) (unaudited)	—	—	—	—	—	—	—	—	116,861	—	—	116,861
Net loss and comprehensive loss (unaudited)	—	—	—	—	—	—	—	—	—	—	(34,869,885)	(34,869,885)
Balance at June 30, 2006 (unaudited)	8,085,108	$ 809	17,675,347	$1,767	53,870,000	$5,387	8,551,740	$ 855	$79,953,466	$ —	$(45,534,734)	$ 34,427,550

See accompanying notes.

Cadence Pharmaceuticals, Inc.
(a development stage company)

STATEMENTS OF CASH FLOWS

	Period from May 26, 2004 (Inception) Through December 31, 2004	Year Ended December 31, 2005	Six Months Ended June 30, 2005 (Unaudited)	Six Months Ended June 30, 2006 (Unaudited)	Period from May 26, 2004 (Inception) Through June 30, 2006 (Unaudited)
Operating activities					
Net loss	$ (3,142,237)	$ (7,522,612)	$ (3,070,008)	$ (34,869,885)	$ (45,534,734)
Adjustments to reconcile net loss to net cash used in operating activities:					
Depreciation	8,389	36,876	15,771	28,862	74,127
Stock-based compensation	811	—	—	116,861	117,672
Non-cash interest expense	—	—	—	41,665	41,665
Changes in operating assets and liabilities:					
Prepaid expenses and other assets	(56,013)	(470,160)	(260,033)	59,799	(466,374)
Accounts payable, accrued liabilities and deferred rent	114,474	1,031,527	1,157,612	3,510,041	4,656,042
Net cash used in operating activities	(3,074,576)	(6,924,369)	(2,156,658)	(31,112,657)	(41,111,602)
Investing activities					
Purchases of marketable securities	(100,000)	(7,000,000)	—	—	(7,100,000)
Maturities of marketable securities	—	—	—	7,000,000	7,000,000
Restricted cash	—	—	—	(1,581,130)	(1,581,130)
Purchases of property and equipment	(117,124)	(45,881)	(10,719)	(681,815)	(844,820)
Net cash provided by (used in) investing activities	(217,124)	(7,045,881)	(10,719)	4,737,055	(2,525,950)
Financing activities					
Proceeds from issuance of common stock, net	22,500	106,000	109,000	456,609	585,109
Proceeds from sale of preferred stock, net of issuance costs	7,540,429	17,618,306	13,661,958	53,775,013	78,933,748
Borrowings under debt agreements	—	—	—	7,000,000	7,000,000
Net cash provided by financing activities	7,562,929	17,724,306	13,770,958	61,231,622	86,518,857
Increase in cash and cash equivalents	4,271,229	3,754,056	11,603,581	34,856,020	42,881,305
Cash and cash equivalents at beginning of period	—	4,271,229	4,271,229	8,025,285	—
Cash and cash equivalents at end of period	$ 4,271,229	$ 8,025,285	$ 15,874,810	$ 42,881,305	$ 42,881,305
Supplemental schedule of non-cash investing and financing activities					
Issuance of warrants in connection with loan and security agreement	$ —	$ —	$ —	$ 313,572	$ 313,572

See accompanying notes.

Cadence Pharmaceuticals, Inc.
(a development stage company)

NOTES TO FINANCIAL STATEMENTS
(Information as of June 30, 2006 and thereafter and for the six months ended June 30, 2005 and 2006 and the period from May 26, 2004 (inception) through June 30, 2006 is unaudited)

1. The Company and Summary of Significant Accounting Policies

The Company and Basis of Presentation

Cadence Pharmaceuticals, Inc. (the "Company") was incorporated in the state of Delaware in May 2004. The Company is a biopharmaceutical company focused on in-licensing, developing and commercializing proprietary product candidates principally for use in the hospital setting.

The Company's primary activities since incorporation have been organizational activities, including recruiting personnel, establishing office facilities, conducting research and development, including clinical trials, and raising capital. To date, the Company has in-licensed rights to two Phase III product candidates. Since the Company has not begun principal operations of commercializing a product candidate, the Company is considered to be in the development stage.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Unaudited Interim Financial Statements

The accompanying unaudited interim balance sheet as of June 30, 2006, the statements of operations and cash flows for the six months ended June 30, 2005 and 2006 and the period from May 26, 2004 (inception) through June 30, 2006 and the statement of stockholders' equity for the six months ended June 30, 2006 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments necessary to present fairly the Company's financial position as of June 30, 2006 and results of operations and cash flows for the six months ended June 30, 2005 and 2006. The results of operations for the six months ended June 30, 2006 are not necessarily indicative of the results to be expected for the year ending December 31, 2006 or for any other interim period or for any other future year.

Unaudited Pro Forma Stockholders' Equity

The unaudited pro forma stockholders' equity information in the accompanying balance sheet assumes the conversion of the outstanding shares of convertible preferred stock at June 30, 2006 into 79,630,455 shares of common stock as though the completion of the initial public offering contemplated by the filing of this prospectus had occurred on June 30, 2006. Common shares issued in such initial public offering and any related estimated net proceeds are excluded from such pro forma information.

Cash and Cash Equivalents

Cash and cash equivalents consists of cash and other highly liquid investments with original maturities of three months or less from the date of purchase.

Cadence Pharmaceuticals, Inc.
(a development stage company)

NOTES TO FINANCIAL STATEMENTS — (Continued)
(Information as of June 30, 2006 and thereafter and for the six months ended June 30, 2005 and 2006 and the period from May 26, 2004 (inception) through June 30, 2006 is unaudited)

Investment Securities Available-for-Sale

The Company classifies all securities as available-for-sale, as the sale of such securities may be required prior to maturity to implement management strategies. These securities are carried at fair value, with the unrealized gains and losses reported as a component of accumulated other comprehensive loss until realized. Realized gains and losses from the sale of available-for-sale securities, if any, are determined on a specific identification basis. As of December 31, 2004 and 2005 and June 30, 2006, the carrying value of the investments approximated their fair market value.

Fair Value of Financial Instruments

The carrying amount of cash and cash equivalents, accounts payable and accrued liabilities are considered to be representative of their respective fair values because of the short-term nature of those instruments.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a significant concentration of credit risk consist primarily of cash and cash equivalents and securities available-for-sale. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. However, management believes the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. Additionally, the Company has established guidelines regarding diversification of its investments and their maturities, which are designed to maintain safety and liquidity.

Property and Equipment

Property and equipment, including leasehold improvements, are stated at cost. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, generally two to five years. Leasehold improvements are amortized over the shorter of their useful lives or the terms of the related leases.

Impairment of Long-Lived Assets

In accordance with Statement of Financial Accounting Standards (“SFAS”) No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*, long-lived assets, such as property and equipment are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized by the amount by which the carrying amount of the asset exceeds the fair value of the asset. Assets to be disposed of would be separately presented in the balance sheet and reported at the lower of the carrying amount or the fair value less costs to sell, and are no longer depreciated. The assets and liabilities of a disposed group classified as held for sale would be presented separately in the appropriate asset and liability sections of the balance sheet. Although the Company has accumulated losses since inception, the Company believes the future cash flows to be received from the long-lived assets will exceed the assets’ carrying value and, accordingly, the Company has not recognized any impairment losses through June 30, 2006.

Cadence Pharmaceuticals, Inc.
(a development stage company)

NOTES TO FINANCIAL STATEMENTS — (Continued)
(Information as of June 30, 2006 and thereafter and for the six months ended June 30, 2005 and 2006 and the period from May 26, 2004 (inception) through June 30, 2006 is unaudited)

Research and Development

The Company accounts for research and development costs in accordance with SFAS No. 2, *Accounting for Research and Development Costs.* SFAS No. 2 specifies that research and development costs should be charged to expense until technological feasibility has been established for the product. Once technological feasibility is established, all product costs should be capitalized until the product is available for general release to customers. The Company has determined that technological feasibility for its product candidates is reached when the requisite regulatory approvals are obtained to make the product available for sale. The Company's research and development expenses consist primarily of license fees, salaries and related employee benefits, costs associated with clinical trials managed by the Company's contract research organizations, or CROs, and costs associated with non-clinical activities, such as regulatory expenses. The Company uses external service providers and vendors to conduct clinical trials, to manufacture product candidates to be used in clinical trials and to provide various other research and development related products and services. Through June 30, 2006, research and development expenses relate predominantly to the in-licensing of IV APAP and Omigard and clinical trials for Omigard.

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized.

Stock-Based Compensation

Effective January 1, 2006, the Company adopted the provisions of SFAS No. 123(R), *Share-Based Payment*, using the prospective transition method and therefore, prior period results will not be restated. SFAS No. 123(R) supersedes Accounting Principles Board ("APB") Opinion No. 25, *Accounting for Stock issued to Employees*, and related interpretations, and revises guidance in SFAS No. 123, *Accounting for Stock-Based Compensation.* Under this transition method, the compensation cost related to all equity instruments granted prior to, but not yet vested as of, the adoption date is recognized based on the grant-date fair value which is estimated in accordance with the original provisions of SFAS No. 123; however, those options issued prior to but unvested on January 1, 2006 and valued using the minimum value method are excluded from the options subject to SFAS No. 123(R). Compensation costs related to all equity instruments granted after January 1, 2006 is recognized at grant-date fair value of the awards in accordance with the provisions of SFAS No. 123(R). Additionally, under the provisions of SFAS No. 123(R), the Company is required to include an estimate of the number of the awards that will be forfeited in calculating compensation costs, which is recognized over the requisite service period of the awards on a straight-line basis.

During the six months ended June 30, 2006, the Company recorded $116,861, or $0.02 per share, of stock-based compensation expense as a result of the adoption of SFAS No. 123(R). Of this amount,

Cadence Pharmaceuticals, Inc.
(a development stage company)

NOTES TO FINANCIAL STATEMENTS — (Continued)
(Information as of June 30, 2006 and thereafter and for the six months ended June 30, 2005 and 2006 and the period from May 26, 2004 (inception) through June 30, 2006 is unaudited)

the Company allocated $20,339, $84 and $96,438 to research and development, sales and marketing and general and administrative expenses, respectively, based on the department to which the associated employee reports. No related tax benefits of the stock-based compensation costs have been recognized since the inception of the Company.

The following table shows the assumptions used to compute the stock-based compensation costs for the stock options granted during the six months ended June 30, 2006 using the Black-Scholes option pricing model:

Employee Stock Options	
Risk-free interest rate	4.36 – 5.08%
Dividend yield	0.00%
Expected life of options (years)	6.06 – 6.08
Volatility	70.00%

The risk-free interest rate assumption was based on the United States Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the award being valued. The assumed dividend yield was based on the Company's expectation of not paying dividends in the foreseeable future. The weighted average expected life of options was calculated using the simplified method as prescribed by Securities and Exchange Commission ("SEC") Staff Accounting Bulletin ("SAB") No. 107. This decision was based on the lack of relevant historical data due to the Company's limited historical experience. In addition, due to the Company's limited historical data, the estimated volatility also reflects the application of SAB No. 107, incorporating the historical volatility of comparable companies whose share prices are publicly available.

The weighted average grant-date fair values of stock options granted during the six months ended June 30, 2006 was $0.29 per share.

As of June 30, 2006, the Company has approximately $1,479,000 of unrecognized stock-based compensation costs related to the non-vested balance of the 5,549,211 stock options granted during the six months ended June 30, 2006 and expects to recognize such compensation over a weighted average period of 3.71 years.

Prior to January 1, 2006, the Company applied the intrinsic-value-based method of accounting prescribed by APB Opinion No. 25, and related interpretations including Financial Accounting Standards Board ("FASB") Interpretation No. 44, *Accounting for Certain Transactions involving Stock Compensation — an interpretation of APB Opinion No. 25*, to account for its equity-based awards to employees and directors. Under this method, if the exercise price of the award equaled or exceeded the fair value of the underlying stock on the measurement date, no compensation expense was recognized. The measurement date was the date on which the final number of shares and exercise price were known and was generally the grant date for awards to employees and directors. If the exercise price of the award was below the fair value of the underlying stock on the measurement date, then compensation cost was recorded, using the intrinsic-value method, and was generally recognized in the statements of operations over the vesting period of the award.

The effect on net loss as if the fair-value-based method had been applied to all outstanding and unvested awards in each period would have been less than a $10,000 increase in the net loss for each period in the period from May 26, 2004 (inception) through December 31, 2005. For purposes of

Cadence Pharmaceuticals, Inc.
(a development stage company)

NOTES TO FINANCIAL STATEMENTS — (Continued)
(Information as of June 30, 2006 and thereafter and for the six months ended June 30, 2005 and 2006 and the period from May 26, 2004 (inception) through June 30, 2006 is unaudited)

disclosures required by SFAS No. 123, the estimated fair value of the options was amortized on a straight-line basis over the vesting period. The fair value of these awards was estimated using the Minimum Value pricing model, with the following weighted-average assumptions for 2004 and 2005: risk-free interest rate of 3.53% and 4.17%, respectively; dividend yield of 0%; expected volatility of 0%; and a life of four years.

Equity instruments issued to non-employees are recorded at their fair value as determined in accordance with SFAS No. 123(R) and Emerging Issues Task Force ("EITF") 96-18, *Accounting for Equity Instruments That are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods and Services*, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period. Compensation expense related to the 10,000 stock options issued to a non-employee was $811 for both the period from May 26, 2004 (inception) through December 31, 2004 and the period from May 26, 2004 (inception) through June 30, 2006. The fair value of these stock options was estimated using the Black-Scholes pricing model, with the following weighted-average assumptions: risk-free interest rate of 4.19%; dividend yield of 0%; expected volatility of 70%; and a life of 10 years.

Comprehensive Income

The Company has applied SFAS No. 130, *Reporting Comprehensive Income*, which requires that all components of comprehensive income, including net income, be reported in the financial statements in the period in which they are recognized. Comprehensive income is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. Net income and other comprehensive income, including foreign currency translation adjustments and unrealized gains and losses on investments, shall be reported, net of their related tax effect, to arrive at comprehensive income. The net loss and comprehensive loss were the same for all periods presented.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, convertible preferred stock, stock options and warrants are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The unaudited pro forma basic and diluted net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period plus the weighted average number of common shares resulting from the assumed conversion of the outstanding shares of convertible preferred stock. The assumed conversion is calculated using the as-if-converted method, as if such conversion had occurred as of the beginning of each period presented or as of the original issuance date, if later.

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(Information as of June 30, 2006 and thereafter and for the six months ended June 30, 2005 and 2006 and the period from May 26, 2004 (inception) through June 30, 2006 is unaudited)

	Period from May 26, 2004 (Inception) Through December 31, 2004	Year Ended December 31, 2005	Six Months Ended June 30, 2005	Six Months Ended June 30, 2006
Historical				
Numerator:				
Net loss	$ (3,142,237)	$ (7,522,612)	$ (3,070,008)	$ (34,869,885)
Denominator:				
Weighted average common shares outstanding	3,680,548	5,277,468	4,770,055	7,826,825
Weighted average unvested common shares subject to repurchase	(22,192)	(653,951)	(243,190)	(2,852,825)
Weighted average common shares outstanding	3,658,356	4,623,517	4,526,865	4,974,000
Basic and diluted net loss per share	$ (0.86)	$ (1.63)	$ (0.68)	$ (7.01)
Pro Forma				
Net loss used above		$ (7,522,612)		$ (34,869,885)
Pro forma basic and diluted net loss per share		$ (0.36)		$ (0.59)
Shares used above		4,623,517		4,974,000
Pro forma adjustments to reflect assumed weighted average effect of conversion of preferred stock		16,025,009		53,737,140
Pro forma shares used to compute basic and diluted net loss per share		20,648,526		58,711,140
Historical weighted average anti-dilutive securities not included in diluted net loss per share calculation				
Preferred stock	5,661,130	16,025,009	8,085,108	53,737,140
Common stock options	—	—	—	1,345,271
Common stock subject to repurchase	22,192	653,951	243,190	2,852,825
	5,683,322	16,678,960	8,328,298	57,935,236

2. Securities Available-for-Sale

As of December 31, 2005, the Company held $7,000,000 of commercial paper issued by U.S. corporations and rated by debt rating agencies.

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3. Property and Equipment

Property and equipment are as follows:

	Useful Lives	December 31, 2004	December 31, 2005	June 30, 2006
Leasehold improvements	2 years	$ 1,146	$ 1,146	$ 1,146
Computer equipment and software	3 years	55,245	63,972	186,006
Furniture and equipment	5 years	60,733	94,982	94,982
Manufacturing equipment	7 years	—	—	122,500
Construction in-process	—	—	—	437,281
		117,124	160,100	841,915
Less accumulated depreciation		(8,389)	(42,360)	(71,222)
		$ 108,735	$ 117,740	$ 770,693

4. Related Party Transactions

From September 2004 through August 2005, the Company paid Mr. Cam L. Garner $5,000 per month plus qualified business expenses for his services as chairman of the Company's board of directors under the terms of a consulting agreement between the Company and a limited liability company affiliated with Mr. Garner. The agreement expired on August 31, 2005. From September 2005 to February 2006, the Company continued to pay Mr. Garner $5,000 per month for his services as chairman of the Company's board of directors. In March 2006, Mr. Garner's monthly compensation for his services as chairman of the Company's board of directors was increased to $8,333 per month. For the period from May 26, 2004 (inception) through December 31, 2004, the year ended December 31, 2005, the six months ended June 30, 2005 and 2006 and the period from May 26, 2004 (inception) through June 30, 2006, the Company expensed $20,000, $60,000, $30,000, $43,333, and $123,333, respectively for payments to Mr. Garner for services as chairman of the Company's board of directors. The unpaid balance as of December 31, 2004 and 2005 and June 30, 2006 was $20,000, $10,000 and $8,333, respectively.

During 2004, a stockholder advanced $500,000 for pre-operating expenses and an exclusivity fee due for the collaboration and license agreement with Migenix (see Note 6). The advance was accounted for in accordance with the SEC SAB Topic 5T (SAB No. 79), *Accounting for Expenses or Liabilities Paid by Principal Stockholder(s)*, which requires the Company to record expenses for services paid by stockholders for the benefit of the Company as if such expenses had been paid directly by the Company. The 531,915 shares of Series A-1 preferred stock issued in settlement of the $500,000 advance were valued at $0.94 per share, the price paid by new Series A-1 investors. The transaction was recorded as a $500,000 cash investment in Series A-1 preferred stock by the stockholder and a corresponding cash payment of $500,000 for operating expenses.

5. Commitments

Loan and Security Agreement

In February 2006, the Company entered into a $7,000,000 loan and security agreement with Silicon Valley Bank and Oxford Finance Corporation to provide growth capital to the Company. In

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June 2006, the Company drew down $7,000,000 under the loan and security agreement with Silicon Valley Bank and Oxford Finance Corporation and has no further credit available under this agreement. The Company will make interest only payments on growth capital advances until the first day of the month following the six month anniversary of each growth capital advance, at which date the Company will make the first of 30 equal principal and interest payments. Interest accrues on all outstanding amounts at the fixed rate equal to the greater of (a) 10.83% or (b) the Treasury Rate plus 6.25% as of the date the first principal and interest payment is due. The loans are collateralized by substantially all the assets of the Company (excluding intellectual property) and are subject to prepayment penalties. Under the terms of the agreement, the Company may be precluded from entering into certain financing and other transactions, including disposing of certain assets and paying dividends, and is subject to certain non-financial covenants. Upon the occurrence of an event of default, including a Material Adverse Change (as defined in the agreement), the lenders may declare all outstanding amounts due and payable.

In conjunction with the loan and security agreement, the Company issued fully exercisable warrants to the lenders to purchase an aggregate of 385,000 shares of the Company's Series A-2 preferred stock at an exercise price of $1.00 per share. Excluding certain mergers or acquisitions, the warrants expire upon the later of: (a) 10 years from issuance or (b) five years after the closing of an initial public offering of the Company's common stock. The $313,572 fair value of the warrants was determined using the Black-Scholes valuation model, recorded as debt issuance costs which are included as other long-term assets in the accompanying balance sheets, and amortized to interest expense over the expected term of the loan agreement. The warrants were valued using the following assumptions: risk-free interest rate of 4.57%; dividend yield of 0%; expected volatility of 70%; and contractual term of 10 years.

Facility Leases

In 2004, the Company subleased its corporate headquarters under a non-cancelable operating lease that expires in September 2006. As of December 31, 2005 and June 30, 2006, the sublessor held a security deposit of $50,685. In May 2006, the Company entered into a six-year operating lease for 23,494 square feet of office space. The Company will receive certain tenant improvement allowances and rent abatement and has an option to extend the lease for five years. Monthly rental payments are adjusted on an annual basis and the lease expires in September 2012. As security for the lease, the landlord required a letter of credit in the amount of $1,581,130. The letter of credit is collateralized by a certificate of deposit in the same amount that is classified as restricted cash in the accompanying balance sheet. The required amount subject to the letter of credit and corresponding certificate of deposit will be reduced by 22% on each of the first four anniversaries of the commencement of the lease. Rent expense was $67,579, $190,911, $89,542, $274,231 and $309,174 for the period from May 26, 2004 (inception) through December 31, 2004, the year ended December 31, 2005, the six months ended June 30, 2005 and 2006 and the period from May 26, 2004 (inception) through June 30, 2006, respectively. As of June 30, 2006, future minimum payments under the operating leases total $186,999, $1,009,000, $1,074,851, $1,112,206, $1,151,676, $1,191,851 and $917,676 for the years ending December 31, 2006, 2007, 2008, 2009, 2010, 2011 and 2012, respectively.

6. License Agreements and Acquired Development and Commercialization Rights

In July 2004, the Company in-licensed from Migenix the technology and the exclusive development and commercialization rights to its omiganan pentahydrochloride product candidate for the prevention and treatment of device-related, wound-related, and burn-related infections in North America

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and Europe. As consideration for the license, the Company paid a $2,000,000 up-front fee, of which $1,900,000 was allocated to the value of the acquired technology and $100,000 was recorded as other long-term assets in the accompanying balance sheet for the 617,284 shares of Migenix common stock acquired. The Company may also be required to make future milestone payments totaling up to $27,000,000 upon the achievement of various milestones related to regulatory or commercial events. The Company is also obligated to pay a royalty on future net sales (as defined) of the licensed products and has the right to grant sublicenses to affiliates. The Company expects results from Phase III clinical trials for the licensed product in the second half of 2007 but does not expect FDA approval prior to 2008. Accordingly, all payments related to the Migenix agreement (other than for the acquisition of common stock) have been recorded as research and development expense.

In March 2006, the Company in-licensed the technology and the exclusive development and commercialization rights to its IV APAP product candidate in the United States and Canada from Bristol-Myers Squibb Company (“BMS”). BMS sublicensed these rights to the Company under a license agreement with SCR Pharmatop S.A. As consideration for the license, the Company paid a $25,000,000 up-front fee, and may be required to make future milestone payments totaling up to $50,000,000 upon the achievement of various milestones related to regulatory or commercial events. The Company is also obligated to pay a royalty on net sales of the licensed products and has the right to grant sublicenses to third parties. The Company expects to initiate Phase III clinical trials for the licensed product in 2006 but does not expect FDA approval prior to 2008. Accordingly, all payments related to the BMS agreement have been recorded as research and development expense.

7. Stockholders’ Equity

Convertible Preferred Stock

In July and August 2004, the Company issued 8,085,108 shares of Series A-1 preferred stock at $0.94 per share for cash of $7,600,002. The Company incurred offering costs of $59,573 resulting in net cash proceeds of $7,540,429.

In June and September 2005, the Company issued an aggregate of 17,675,347 shares of Series A-2 preferred stock at $1.00 per share for cash of $17,675,347. The Company incurred offering costs of $57,041 resulting in net cash proceeds of $17,618,306.

In March 2006, the Company issued 53,870,000 shares of Series A-3 preferred stock at $1.00 per share for cash of $53,870,000. The Company incurred offering costs of $94,987 resulting in net cash proceeds of $53,775,013.

Each holder of Series A-1, A-2 and A-3 preferred stock has the right, at the option of the holder at any time, to convert shares of preferred stock into shares of common stock at a conversion ratio of one-to-one, subject to adjustment for stock splits, certain capital reorganizations and dilutive stock issuances. As of June 30, 2006, there have been no adjustments to the conversion ratios of any series of preferred stock. Each share of preferred stock will automatically convert into shares of common stock, at the then effective applicable conversion rate upon the earlier of: (i) the day preceding the closing of the sale of the Company’s common stock in connection with a firmly underwritten public offering in which the Company receives gross proceeds of at least $30,000,000 at a price of at least $3.00 per share (as adjusted from time to time) or (ii) the consent of at least 60% of the then outstanding shares of preferred stock, as a single class.

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Unless 60% of the Series A-3 preferred stockholders vote otherwise, certain Series A-3 preferred stockholders that fail to participate in future equity financings up to specified amounts will lose their right of first offer related to any subsequent equity financings and any Series A-1 preferred stock held by them will automatically convert into newly created Series A-4 preferred stock and any Series A-2 and A-3 preferred stock held by them will automatically convert into newly created Series A-5 preferred stock. Series A-4 and A-5 preferred stock shall have identical rights and preferences as Series A-1, A-2 and A-3 preferred stock with the exception of certain anti-dilution protections.

The holders of Series A-1, A-2 and A-3 preferred stock are entitled to receive, when, as and if declared by the Company's Board of Directors out of legally available funds, non-cumulative dividends payable to holders of the preferred stock in an amount equal to $0.0752, $0.08 and $0.08 per share, respectively, in preference and priority to the payment of any dividends on common stock. As of December 31, 2005 and June 30, 2006, no dividends have been declared by the Board of Directors.

In the event of any liquidation, dissolution or winding up of the Company, the holders of Series A-1, A-2 and A-3 preferred stock will be entitled to receive in preference to the holders of common stock, the amount of their original purchase price per share, plus declared and unpaid dividends, if any. If the assets and funds available to be distributed among the holders of the preferred stock shall be insufficient to permit the payment to such holders of the full preferences, then the entire assets and funds legally available for distribution to such holders shall be distributed ratably based on the total due each such holder. Any remaining assets of the Company will be distributed ratably among the holders of the common stock and preferred stock, with the preferred stock limited to the aggregate of three times the original purchase price per share, based upon the number of shares of common stock held by each stockholder, treating each share of preferred stock as if it were converted into shares of common stock at the then-applicable conversion rate.

Preferred stockholders are entitled to the number of votes they would have upon conversion of their preferred shares into common stock at the then-applicable conversion rate. The preferred stockholders have been granted certain rights with regard to the election of board members and various other corporate actions.

Stock Options

In 2004, the Company adopted the Cadence Pharmaceuticals, Inc. 2004 Equity Incentive Plan (the "2004 Plan"). The 2004 Plan allows for the grant of options, restricted stock awards, performance share awards, dividend equivalents, restricted stock units, stock payments and stock appreciation rights to employees, directors and consultants of the Company. As of December 31, 2005 and June 30, 2006, respectively, the 2004 Plan had 4,500,000 and 11,500,000 shares of common stock reserved for issuance. Options granted under the 2004 Plan expire no later than 10 years from the date of grant. Options generally vest over a four-year period and may be immediately exercisable. After one year, the options generally vest 25%. Thereafter, options generally vest monthly in 36 equal installments. The exercise price of incentive stock options shall not be less than 100% of the fair value of the Company's common stock on the date of grant. The exercise price of any option granted to a 10% stockholder may be no less than 110% of the fair value of the Company's common stock on the date of grant. The fair value of the Company's common stock is established contemporaneously by the Company's board of directors all of whom are related parties. From May 26, 2004 (inception) through February 2006 the valuations were performed by the Company's board of directors who have experience in valuing early stage companies. Beginning in

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March 2006 the board of directors established the fair value of the Company's common stock based on contemporaneous independent valuations of the Company's common stock performed by an unrelated valuation specialist.

The Company has applied the guidance in the American Institute of Certified Public Accountants ("AICPA") Audit and Accounting Practice Aid Series, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, to determine the fair value of its common stock for purposes of setting the exercise prices of stock options granted to employees and others. This guidance emphasizes the importance of the operational development in determining the value of the enterprise. As a development stage enterprise, the Company is at an early stage of existence, primarily focused on product development with an unproven business model. To date, the Company has been funded primarily by venture capitalists with a history of funding start-up, high-risk entities with the potential for high returns in the event the investments are successful. Prior to the licensing of IV APAP in March 2006, the Company was considered to be in a very early stage of development as defined in the AICPA guidance where the preferences of the preferred stockholders, in particular the liquidation preferences, are very meaningful. Subsequent to the Company's licensing of IV APAP but prior to the initiation of the Company's initial public offering process on June 14, 2006, based on a contemporaneous independent valuation performed by an unrelated valuation specialist, the Company allocated additional enterprise value to its common stock with an increase in the common stock valuation to $0.34 per share. Subsequent to the initiation of the initial public offering process, based on a contemporaneous independent valuation performed by an unrelated valuation specialist, the Company increased its common stock valuation to $0.80 per share.

At December 31, 2005 and June 30, 2006, respectively, a total of 228,000 and 1,678,789 shares of common stock remained available for issuance under the 2004 Plan. A summary of the Company's stock option activity under the 2004 Plan and related information are as follows:

	Options Outstanding	Weighted Average Exercise Price
Granted	1,225,000	$ 0.10
Exercised	(180,000)	$ 0.10
Balance at December 31, 2004	1,045,000	$ 0.10
Granted	3,077,000	$ 0.10
Exercised	(2,966,000)	$ 0.10
Balance at December 31, 2005	1,156,000	$ 0.10
Granted	5,549,211	$ 0.43
Exercised	(935,740)	$ 0.30
Balance at June 30, 2006	5,769,471	$ 0.38

	December 31, 2005				
	Options Outstanding			Options Exercisable	
Exercise Price	Number Outstanding	Weighted Average Remaining Contractual Life (in years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$0.10	1,156,000	9.24	$ 0.10	989,521	$ 0.10

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	June 30, 2006					
	Options Outstanding			Options Exercisable		
Exercise Price	Number Outstanding	Weighted Average Remaining Contractual Life (in years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Remaining Contractual Life (in years)	Weighted Average Exercise Price
$0.10	1,017,000	8.72	$ 0.10	852,394	8.69	$ 0.10
$0.34	3,714,471	9.86	$ 0.34	3,561,771	9.86	$ 0.34
$0.80	1,038,000	9.96	$ 0.80	1,005,000	9.96	$ 0.80
	5,769,471	9.68	$ 0.38	5,419,165	9.70	$ 0.39

During the period from May 26, 2004 (inception) through December 31, 2004 and the quarterly periods ended March 31, 2005, June 30, 2005, September 30, 2005, December 31, 2005, March 31, 2006, and June 30, 2006 the Company granted options to purchase shares of the Company's common stock in the amount of 1,225,000, 650,000, 360,000, 191,000, 1,876,000, 15,000 and 5,534,211, respectively. All such grants had both a fair value and exercise price of $0.10 for periods through March 31, 2006. During the quarterly period ended June 30, 2006, both the fair value and exercise price of 4,496,211 and 1,038,000 option grants was $0.34 and $0.80, respectively.

As of December 31, 2005 and June 30, 2006, respectively, 186,813 and 341,768 of the outstanding options under the 2004 plan were vested and 2,767,875 and 3,440,257 of the options exercised were subject to repurchase by the Company since they were unvested.

The aggregate fair value of options that vested during the six months ended June 30, 2006 was approximately $12,000. The aggregate intrinsic value of options exercised during the six months ended June 30, 2006 was approximately $360,000.

The aggregate intrinsic value of options outstanding and options exercisable as of June 30, 2006 was approximately $2,421,000 and $2,235,000, respectively.

Shares Reserved For Future Issuance

The following shares of common stock are reserved for future issuance:

	December 31, 2005	June 30, 2006
Conversion of preferred stock	25,760,455	79,630,455
Common stock options granted and outstanding	1,156,000	5,769,471
Preferred stock warrants outstanding	—	385,000
Common stock options reserved for future issuance	228,000	1,678,789
	27,144,455	87,463,715

8. Income Taxes

Significant components of the Company's deferred tax assets for federal and state income taxes at December 31, 2004 and 2005 are shown below. A valuation allowance has been established as realization

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of such deferred tax assets has not met the more likely than not threshold requirement under SFAS No. 109.

	December 31, 2004	December 31, 2005
Deferred tax assets:		
Net operating loss carryforwards	$ 361,000	$ 3,528,000
Tax credit carryforwards	29,000	359,000
Capitalized research and development	591,000	520,000
Other, net	157,000	111,000
Total deferred tax assets	1,138,000	4,518,000
Valuation allowance for deferred tax assets	(1,138,000)	(4,518,000)
Net deferred taxes	$ —	$ —

At December 31, 2005, the Company had federal and state net operating loss carryforwards of approximately $8,659,000 and $8,663,000, respectively. The federal and state tax loss carryforwards will begin to expire in 2024 and 2014, respectively, unless previously utilized. The Company also had federal research and development tax credit carryforwards of approximately $283,000 which will begin expiring in 2024 unless previously utilized. The Company had state research and development tax credit carryforwards of approximately $116,000, which carryforward indefinitely.

Utilization of the net operating loss carry forwards and credits may be subject to a substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization.

9. Employee Benefit Plan

Effective January 1, 2005, the Company established a 401(k) plan covering substantially all employees. Employees may contribute up to 100% of their compensation per year (subject to a maximum limit prescribed by federal tax law). The Company may elect to make a discretionary contribution or match a discretionary percentage of employee contributions. As of December 31, 2005 and June 30, 2006, the Company had not elected to make any contributions to the plan.

Through and including , 2006 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Shares

Common Stock

PROSPECTUS

Merrill Lynch & Co.
Deutsche Bank Securities
Pacific Growth Equities, LLC
JMP Securities

, 2006

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. *Other Expenses of Issuance and Distribution*

The following table sets forth the fees and expenses, other than underwriting discounts and commissions, payable by us in connection with the registration of the common stock hereunder. All amounts shown are estimates except for the SEC registration fee, the NASD filing fee and the Nasdaq Global Market listing fee.

Item	Amount to be Paid
SEC Registration Fee	$ 9,229
NASD Filing Fee	9,125
Nasdaq Global Market Listing Fee	100,000
Legal Fees and Expenses	*
Accounting Fees and Expenses	*
Printing and Engraving Expenses	*
Blue Sky, Qualification Fees and Expenses	*
Transfer Agent and Registrar Fees	*
Miscellaneous Expenses	*
Total	$ *

* To be completed by amendment.

Item 14. *Indemnification of Directors and Officers*

Section 145 of the Delaware General Corporation Law permits a corporation to include in its charter documents, and in agreements between the corporation and its directors and officers, provisions expanding the scope of indemnification beyond that specifically provided by the current law.

Our amended and restated certificate of incorporation provides for the indemnification of directors to the fullest extent permissible under Delaware law.

Our amended and restated bylaws provide for the indemnification of officers, directors and third parties acting on our behalf if such persons act in good faith and in a manner reasonably believed to be in and not opposed to our best interest, and, with respect to any criminal action or proceeding, such indemnified party had no reason to believe his or her conduct was unlawful.

We are entering into indemnification agreements with each of our directors and executive officers, in addition to the indemnification provisions provided for in our charter documents, and we intend to enter into indemnification agreements with any new directors and executive officers in the future.

The underwriting agreement (to be filed as Exhibit 1.1 hereto) will provide for indemnification by the underwriters of us, our executive officers and directors, and indemnification of the underwriters by us for certain liabilities, including liabilities arising under the Securities Act of 1933, as amended, in connection with matters specifically provided in writing by the underwriters for inclusion in the registration statement.

We intend to purchase and maintain insurance on behalf of any person who is or was a director or officer against any loss arising from any claim asserted against him or her and incurred by him or her in that capacity, subject to certain exclusions and limits of the amount of coverage.

Item 15. ***Recent Sales of Unregistered Securities***

Since inception, we have issued and sold the following unregistered securities:

1. In July 2004, we issued 4,500,000 shares of common stock to a limited liability company and individual investors for aggregate consideration of $4,500.

2. In July and August 2004, we issued and sold an aggregate of 8,085,108 shares of Series A-1 preferred stock to certain venture capital funds and individual investors at a per share price of $0.94, for aggregate consideration of $7,600,001.52. Upon completion of this offering, these shares of Series A-1 preferred stock will convert into 8,085,108 shares of our common stock.

3. In June and September 2005, we issued and sold an aggregate of 17,675,347 shares of Series A-2 preferred stock to certain existing and new investors at a per share price of $1.00, for aggregate consideration of $17,675,347. Upon completion of this offering, these shares of Series A-2 preferred stock will convert into 17,675,347 shares of our common stock.

4. In February 2006, in connection with a loan and security agreement, we issued two warrants to two lenders to purchase an aggregate of 385,000 shares of Series A-2 preferred stock, at an initial exercise price of $1.00 per share, subject to adjustment. The warrants are exercisable through the later of February 2016 or five years from the closing of this offering. These warrants will be exercisable for an aggregate of 385,000 shares of common stock at an exercise price of $1.00 per share upon the completion of this offering.

5. In March 2006, we issued and sold an aggregate of 53,870,000 shares of Series A-3 preferred stock to certain existing and new investors at a per share price of $1.00, for aggregate consideration of $53,870,000. Upon completion of this offering, these shares of Series A-3 preferred stock will convert into 53,870,000 shares of our common stock.

6. Since our inception through June 30, 2006, we granted stock options to purchase 9,851,211 shares of our common stock at exercise prices from $0.10 to $0.80 per share to our employees, consultants and directors under our 2004 equity incentive award plan. Since our inception through June 30, 2006, we issued and sold an aggregate of 4,081,740 shares of our common stock to our employees, consultants and directors at prices from $0.10 to $0.34 per share pursuant to exercises of options granted under our 2004 equity incentive award plan. During this period, 30,000 unvested shares were repurchased by us at $0.10 per share resulting in a net of 4,051,740 shares issued and sold under our 2004 equity incentive award plan.

The issuance of securities described above in paragraphs (1) through (5) were exempt from registration under the Securities Act of 1933, as amended, in reliance on Section 4(2) of the Securities Act of 1933, as amended, and Regulation D promulgated thereunder, as transactions by an issuer not involving any public offering. The purchasers of the securities in these transactions represented that they were accredited investors or qualified institutional buyers and they were acquiring the securities for investment only and not with a view toward the public sale or distribution thereof. Such purchasers received written disclosures that the securities had not been registered under the Securities Act of 1933, as amended, and that any resale must be made pursuant to a registration statement or an available exemption from registration. All purchasers either received adequate financial statement or non-financial statement information about the registrant or had adequate access, through their relationship with the registrant, to financial statement or non-financial statement information about the registrant. The sale of these securities was made without general solicitation or advertising.

The issuance of securities described above in paragraph (6) was exempt from registration under the Securities Act of 1933, as amended, in reliance on Rule 701 of the Securities Act of 1933, as amended, pursuant to compensatory benefit plans approved by the registrant’s board of directors.

All certificates representing the securities issued in these transactions described in this Item 15 included appropriate legends setting forth that the securities had not been offered or sold pursuant to a

registration statement and describing the applicable restrictions on transfer of the securities. There were no underwriters employed in connection with any of the transactions set forth in this Item 15.

Item 16. ***Exhibits and Financial Statement Schedules***

(a) *Exhibits*

Exhibit Number	Description
1.1*	Form of Underwriting Agreement
3.1(1)	Restated Certificate of Incorporation of the Registrant, as currently in effect
3.2(2)	Certificate of Amendment to Restated Certificate of Incorporation of the Registrant, as currently in effect
3.3(2)	Form of Amended and Restated Certificate of Incorporation of the Registrant, to be in effect upon completion of the offering
3.4(1)	Amended and Restated Bylaws of the Registrant, as currently in effect
3.5(2)	Form of Amended and Restated Bylaws of the Registrant, to be in effect upon completion of the offering
4.1*	Form of the Registrant's Common Stock Certificate
4.2(1)	Amended and Restated Investor Rights Agreement dated February 21, 2006
4.3(1)	Warrant issued by Registrant in February 2006 to Silicon Valley Bank
4.4(1)	Warrant issued by Registrant in February 2006 to Oxford Finance Corporation
5.1*	Opinion of Latham & Watkins LLP
10.1(2)	Form of Director and Executive Officer Indemnification Agreement
10.2(2)	Form of Executive Officer Employment Agreement
10.3#(1)	2004 Equity Incentive Award Plan and forms of option agreements thereunder
10.4#(2)	Director Equity Compensation Policy
10.5#(2)	2006 Equity Incentive Award Plan and forms of option and restricted stock agreements thereunder
10.6(2)	Form of Amended and Restated Restricted Common Stock Purchase Agreement
10.7#(2)	2006 Corporate Bonus Plan
10.8(1)	Sublease dated August 31, 2004 by and between the Registrant and Townsend and Townsend and Crew, LLP
10.9(1)	Lease dated May 12, 2006 by and between the Registrant and Prentiss/ Collins Del Mar Heights LLC
10.10†	Collaboration and License Agreement dated July 30, 2004 by and between the Registrant and Migenix Inc. (formerly Micrologix Biotech Inc.)
10.11†	IV APAP Agreement (US and Canada) dated February 21, 2006 by and between the Registrant and Bristol-Myers Squibb Company
10.12†	License Agreement dated December 23, 2002 by and among SCR Pharmatop and Bristol-Myers Squibb Company
10.13(1)	Loan and Security Agreement dated February 17, 2006 by and among the Registrant, Silicon Valley Bank and Oxford Finance Corporation
10.14†	Clinical Supply Agreement dated February 21, 2006 by and between the Registrant and Lawrence Laboratories
10.15†	Engagement Letter dated May 19, 2005 by and between the Registrant and Clearview Projects, Inc.
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm
23.2*	Consent of Latham & Watkins LLP (included in Exhibit 5.1)

Exhibit Number	Description
24.1(1)	Power of Attorney
24.2(2)	Power of Attorney

* To be filed by amendment.

(1) Filed with the Registrant's Registration Statement on Form S-1 on July 17, 2006.

(2) Filed with Amendment No. 1 to the Registrant's Registration Statement on Form S-1 on August 30, 2006.

† Confidential treatment has been requested for portions of this exhibit. These portions have been omitted from the Registration Statement and submitted separately to the Securities and Exchange Commission.

# Indicates management contract or compensatory plan.

(b) *Financial Statement Schedules*

Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. ***Undertakings***

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933, as amended, and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933, as amended, and will be governed by the final adjudication of such issue.

We hereby undertake that:

(a) We will provide to the underwriters at the closing as specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

(b) For purposes of determining any liability under the Securities Act of 1933, as amended, the information omitted from a form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in the form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933, as amended, shall be deemed to be part of this registration statement as of the time it was declared effective.

(c) For the purpose of determining any liability under the Securities Act of 1933, as amended, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, Cadence Pharmaceuticals, Inc. has duly caused this Amendment No. 2 to Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in San Diego, California on the 25th day of September, 2006.

CADENCE PHARMACEUTICALS, INC.

By: /s/ THEODORE R. SCHROEDER

Theodore R. Schroeder
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this Amendment No. 2 to Registration Statement on Form S-1 has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ THEODORE R. SCHROEDER Theodore R. Schroeder	President, Chief Executive Officer and Director (Principal Executive Officer)	September 25, 2006
/s/ WILLIAM R. LARUE William R. LaRue	Senior Vice President, Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer)	September 25, 2006
* Cam L. Garner	Chairman of the Board of Directors	September 25, 2006
* Brian G. Atwood	Director	September 25, 2006
* Samuel L. Barker, Ph.D.	Director	September 25, 2006
* Michael A. Berman, M.D.	Director	September 25, 2006
* James C. Blair, Ph.D.	Director	September 25, 2006
* Alan D. Frazier	Director	September 25, 2006

Signature	Title	Date
*	Director	September 25, 2006
Alain B. Schreiber, M.D.		
*	Director	September 25, 2006
Christopher J. Twomey		

*By: /s/ Theodore R. Schroeder
Theodore R. Schroeder
Attorney-in-Fact

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† Confidential treatment has been requested for portions of this exhibit. These portions have been omitted from the Registration Statement and submitted separately to the Securities and Exchange Commission.

# Indicates management contract or compensatory plan.

Exhibit 10.10

CERTAIN MATERIAL (INDICATED BY AN ASTERISK) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

COLLABORATION AND LICENSE AGREEMENT

between

MICROLOGIX BIOTECH INC.

and

STRATA PHARMACEUTICALS INC.

Dated: July 30, 2004

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COLLABORATION AND LICENSE AGREEMENT

This Collaboration and License Agreement (this "**Agreement**") is made as of July 30, 2004 (the "**Effective Date**") by and between **Micrologix Biotech Inc.**, a British Columbia corporation having its offices at BC Research Complex, 3650 Wesbrook Mall, Vancouver, BC, Canada V6S 2L2 ("**Micrologix**") and **Strata Pharmaceuticals Inc.**, a corporation having its offices at 10923 Coverhurst Way, San Diego, California 92130, USA ("**Strata**"). Micrologix and Strata are sometimes referred to collectively herein as the "**Parties**" or singly as a "**Party**".

R E C I T A L S

WHEREAS, Micrologix has developed and owns or controls certain proprietary technology, patents, patent applications, and know-how relating to Micrologix's proprietary Compound (as defined below);

WHEREAS, on June 2, 2004, the Parties signed a term sheet (the "**Term Sheet**"), whereby Strata paid Micrologix the Exclusivity Fee, in exchange for, among other things, Micrologix's agreement to negotiate solely and exclusively with Strata with respect to any license to the Compound and the Micrologix Technology for development and commercialization in the Field in the Territory (as such terms are defined herein); and

WHEREAS, Micrologix wishes to grant to Strata, and Strata wishes to obtain from Micrologix, an exclusive license under the Micrologix Technology to use, market, advertise, promote, distribute, offer for sale, sell, manufacture, have manufactured, export and import, and co-develop with and/or in addition to Micrologix, the Compound in the Field in the Territory, or have the foregoing done on its behalf, subject to the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the foregoing Recitals and the mutual covenants and agreements contained herein, the Parties hereby agree as follows:

ARTICLE 1
DEFINITIONS

As used in this Agreement, the following terms shall have the meanings set forth below:

Section 1.1 "Acceptance for Filing"

means notification from the FDA indicating receipt of an NDA submission in the United States or equivalent marketing application pursuant to Applicable Laws in each country in the Territory.

Section 1.2 "Act"

means the Federal Food Drug and Cosmetic Act (21 U.S.C. Section 301 et seq.) in the United States and any other comparable, applicable legislation in any other country in the Territory.

Section 1.3 “Affiliate”

means any company or entity controlled by, controlling or under common control with a Party. As used in this Section 1.3, “control” means (a) that an entity or company owns, directly or indirectly, fifty percent (50%) or more of the voting stock of another entity, or (b) that an entity, person or group has the actual ability to control and direct the management of the entity, whether by contract or otherwise.

Section 1.4 “Applicable Law(s)”

means the Act, Regulations and all other applicable laws, rules, regulations and guidelines within the Territory that apply to the import, export, research and development, manufacture, marketing, distribution or sale of the Product in the Field in the Territory or the performance of either Party’s obligations under this Agreement (including disclosure obligations as required by the United States Securities and Exchange Commission or other comparable exchange or securities commission having authority over a Party) to the extent applicable and relevant to such Party.

Section 1.5 “Approval Letter”

means a letter issued by the FDA indicating approval of a product for commercialization, as defined in 21 CFR § 314.105 in the United States, or equivalent letter issued by the applicable Competent Authority in any other country in the Territory, pursuant to Applicable Laws in each country in the Territory.

Section 1.6 “Books and Records”

means, in whatever media, any and all books and records, documents, reports and accounts in connection with or relative to: any Reimbursable Costs, any costs Strata or Micrologix is obligated to reimburse or pay to the other Party under this Agreement; the Development; the Development Plan; as well as any other books and records as may be required from time to time by Applicable Laws or this Agreement. Books and Records shall not include any market research and competitive reports, marketing reports and data.

Section 1.7 “CFR”

means the United States Code of Federal Regulations in the United States and any other comparable, applicable code of regulations in any other country in the Territory.

Section 1.8 “cGMP”

means the current good manufacturing protocols as defined in 21 CFR § 210 and § 211 in the United States or other comparable, applicable regulations in other countries in the Territory.

Section 1.9 “Collaboration”

means the activities of the Parties carried out in performance of, and the relationship between the Parties established by this Agreement.

Section 1.10 “Commercially Reasonable Efforts”

means, except as otherwise explicitly set forth in this Agreement, those diligent efforts consistent with the exercise of prudent scientific and business judgment, as applied to products having comparable market potential and comparable developmental and regulatory risks and challenges and otherwise in accordance with generally accepted practices in the pharmaceutical industry. “Comparable market potential” shall be fairly determined based upon relevant factors, including market size, price, competition, patent rights, product liability issues and general marketing parameters. Except as expressly set out in this Agreement, “Commercially Reasonable Efforts”, as applied to development and commercialization efforts, shall be as applied to, and assessed upon, the Territory taken as a whole, and therefore, Strata shall not be required to:

(a) manufacture, develop, pursue regulatory approval or commercialize the Product in any particular country or countries in the Territory; or

(b) obtain regulatory approval for all uses of the Product in any particular country or countries in the Territory;

except as may be required in respect of the Product and uses of the Product when using Commercially Reasonable Efforts in respect of the Territory taken as a whole. In addition to the foregoing, during the first [***] immediately following the Effective Date, when assessing whether Commercially Reasonable Efforts have been applied by a Party to an obligation under this Agreement other than the obligations set out in Section 2.1(b), in addition to the foregoing considerations, the Parties shall take into account the efforts that ought to be made by companies of similar size, financial strength, and stage of corporate development to the Party whose efforts are being assessed.

Section 1.11 “Common Shares”

means common shares in the capital of Micrologix.

Section 1.12 “Competent Authority(ies)”

means collectively the entities in each country in the Territory responsible for: (i) the regulation of medicinal products intended for human use, including the FDA; or (ii) the establishment, maintenance and/or protection of rights related to the Micrologix Patent Rights, or any other successor entities thereto.

Section 1.13 “Compound”

means omiganan pentahydrochloride.

Section 1.14 “Confidential Information”

means any and all information (including the Micrologix Technology) of a Party relating to any trade secret, Reimbursable Costs, Books and Records, process, method, compound, research project, work in process, future development, scientific, engineering, manufacturing, marketing, sales, business plan, financial or personnel matter relating to the disclosing Party, its present or future products, sales, suppliers, customers, employees, investors or business, whether in oral,

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

written, graphic or electronic form. Confidential Information shall not include any information which the receiving Party can prove by competent evidence:

(a) is now, or hereafter becomes, through no act or failure to act on the part of the receiving Party, generally known or available;

(b) is known by the receiving Party at the time of receiving such information, as evidenced by its written records maintained in the ordinary course of business;

(c) is hereafter furnished to the receiving Party by a Third Party, as a matter of right and without restriction on disclosure;

(d) is independently developed by the receiving Party, as evidenced by its written records, without knowledge of, and without the aid, application or use of, the disclosing Party's Confidential Information; or

(e) is the subject of a written permission to disclose provided by the disclosing Party.

Section 1.15 "Control"

means the possession of the ability to grant a license or sublicense as provided for herein without violating the terms of any agreement or other arrangement with any Third Party, licensee or sublicensee or the payment of any material licensing fees or royalties to any Third Party, licensee or sublicensee.

Section 1.16 "Costs"

means any and all costs, expenses, fees (including attorneys' fees and costs), charges, monies, license fees, upfront fees and royalties paid in connection with any proceeding, action, suit or claim and/or paid to any Third Party.

Section 1.17 "CRBSI"

means catheter related blood stream infection.

Section 1.18 "Development"

means work conducted under the Development Plan(s) and as set out in Section 2.3.

Section 1.19 "Development Plan(s)"

means the detailed plan(s) related to the research and the development (including work to obtain Governmental Approvals, including Marketing Authorizations), and the budget therefor as amended from time to time pursuant to which the Parties shall conduct the Development under the terms of this Agreement. The initial Development Plan is attached hereto as Exhibit "A".

Section 1.20 "Development Subcontract"

has the meaning set out in Section 2.1.

Section 1.21 “DMF”

means drug master file.

Section 1.22 “Europe”

means the European Union as of the Effective Date, European Union Candidate Countries (namely, Bulgaria, Croatia, Romania and Turkey), and the following European Countries: Albania, Andorra, Belarus, Bosnia-Herzegovina, Former Yugoslav Republic of Macedonia, Iceland, Liechtenstein, Moldova, Monaco, Norway, Russia, San Marino, Serbia & Montenegro, Switzerland, Ukraine, and Vatican City.

Section 1.23 “Exclusivity Fee”

means the $200,000 payment made by Strata to Micrologix under the Term Sheet which Micrologix acknowledges it received in two $100,000 payments, the first on June 3, 2004 and the second on July 6, 2004.

Section 1.24 “Exclusivity Period”

has the meaning set out in Section 3.7(b).

Section 1.25 “Extended Field”

has the meaning set out in Section 3.7(a).

Section 1.26 “FDA”

means the United States Food and Drug Administration in the United States and any other comparable, applicable administrative agency in any other country in the Territory, or any successor entity thereto.

Section 1.27 “Field”

means any or all of the following: (i) the topical administration to a burn site or a surgical wound site for the treatment or prevention in humans of burn-related or surgery-related infections; and (ii) the topical administration to a device or the site around the device for the treatment or prevention in humans of device-related infections, including LCSI and CRBSI. For the avoidance of doubt, the Field specifically excludes the treatment or prevention of dermatological diseases or disorders, including acne, psoriasis, rosacea and atopic dermatitis.

Section 1.28 “First Commercial Sale”

means (a) with respect to a country in the Territory, the first sale for use, consumption or resale of the Product by Strata, its sublicensees or its Affiliates in such country (excluding any sales for clinical trials or other non-commercial purposes) and (b) with respect to the Territory, the First Commercial Sale in any country within the Territory. A sale to a sublicensee or an Affiliate shall not constitute a First Commercial Sale unless the sublicensee or Affiliate is the end user of the Product.

Section 1.29 “First Phase III Study” means the Phase III Study for the Product completed prior to the Effective Date, namely #226-98-002.

Section 1.30 “GAAP”

means United States generally accepted accounting principles, as consistently applied in the Territory.

Section 1.31 “Good Clinical Practices” or “GCP”

means good clinical practices as defined in 21 CFR § 50 et seq., § 56 et seq., and § 312 et seq. in the United States or other comparable, applicable regulations in other countries in the Territory.

Section 1.32 “Governmental Approval(s)”

means any and all permits, licenses and authorizations, including Marketing Authorizations required by any Competent Authority as a prerequisite to the development, manufacturing, packaging, marketing and selling of the Product in the Field in the Territory; excluding however import permits.

Section 1.33 “IMS Data”

means the data reported from IMS Health Incorporated of Plymouth Meeting, PA, or any successor to IMS Health Incorporated or any other independent reporting service used by Strata to provide information related to the marketing of the Product and other pharmaceutical products.

Section 1.34 “Improvements”

means, subject to Section 3.6, any and all developments, derivative works, enhancements, modifications, inventions or discoveries relating to the Compound, the Product, for use in the Field and under the Control of Micrologix or developed, created or acquired by Micrologix at any time during the Term, whether patentable or not, and shall include, but not be limited to, developments, inventions or discoveries intended to enhance the safety or efficacy of the Product and all intellectual property rights related thereto.

Section 1.35 “IND(s)”

means an investigational new drug application as defined in 21 C.F.R. Section 312 et seq for the FDA in the United States or equivalent application to the Competent Authorities of other countries in the Territory, to commence clinical testing of a drug in humans, as defined by the FDA in the United States, or other applicable Competent Authority, as the same may be amended, supplemented or replaced from time to time.

Section 1.36 “Know-How”

means any and all know-how, trade secrets, inventions, data, processes, techniques, procedures, compositions, devices, methods, formulas, protocols, any and all pre-clinical and clinical data, and information, whether or not patentable, which are not generally publicly known, including

but not limited to any and all chemical, biochemical, toxicological, and scientific research information, whether in written, electronic, graphic or video form or any other form or format.

Section 1.37 “knowledge” or “best of its knowledge”

means, with respect to each Party, the actual knowledge of the senior officers of such Party, without the duty of inquiry.

Section 1.38 “Labelled” or “Labelling”

means any and all labels and other written, printed or graphic matter, including artwork, upon (a) the Product or any container utilized with the Product; (b) packaging; or (c) the package inserts.

Section 1.39 “LCSI”

means local catheter site infection.

Section 1.40 “Major European Market Country”

means France, Germany and United Kingdom.

Section 1.41 “manufacture(d)” or “manufacturing”

means the storage, handling, assembly, production, processing, Labelling, testing, disposition, packaging and quality control of raw materials and components and the Product.

Section 1.42 “Manufacturing Development Costs”

has the meaning set out in Section 5.3(f).

Section 1.43 “Market Price”

of the Common Shares means the U.S. Dollar Equivalent of the weighted average of the trading prices of the Common Shares on The Toronto Stock Exchange, for the five consecutive Trading Days ending on the last Trading Day prior to the Effective Date.

Section 1.44 “Marketing Authorization”

means all necessary and appropriate regulatory approvals, including NDAs and Pricing and Reimbursement Approvals, where applicable, to allow the Product to be marketed and sold in the Field in a particular country in the Territory.

Section 1.45 “MBI 594AN”

means [***].

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

Section 1.46 “Micrologix Know-How”

means any and all Know-How related to the Compound or the Product, including research and development and clinical studies hereunder and other obligations of Micrologix hereunder, and which is under the Control of Micrologix as of the Effective Date and any and all Improvements thereto, which is not covered by the Micrologix Patent Rights, but is necessary or useful to the use, development, manufacture, marketing, promotion, distribution, sale and/or commercialization of the Product in the Territory for use in the Field.

Section 1.47 “Micrologix Patent Rights” or “Micrologix Patent”

means any and all Patent Rights that claim Micrologix’s proprietary technology for the Product or the Compound which is under the Control of Micrologix as of the Effective Date and any and all Patent Rights covering Improvements thereto, which are necessary or useful to the use, development, manufacture, marketing, promotion, distribution, sale and/or commercialization of the Product in the Territory for use in the Field. The Micrologix Patent Rights as of the Effective Date are set forth on Exhibit “B”. Any Micrologix Patent Rights issued after the Effective Date shall be added to Exhibit “B”.

Section 1.48 “Micrologix Technology”

means the Micrologix Patent Rights and the Micrologix Know-How.

Section 1.49 “NDA”

means a New Drug Application, and all amendments and supplements thereto, for regulatory approval by the FDA as defined in 21 CFR § 314.50 et seq., as such act or regulations may be amended, supplemented or replaced from time to time, to commence commercial sale of the Product in the United States and any other comparable term and act as applicable with regard to a new drug application and all amendments, supplements or replacements to such act or regulations in any other country in the Territory.

Section 1.50 “Negotiation Period”

has the meaning set out in Section 3.7(c).

Section 1.51 “Net Sales”

means collectively, the gross amount invoiced by Strata, its sublicensees, or its Affiliates for sales of the Product to a Third Party (excluding sales among Strata and a sublicensee or Affiliate of Strata for resale, but including the subsequent final sales to Third Parties by such sublicensees or Affiliates), less the following as they pertain to the Product:

(a) any and all normal and customary trade and quantity discounts and customary allowances actually granted to purchasers of the Product for returns or credits, recalls (whether in the form of a credit or free replacement actually given in place of a returned or recalled Product), allowances to end users, which are reasonable and customary in accordance with generally accepted practices in the pharmaceutical industry (whether in the form of a credit or free Product), taxes (the legal incidence of which is on the purchaser and is shown separately on a Party's invoices) and transportation, insurance and postage charges (if billed on a Party's invoices as a separate item), and payments and rebates (including Medicaid rebates given pursuant to an agreement with U.S. Department of Health and Human Services and other rebates given pursuant to a government based rebate program, including local and state rebate programs), accrued, paid or deducted pursuant to agreements (including managed care agreements and group purchasing agreements) or Applicable Laws, chargebacks and reporting rebates paid to wholesalers and other distributors.

(b) Excise and value added taxes applicable to sales of the Product in finished package from which a Party has to pay or absorb on such sales.

The Product shall be considered "sold" when billed out or invoiced.

No deductions shall be made from Net Sales for items (a) and (b) above except to the extent of amounts for such items actually granted or paid with respect to the Product; provided that a Party may reconcile all such amounts within a given calendar quarter regardless of when such amounts were actually granted or paid.

No deductions shall be made from Net Sales for commissions paid to individuals whether they are with independent sales agencies or are regularly employed by a Party or its Affiliates or sublicensees and are on its or their payroll, or for the cost of collections.

Components of Net Sales shall be determined in the ordinary course of business using the accrual method of accounting in accordance with GAAP, provided that a Party may reconcile all such amounts within a given calendar quarter regardless of when such amounts were actually granted or paid.

In the event a Party transfers Product to a Third Party in a bona fide arm's length transaction, for consideration, in whole or in part, other than cash or to a Third Party in other than a bona fide arm's length transaction, the Net Sales price for such Product shall be deemed to be the standard invoice price then being invoiced by a Party in an arm's length transaction with similar customers.

Notwithstanding anything herein to the contrary, the transfer of a Product to a Third Party without consideration to Strata in connection with the development or testing of a Product shall not be considered a sale of a Product under this Agreement.

Section 1.52 "Notification Period"

has the meaning set out in Section 3.7(c).

Section 1.53 “packaging”

means any and all containers, cartons, shipping cases, inserts, package inserts or other similar material used in packaging or accompanying the Product.

Section 1.54 “Patent Rights”

means any and all rights under patents and patent applications, and any and all patents issuing therefrom (including utility, model and design patents and certificates of invention), together with any and all substitutions, extensions (including supplemental protection certificates), registrations, confirmations, reissues, divisionals, continuations, continuations-in-part, re-examinations, renewals, and foreign counterparts of the foregoing and all supplements and modifications thereto.

Section 1.55 “Phase III Study”

means that portion of the clinical development program that provides for human clinical trials, performed after preliminary evidence suggesting dose and effectiveness of a Product has been obtained, which is intended to gather the additional information about the effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the Product and to provide adequate basis for labelling, performed in accordance with the *U.S.A. Federal Food, Drug and Cosmetic Act* and applicable regulations promulgated thereunder (including 21 CFR Part 312), as amended from time to time.

Section 1.56 “Phase IV Study”

means, as applicable, a study or program, designed to: (a) obtain additional safety or efficacy data in support of the Product; or (b) determine effectiveness for additional labelled indications, in either case commenced after Governmental Approval of the Product in the subject country in the Territory.

Section 1.57 “Post Marketing Commitments”

means any post-approval commitments required by the FDA in the United States or any other Competent Authority in any other country in the Territory.

Section 1.58 “Pricing and Reimbursement Approvals”

means any pricing and reimbursement approvals which must be obtained before placing the Product on the market in the Field in any country in the Territory in which such approval is required.

Section 1.59 “Prime Rate of Interest”

means the prime rate of interest published from time to time in The Wall Street Journal as the prime rate; provided, however that if The Wall Street Journal does not publish the Prime Rate of Interest, then the term “Prime Rate of Interest” shall mean the rate of interest publicly announced by Bank of America, N.A., as its prime rate, base rate, reference rate or the equivalent of such rate, whether or not such bank makes loans to customers at, above, or below said rate.

Section 1.60 “Product”

means any and all pharmaceutical formulations containing any and all concentrations, sizes of volume, configurations and combinations of the Compound.

Section 1.61 “Promotional Material(s)”

has the meaning set out in Section 6.6(a).

Section 1.62 “raw materials and components”

means any and all raw materials and components (such as bulk drug, chemicals, containers, closures, packaging, Labelling, etc.) needed to manufacture the Product.

Section 1.63 “Regulations”

means regulations, statutes, rules, guidelines and procedures promulgated by the FDA or other Competent Authority pursuant to the Act or other Applicable Laws, including current Good Clinical Practices, current Good Manufacturing Practices, as well as those regulations currently contained in Title 21 of the CFR.

Section 1.64 “Reimbursable Costs” means the fees and costs owed by Strata pursuant to Section 2.5. Reimbursable Costs do not include [***]. Marketing Authorizations will be paid for by Strata in accordance with Section 2.3(c).

Section 1.65 “Representatives”

means, in respect of a Party, its Affiliates, licensees, sublicensees, and their respective employees, agents, consultants, Subcontractors, and other representatives.

Section 1.66 “Royalty Term”

means the period of time commencing on the First Commercial Sale of the Product in a particular country in the Territory and ending on the expiration of the last to expire of the Micrologix Patent Rights containing Valid Claims covering such Product in such country in the Territory; provided, however, that with respect to a country in the Territory in which a Micrologix Patent has not been issued at the time of the First Commercial Sale in that country, the Royalty Term shall commence on the First Commercial Sale in such country and continue for the greater of (i) the period in which a Valid Claim covering such Product exists in the United States; or (ii) if a Micrologix Patent is subsequently issued in such country, for the period of time in which a Valid Claim covering such Product exists in such country. The Royalty Term shall apply on a country-by-country basis. Notwithstanding anything to the contrary provided in this Section 1.66, if no Valid Claim covering such Product exists in a given country in the Territory, then the Royalty Term in such country shall be for a period of ten (10) years from the date of the First Commercial Sale in that country.

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Section 1.67 “Second Phase III Study”

means a Phase III Study to support a Marketing Authorization for a LCSI, and if reasonably prudent to pursue same, for CRBSI.

Section 1.68 “Subcontractors”

means Third Parties engaged to perform obligations of the Parties as permitted by this Agreement.

Section 1.69 “Territory”

means North America (including the United States, Canada and Mexico) and Europe, and as may be expanded or reduced pursuant to the terms of this Agreement.

Section 1.70 “Third Party”

means any entity, other than Micrologix or Strata.

Section 1.71 “Trading Day”

means any day on which the Toronto Stock Exchange is open for business.

Section 1.72 “U.S.” or the “United States”

means the 50 states of the United States of America, its territories or possessions, and the District of Columbia and Puerto Rico.

Section 1.73 “U.S. Dollar Equivalent”

means the equivalent amount of U.S. dollars calculated from Canadian currency using the Bank of Canada noon rate for such conversion as reported on the Bank of Canada’s website on the business day prior to the applicable date.

Section 1.74 “U.S. PTO”

means the Unites States Patent and Trademark Office or any successor entity thereto.

Section 1.75 “Valid Claim”

means a claim of an issued and unexpired Micrologix Patent that, with respect to a specific country in the Territory: (i) has not been revoked, declared unenforceable or unpatentable, or held invalid by a court or other governmental agency of competent jurisdiction that is unappealable or unappealed within the time allowed for appeal, (ii) has not been admitted to be rendered invalid or unenforceable through reissue, disclaimer or otherwise, and (iii) has not been finally cancelled, withdrawn, abandoned, allowed to lapse, or rejected by any governmental agency of competent jurisdiction.

ARTICLE 2
PRODUCT DEVELOPMENT

Section 2.1 Objectives.

(a) Pursuant to the Development Plan(s) and under the oversight of the JDMC, Strata, (along with the collaboration and assistance of Micrologix as described in any applicable development subcontract ("**Development Subcontract**")), shall use Commercially Reasonable Efforts to obtain Marketing Authorizations for the Product in the Field in the Territory.

(b) Strata shall use Commercially Reasonable Efforts:

(i) to submit a protocol and request a special protocol assessment for the Second Phase III Study in the US, in sufficient time to obtain feedback from the FDA, on or before the end of the [***]; and

(ii) within [***] after receiving satisfactory feedback from the FDA on such protocol, provided that Strata has secured an adequate supply of Product ready for use in human trials, enrol a patient in the Second Phase III Study;

(iii) within [***] after filing an NDA in the US, provided that no Competent Authority in Europe requires an additional phase III clinical study in order to file a common technical document in Europe, file a common technical document in Europe.

(c) After receiving satisfactory feedback from the FDA on the protocol referred to in Section 2.1(b)(ii), Strata shall use Commercially Reasonable Efforts to conduct a financing with proceeds to Strata sufficient to obtain, at a minimum, data from the LCSI endpoint from the Second Phase III Study.

(d) In addition, in its absolute discretion, Strata may file an NDA and seek Marketing Authorization for CRBSI based on [***].

(e) Strata shall use Commercially Reasonable Efforts to market and sell the Product as contemplated hereunder.

Section 2.2 Collaboration Guidelines; Amendments to the Development Plan(s).

(a) In all matters related to the Collaboration, the Parties shall strive to balance as best they can the legitimate interests and concerns of the Parties and to realize the economic potential of the Product.

(b) Any Development Plan may only be modified by the JDMC. The Development Plan(s) and any modifications thereto, as each may be approved by the JDMC in

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accordance with this Section 2.2(b), shall be incorporated into this Agreement as though fully set forth herein and without requiring formal or additional amendment to this Agreement.

Section 2.3 Development.

(a) Strata shall have responsibility for the Development under the oversight and based on the Development Plan, including a timeline, as approved by the JDMC. In addition to any other responsibilities as may be provided in the Development Plan(s), Strata shall:

(i) use Commercially Reasonable Efforts to develop the Product in accordance with the Development Plan(s) and as otherwise in accordance with the terms and conditions of this Agreement;

(ii) use Commercially Reasonable Efforts to secure the Marketing Authorizations, in accordance with the Development Plan(s) and/or otherwise in accordance with Article 6;

(iii) promptly advise Micrologix of any issues of which Strata becomes aware that materially and adversely affect Strata's ability to develop the Product or meet the timelines on the critical path set out in the Development Plan(s);

(iv) use Commercially Reasonable Efforts to manufacture or have manufactured the Compound and the Product to supply the Product to carry out the Development Plan(s).

(b) Strata may from time to time and where appropriate, engage Micrologix to perform regulatory, clinical and other development work pursuant to a Development Subcontract consistent with the provisions of this Article 2.

(c) Strata shall pay one hundred percent (100%) of the Reimbursable Costs incurred by Micrologix, including those arising under Section 2.5. Micrologix shall invoice Strata for such Reimbursable Costs on a quarterly basis within forty-five (45) days after the end of each calendar quarter and such invoices shall be accompanied by the appropriate documentation, including a listing of expenditures, in reasonably specific detail. Strata shall pay such invoices within thirty (30) days after receipt of the invoice. Micrologix shall keep Books and Records as necessary to document the inclusion of the out-of-pocket and internal costs within the Reimbursable Costs including time sheets, invoices, etc. Pursuant to Section 11.4, Strata has the right to inspect such Books and Records upon request and during normal business hours, and Micrologix shall provide copies of such Books and Records to Strata.

(d) Notwithstanding anything to the contrary contained in this Agreement, if the Second Phase III Study is commenced, Strata shall not terminate such study except on notice to Micrologix:

(i) at any time within [***] after Strata's receipt of any interim results or the executive summary following database lock of the LCSI endpoint;

(ii) if Strata elects to continue such study by enrolling patients thereafter, at any time within [***] after Strata's receipt of any subsequent interim results or the executive summary following database lock of the CRBSI endpoint;

unless Strata terminates this Agreement for Micrologix's breach pursuant to Section 13.2.

Section 2.4 Joint Development Management Committee.

(a) **Creation of JDMC; Scope**. Within ten (10) days after the Effective Date, the Parties will form a Joint Development Management Committee ("**JDMC**"), which shall oversee, review and coordinate the Development under the Development Plan(s) and otherwise under the terms and conditions of this Agreement. The JDMC may delegate certain responsibilities to the Parties. The JDMC shall be responsible for (i) coordinating the Parties' respective duties and efforts under this Article 2; (ii) overseeing the Development, including responsibility for all regulatory strategies involving Marketing Authorizations, meetings with the FDA and other Competent Authorities, review of draft submissions to the FDA and other Competent Authorities, as well as shelf-life and other manufacturing issues; (iii) making all decisions related to development, clinical trials and budgets in connection with the Development and the Development Plan(s); (iv) managing the Development conducted under the Development Plan(s); (v) coordinating the Parties' respective obligations under Section 2.3(a) and Section 2.3(b); (vi) managing the manufacturing development for the Compound referred to in Section 5.3(a)(i)(C); (vii) monitoring the progress and results of such work, all based on the principles of prompt, diligent and commercially reasonable development of the Product consistent with generally accepted practices in the pharmaceutical industry; and (viii) performing any Post Marketing Commitments. Any changes to any Development Plan shall be approved in advance by the JDMC. Notwithstanding the foregoing and anything to the contrary in this Agreement, the JDMC shall have a consulting role only in regard to, and no right to vote upon, any matters relating to burns and surgical infections indications for the Product. The JDMC shall not have any responsibilities in connection with: (i) any Phase IV Study; (ii) any commercialization or marketing activities in connection with the Product; or (iii) subject to Section 2.4(a)(vi), any manufacturing of commercial supplies of the Compound or the Product. Subject to the obligations to make Commercially Reasonable Efforts set out in Section 2.1 and Section 2.3 of this Agreement: (i) any such commercialization, marketing and manufacturing activities shall be the sole right and responsibility of Strata; and (ii) any Phase IV Study(ies) shall be the sole right and responsibility, but not obligation, of Strata.

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(b) **Membership**. The JDMC shall be comprised of three (3) voting representatives of each of Micrologix and Strata. Each Party may change its representatives on the JDMC at any time upon written notice to the other Party. Strata shall select one (1) member of the JDMC to act as the chairperson of the JDMC and Micrologix shall select one member of the JDMC to act as the secretary of the JDMC.

(c) **Meetings of the JDMC**. The JDMC shall meet on a quarterly basis or at such other frequency and at such time (and place, as applicable) as agreed to by the members of the JDMC or upon the reasonable request of either Party. Such meetings may be conducted in person or via teleconference. The JDMC Secretary will be responsible for calling meetings, preparing and circulating an agenda in advance of each meeting, and preparing and issuing minutes of each meeting within thirty (30) days thereafter. Any such agenda or minutes shall be approved by the other Party in advance of any issuance. A reasonable number of additional representatives of a Party may attend meetings of the JDMC in a non-voting observer capacity.

(d) **Decisions of the JDMC**. A quorum of the JDMC shall be deemed to be present at any meeting of the JDMC if at least two (2) JDMC members or their designees of each Party are present at such meeting in person or by telephone. If a quorum exists at any meeting, a majority vote of the members of the JDMC present at such meeting is required to take any action on behalf of the JDMC. In the event that any vote within the JDMC results in a tie, Strata shall have the tie-breaking vote, which shall be exercised in good faith, and make the final determination. Such final determination shall be binding upon the Parties.

(e) **Limitation of Powers**. The JDMC shall not have the right to amend or interpret this Agreement. Issues regarding the interpretation of this Agreement shall be referred to the respective Chief Executive Officers of each Party, or their designees (who must be members of a Party's senior management), as provided in Section 14.1. The actions or decisions of the JDMC shall not substitute for either Party's ability to exercise any right set forth herein or excuse the performance of any obligation set forth herein.

(f) **Liaisons**. Each Party will designate an individual to serve as the liaison between the Parties to undertake and coordinate any day-to-day communications as may be required between the Parties relating to their respective activities under this Agreement. Each Party may change such liaison from time to time during the Term upon written notice thereof to the other Party.

Section 2.5 Technology Transfer.

(a) Micrologix shall, upon Strata's request, transfer to or make available to Strata the then most-current version of all relevant Micrologix Know-How to enable Strata's reasonably capable personnel to understand such Micrologix Know-How as reasonably necessary to undertake the manufacture, development and commercialization of the Compound and generally any Product in the Field under this Agreement. Such transfer shall include:

(i) transfer of the results of the clinical trials conducted prior to and as of the Effective Date relating to the Product to Strata (including all regulatory information, clinical data, hard-copy CRFs and reports together with any patient samples (such as blood samples, microbiology samples, and tissue samples), if available, without regard to the condition of such samples);

(ii) transfer of any communications with the FDA and the minutes of any meetings with the FDA relating to the Product to Strata;

(iii) transfer of the data and results of any CMC related activities incident to Section 2.5(a)(i) and Section 2.5(a)(ii);

(iv) coordination of communication between Strata and the clinical trial groups that conducted the clinical trials referred to in Section 2.5(a)(i) prior to and as of the Effective Date; and

(v) providing Strata reasonable access to Micrologix personnel with relevant clinical and regulatory expertise to explain the information transferred pursuant to Section 2.5(a)(i), Section 2.5(a)(ii) and Section 2.5(a)(iii).

(b) Micrologix shall update the Micrologix Know-How related to the Compound and Products previously transferred to Strata regularly at JDMC meetings.

(c) Micrologix shall work cooperatively with and provide reasonable assistance to Strata upon Strata's request, under the oversight of the JDMC, to prepare the first NDA filing in the United States pursuant to a Development Subcontract.

(d) Strata shall pay for the maintenance by Micrologix of the certain Governmental Approvals in connection with the research and development of the Product pursuant to Section 6.7(b) and the services of Micrologix personnel provided pursuant to this Section 2.5, as follows:

(i) For the first three months from the Effective Date, Strata shall pay to Micrologix Micrologix's documented out-of-pocket costs of providing such services.

(ii) Commencing after the expiry of three months from the Effective Date, Strata shall pay to Micrologix the hourly rate of [***] ($[***]) per hour, plus the documented out-of-pocket costs of providing such services.

(iii) Strata is responsible for, and will pay all reasonable, documented, actual travel and associated accommodation expenses of Micrologix personnel who, at Strata's request, travels to provide transition support under this Section.

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ARTICLE 3
LICENSE

Section 3.1 License Terms.

Subject to the terms and conditions of this Agreement, Micrologix hereby grants to Strata an exclusive, royalty-bearing license under the Micrologix Technology to use, market, advertise, promote, distribute, offer for sale, sell, make, manufacture, have manufactured, export and import, and develop the Product in the Territory for use in the Field with the right to sublicense (as provided in Section 3.5), and/or assign (as provided Section 15.2) the foregoing.

Section 3.2 Micrologix's Reservation of Rights.

Except as otherwise licensed to Strata hereunder and subject to Section 11.1, Micrologix may exploit the Micrologix Technology for any purpose, including to use, develop, market, advertise, promote, distribute, offer for sale, make, manufacture, sell, export and import the Product:

(a) outside the Territory; and

(b) inside the Territory but outside the Field.

Section 3.3 Third Party Licensees of Micrologix.

In the event that Micrologix or a licensee of Micrologix develops and/or markets a Product outside the Territory but inside the Field, Micrologix shall use Commercially Reasonable Efforts to work cooperatively with Strata to coordinate the development and marketing activities of Micrologix or such licensee of Micrologix with the development and marketing activities hereunder.

Section 3.4 Work Product and Intellectual Property.

(a) Strata acknowledges that it shall have no right, title or interest in or to the Micrologix Technology except as set forth in this Agreement. Nothing in this Agreement shall be construed to grant Strata any rights or license to any intellectual property of Micrologix other than as expressly set forth in this Agreement.

(b) Except as set forth in Section 5.2 and the termination Sections of this Agreement

(i) Micrologix acknowledges that it shall have no right, title or interest in or to any data, inventions, discoveries, improvements, derivative works, and/or any other work product, whether patentable or not, developed hereunder by Strata or on behalf of Strata by its Representatives ("**Strata Work Product**").

(ii) Nothing herein shall be construed to grant Micrologix any rights or license to the Strata Work Product or any other intellectual property of Strata (collectively, "**Strata Intellectual Property**"). Strata reserves all rights in and to any such Strata Work Product and the Strata Intellectual Property.

Section 3.5 Sublicenses.

(a) Strata shall have the right to sublicense rights granted in Section 3.1 to its Affiliates. Strata shall cause its Affiliates to comply with and be bound by those terms and conditions of Strata under this Agreement that by their terms are intended to obligate Strata or its Affiliates commercializing the Product as permitted hereunder, including Section 3.4, Section 3.5, Article 5, Article 6, Article 7, Article 8, Article 9, Article 10, Article 11 (excluding however Section 11.1), Article 12 and Section 14.5. Notwithstanding the foregoing, Strata shall remain primarily responsible for complying with such applicable terms and conditions. A breach by any such Affiliate of any such obligation shall constitute a breach by Strata of this Agreement and shall entitle Micrologix to exercise its rights hereunder, in addition to any other rights and remedies to which Micrologix may be entitled.

(b) Strata shall also have the right to sublicense rights granted in Section 3.1 to Third Parties, subject to the following: Strata shall give Micrologix prompt notice of the execution of any sublicense. Within ten (10) calendar days after execution of a sublicensing agreement, Strata shall provide Micrologix with a copy thereof (provided that Strata shall be permitted to redact the financial terms and other confidential information in such agreement). Each sublicense shall contain covenants by the sublicensee for such sublicensee to observe and perform materially the same terms and conditions as those set out for Strata in this Agreement to the extent applicable. In the event Strata grants sublicenses to others to sell Product, such sublicenses shall include an obligation for the sublicensee to account for and report its Net Sales on the same basis as if such sales were Net Sales by Strata, and Micrologix shall receive royalties from Strata in the same amounts as if the Net Sales of the sublicensee were Net Sales of Strata. In the event that Strata becomes aware of a material breach of any such sublicense by the sublicensee, Strata shall promptly notify Micrologix of the particulars of same and use its Commercially Reasonable Efforts to enforce the terms of such sublicense. Upon the request of Micrologix, Strata shall act reasonably in considering any request of Micrologix for Strata to terminate such sublicense for cause, but Strata shall have the final and sole right and responsibility and decision making authority with respect to any such sublicense (provided that Strata acts reasonably in such regard).

(c) The terms of this Section 3.5 shall apply to each subsequent sublicensee or sub-sublicensee, as if same were Strata’s original sublicensee.

(d) Micrologix will, upon request by any sublicensee of Strata, provide such sublicensee with a letter whereby Micrologix agrees that if Micrologix gives notice of default to Strata pursuant to Section 13.2 or Section 13.4, then, prior to any termination of this Agreement, Micrologix will give such sublicensee written notice of such default or intention to terminate this Agreement, and in the event of any breach or default by Strata, which may be cured pursuant to Section 13.2 or Section 13.4, will for 60 days from the date of such notice to the sublicensee, give the sublicensee the opportunity to cure such default or breach on the terms provided in Section 13.2 or Section 13.4, mutatis mutandis. Further, such letter

shall evidence Micrologix's agreement that if this Agreement is terminated, and provided that the sublicense between Strata and the sublicensee is in good standing at such time, Micrologix will then grant to the sublicensee a license of the same rights conferred on the sublicensee by the sublicense agreement on substantially those same terms and conditions as are contained in this Agreement as would correspond to the sublicense rights granted in the sublicense agreement, on the financial terms set out in the relevant sublicense agreement.

Section 3.6 Certain Improvements.

(a) When Micrologix enters into any agreement or other arrangement with a Third Party or licensee or sublicensee that may result in the development, creation or acquisition by Micrologix of any developments, derivative works, enhancements, modifications, inventions or discoveries relating to the Compound or the Product for use in the Field (collectively, **"Certain Improvements**"), Micrologix will use Commercially Reasonable Efforts not to limit or otherwise restrict Micrologix's ability to grant a license or sublicense to any such Certain Improvements as provided for herein without violating the terms of any such agreement or other arrangement.

(b) If Micrologix develops, creates or acquires any developments, derivative works, enhancements, modifications, inventions or discoveries relating to the Compound or the Product for use in the Field, where the grant of a license or sublicense to same as provided for herein requires the payment of material licensing fees or royalties to any Third Party, licensee or sublicensee, then Micrologix shall in a timely fashion offer to Strata in writing a license or sublicense to the rights to such developments, derivative works, enhancements, modifications, inventions or discoveries. Within a reasonable period of time (but not to exceed [***] after receipt of Micrologix's offer), Strata shall either accept the license or sublicense of same and pay to Micrologix the amount of such material licensing fees or royalties owed by Micrologix to such Third Party due to Strata's activities under such license or sublicense, or advise Micrologix that Strata does not wish to obtain such rights.

(c) In the event that:

(i) Micrologix, using Commercially Reasonable Efforts, fails to obtain the ability to grant a license or sublicense as provided for in Section 3.6(a) without violating the terms of any such agreement or other arrangement, then the rights to any such Certain Improvements shall be excluded from the definition of Improvements under this Agreement; or

(ii) Strata advises Micrologix that Strata does not wish to obtain the rights referred to in Section 3.6(b), or if Strata fails to notify Micrologix within a reasonable period of time (not to exceed [***] as noted above) that it

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accepts such license or sublicense, then such rights shall be excluded from the definition of Improvements under this Agreement; or

(iii) Strata advises Micrologix that Strata does wish to obtain the rights referred to in Section 3.6(b) within a reasonable period of time (not to exceed [***] as noted above) and pays such licensing fees or royalties, then such rights shall be included in the definition of Improvements under this Agreement without further formality.

Section 3.7 Exclusive Option to Extend Field.

(a) Subject to the terms and conditions of this Section, Micrologix hereby grants to Strata the right of first negotiation to obtain an exclusive license under the Micrologix Technology to use, market, advertise, promote, distribute, offer for sale, sell, make, manufacture, have manufactured, export and import, and develop the Product to reduce or eliminate the nasal carriage of infectious organisms (the "**Extended Field**") in the Territory.

(b) From the Effective Date and for a period of [***] thereafter (the "**Exclusivity Period**"), Micrologix shall notify Strata in writing prior to any:

(i) use, marketing, advertising, promotion, distribution, offer for sale, sale, making, manufacturing, having manufactured, exporting, importing or developing the Product or the Compound for the Extended Field in all or any part of the Territory for itself or through its Affiliates, or

(ii) grant to any Third Party any rights to do any of the foregoing.

(c) Strata shall have a period of [***] from its receipt of a notice described in Section 3.7(b) (the "**Notification Period**") to notify Micrologix in writing if Strata is interested in obtaining such license for the Extended Field for such territory. If, by the end of the Notification Period, Micrologix receives written notice from Strata that it desires to obtain such a license, then Micrologix and Strata for a period of [***] or such longer period of time as mutually agreed to by the Parties in writing (the "**Negotiation Period**") shall negotiate in good faith, on an exclusive basis, a definitive license agreement(s) for an exclusive license to the Extended Field upon such terms and conditions as are mutually agreeable to the Parties.

(d) If the Parties fail to execute such definitive license agreement(s) as described in Section 3.7(c), by the end of the Negotiation Period or if Strata fails to give notice of its interest in obtaining a license to the Extended Field before the expiry of the Notification Period, then Strata's right of first negotiation with respect to the Extended Field shall terminate; provided, however, that if Micrologix disposes of rights to the Micrologix Technology for the Extended Field to a Third Party prior

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to the end of the Exclusivity Period, then the financial terms of such transaction shall not be substantially less favorable to Micrologix in the aggregate than the best terms offered to Strata by Micrologix in writing during the Negotiation Period. If, prior to the end of the Exclusivity Period, Micrologix desires to offer a Third Party rights to the Extended Field on financial terms substantially less favorable to Micrologix in the aggregate than the best terms offered to Strata by Micrologix in writing during the Negotiation Period, then Micrologix shall first offer such terms to Strata, and if within [***] of such offer, Strata informs Micrologix that it is prepared to enter into an agreement with Micrologix in accordance with such terms, Micrologix shall conclude such agreement with Strata upon such terms. If no such statement is made by Strata within said [***], Micrologix shall be free to enter into an agreement in accordance with such terms with a Third Party.

ARTICLE 4
ADDITIONAL PAYMENTS

Section 4.1 License Fee.

(a) **Upfront Payment to Micrologix.** In partial consideration for the licenses granted under Section 3.1, Strata shall pay to Micrologix a one-time, non-refundable license fee equal to One and One Half Million Dollars ($1,500,000) one business day after the Effective Date by wire transfer of immediately available funds to an account designated in writing by Micrologix to Strata prior to the Effective Date (the "**Upfront Fee**"). Strata may deduct the Exclusivity Fee from the Upfront Fee.

(b) **Upfront Equity Investment in Micrologix.** Strata shall purchase from Micrologix on the Effective Date such number of Common Shares as equals Five Hundred Thousand Dollars ($500,000), based on the Market Price plus a [***] ([***]) premium, and as issued pursuant to a separate stock purchase agreement.

Section 4.2 Product Milestone Payments.

Strata shall pay to Micrologix, as licensing fees, the following non-refundable milestone payments as follows:

(a) for milestones referred to in Section 4.3 and Section 4.4,

(i) if Strata can make the payment respecting such milestone within 45 days of the date on which Strata receives a copy of the applicable letter or notice from the FDA in the U.S. or from a foreign equivalent in the Territory, Strata shall pay to Micrologix such milestone within [***] of achieving such milestone;

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(ii) if Strata cannot make the payment respecting such milestone within [***] of the date on which Strata receives a copy of the applicable letter or notice from the FDA in the U.S. or from a foreign equivalent in the Territory, Strata shall:

(A) within [***] of achieving such milestone, notify Micrologix in writing that it cannot make the payment respecting such milestone; and

(B) provided that Micrologix receives such notice within the period for the receipt of same, Strata shall pay to Micrologix such milestone within [***] of achieving such milestone, [***].

(b) for milestones referred to in Section 4.5, [***] after Strata receives a copy of the applicable letter or notice from the FDA in the U.S. or from a foreign equivalent in the Territory.

Section 4.3 Milestones for a Second Phase III.

For NDA Filings and Marketing Authorizations for either LCSI or CRBSI based upon a second Phase III trial, the following milestones shall apply:

[***]

Section 4.4 Milestones for the First Phase III.

For an NDA Filing and Marketing Authorization for CRBSI based upon the First Phase III Study, the following milestones shall apply; provided however that notwithstanding anything in this Agreement to the contrary, the milestone for receipt of [***] in the United States in this Section 4.4 shall only be payable when the milestone for [***] in the United States in this Section 4.4 becomes payable:

[***]

The CRBSI milestones set forth in Section 4.3 and Section 4.4 regarding the CRBSI indication in the United States are alternative milestones and as such only one milestone shall be due and payable for [***] and [***], as applicable, under Section 4.3 and Section 4.4, but not both.

Section 4.5 Burns or Surgical Infections milestones.

For Marketing Authorizations for burns or surgical infection indications, the following milestones shall apply:

[***]

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Section 4.6 Commercial Milestone Payments.

Strata shall pay to Micrologix, as additional licensing fees, the following one-time, non-refundable milestone payments within [***] following the end of the calendar quarter in which the relevant commercial milestone is achieved.

[***]

Section 4.7 Royalties.

(a) **Royalty Payment**. During the Royalty Term, Strata shall owe and pay to Micrologix the following royalties on Net Sales:

(i) [***]% of Net Sales, on aggregate Net Sales in each calendar year which does not exceed [***] ($[***]);

(ii) [***]% of Net Sales, on aggregate Net Sales in each calendar year which is greater than [***] ($[***]) but does not exceed [***] ($[***]); and

(iii) [***]% of Net Sales, on aggregate Net Sales in each calendar year which is greater than [***]($[***]).

(b) **Reductions in Royalty Rates**. Strata's royalty obligation under Section 4.7(a) shall be [***] in the manner herein described:

(i) In the event (and for the period that) a non-proprietary version or versions of the Product enters the market in a country in the Territory in any calendar quarter during the Term, [***]. For the purposes of this Section, "non-proprietary" means a product containing the amino acid sequence [***] for use in the Field which does not infringe a Valid Claim. The [***] shall be effective beginning on the first calendar quarter of the launch of such generic product. The royalty rate shall be adjusted quarterly and shall be reconciled quarterly at such time as the applicable IMS Data has been made available to Strata.

(ii) Any such [***] in Section 4.7(b)(i) shall be credited against the next payment(s) owed Micrologix. [***].

(c) **Certain Recoveries**. If Micrologix owes Strata Micrologix's share of the Costs pursuant to Section 7.3, Section 7.4 or Section 10.4, Strata shall recover such amounts [***]. The Parties acknowledge and agree that the maximum amount of any such [***] in accordance with Section 7.3, Section 7.4 and Section 10.4 from any royalty payments due Micrologix hereunder in a given quarter shall not exceed [***] of the royalty payment owed in such quarter (the [***]). Any

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amounts in excess of [***] for any quarter(s) shall be [***] against subsequent quarterly royalty payments owed to Micrologix, subject to the [***] limitation for any such subsequent quarter, [***].

(d) **After Royalty Term**. After the expiration of the Royalty Term in any relevant country, Strata shall have no further obligation to pay royalties to Micrologix in such country.

(e) **Payment of Royalties and Reports**. Within [***] of the end of each calendar quarter following the First Commercial Sale, Strata shall provide Micrologix with a written report, in a form to be agreed between the parties, acting reasonably, accompanied by full payment of all royalties accrued and owing to Micrologix during such quarter, of: (i) Net Sales during such quarter and cumulative Net Sales for the current calendar year; (ii) deductions from Net Sales; (iii) withholding taxes, if any, required by Applicable Laws to be deducted with respect to such sales; (iv) the dates of the First Commercial Sale of the Product in any country in the Territory during the reporting period; (v) the exchange rates, if any used to determine the amount of United States dollars; and (vi) the calculation of the royalties owed (collectively, the "**Royalty Statement**"). The Royalty Statement shall be in reasonably specific detail, on a country-by-country basis, and segmented according to sales by Strata, each Affiliate and each sublicensee.

(f) **Exchange Rate; Manner and Place of Payment**. All payments hereunder shall be payable in United States dollars. With respect to each month in each calendar quarter, whenever conversion of payments from any foreign currency shall be required, such conversion shall be made at the rate of exchange reported in The Wall Street Journal on the last business day of such month within the applicable calendar quarter. All payments owed under this Agreement shall be made by wire transfer to a bank account designated in writing by the receiving Party.

(g) **Late Payments**. In the event that any payments due hereunder are not made when due, each such payment shall accrue interest from the date due until paid at the Prime Rate of Interest. The payment of such interest shall not limit or otherwise be deemed to be in satisfaction of a Party exercising any other rights it may have under this Agreement arising from the other Party's failure to make such payment when due.

(h) **Taxes**. All taxes levied on account of the payments accruing to either Party (the "**Receiving Party**") under this Agreement shall be paid by the Receiving Party for its own account, including taxes levied thereon as income to the Receiving Party. If provision is made under Applicable Laws for withholding, such tax shall be deducted from the payment made by the other Party paid to the proper taxing authority and a receipt of payment of the tax secured and promptly delivered to the Receiving Party, provided that it is understood that if this Agreement is assigned by Strata, Micrologix should be no worse off than if this Agreement was made and remained with a United States company and the payments to Micrologix were made from the United States to Canada. Each Party agrees to assist the other Party in claiming exemption from such deductions or withholdings

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under any double taxation or similar agreement or treaty from time to time in force.

(i) **Prohibited Payments**. Notwithstanding any other provision of this Agreement, if either Party is prevented from paying any payments by virtue of the Applicable Laws of the country from which the payment is to be made, then such payment may be paid by depositing funds in the currency in which it accrued to the Receiving Party's account in a bank acceptable to the Receiving Party in the country whose currency is involved.

(j) **Non-Monetary Consideration**. In the event Strata, its sublicensee(s) or its Affiliate(s) receive any non-monetary consideration in connection with the sale of the Product, the Net Sales of such Product shall be calculated based on the fair market value of such other consideration. Strata shall disclose the terms of such arrangement to Micrologix and the Parties shall endeavour in good faith to agree on such fair market value as promptly as possible.

(k) **Manufacturing Development Costs**. Strata shall recover Manufacturing Development Costs owed by Micrologix pursuant to Section 5.3(f) [***].

ARTICLE 5
COMMERCIALIZATION OF THE PRODUCT

Section 5.1 Marketing Efforts.

(a) Subject to Section 2.4(a) and Section 5.3(f), Strata shall: (i) have the exclusive right, at its cost, to make, manufacture, market, advertise, promote, sell, distribute, and commercialize the Product in the Field in the Territory; (ii) be solely responsible using Commercially Reasonable Efforts, for the making, manufacture, marketing, advertising promotion, sale, distribution and commercialization of the Product in the Field in the Territory; and (iii) have the sole responsibility and decision making authority using Commercially Reasonable Efforts with regard to any and all aspects of the making, manufacturing, marketing, advertising, promotion, sale, distribution and commercialization of the Product in the Field in the Territory, including all Labelling, marketing plans, marketing strategy, pricing decisions, and the nature and type of advertising and marketing materials, including all Promotional Materials.

(b) Subject to the terms of this Agreement, Strata agrees to: (i) use Commercially Reasonable Efforts to market, advertise, promote, sell, distribute, and commercialize the Product in the Field in the Territory; and (ii) commence commercial sales of the Product in each country in the Territory within six (6) months after receiving a copy of each of the relevant Marketing Authorization.

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(c) Strata shall promptly advise Micrologix of any issues of which Strata becomes aware that materially and adversely affect Strata's ability to market or sell the Product in the Territory. In such event, senior executives of Strata and Micrologix shall meet and in good faith discuss what actions should be taken in light of such issues. If the Parties cannot resolve any such issue, either Party may invoke the dispute resolution procedure in Article 14.

(d) Strata shall provide Micrologix prompt notice of the following events during the Term: (i) the First Commercial Sale of Product in each country in the Territory, if and when such occurrence takes place; and (ii) when any milestone referred to in Section 4.3, Section 4.4, Section 4.5, or Section 4.6 has occurred.

Section 5.2 Marketing Update.

(a) Following receipt of an Approval Letter from the FDA for the Product or an equivalent letter from a Competent Authority, Strata shall provide Micrologix on an annual basis during the Term, through the JDMC or otherwise, with reports in reasonable detail describing Strata's material marketing efforts with respect to the Product in the Territory during the preceding year and forecasts and plans for such efforts for the following year.

(b) Strata agrees to consider Micrologix's input and comments that Micrologix may provide related to any such report for any applicable period; provided, however, Strata shall have the right to either accept or reject such input and/or comments in whole or in part in Strata's sole discretion for any reason whatsoever, and Strata shall have the final and sole right and responsibility and decision-making authority for all matters related to any such report(s).

Section 5.3 Manufacturing.

(a) Unless Strata is prevented, restricted, interfered with or delayed in making such sales by reason of: (i) Force Majeure; or (ii) otherwise due to any breach of this Agreement by Micrologix; Strata shall use Commercially Reasonable Efforts to:

(i) identify, select, qualify, and enter into definitive agreement(s) with Third Party(ies) to:

(A) manufacture commercial supplies of the Product for use in the Field in the Territory; and

(B) supply raw materials and components for such commercial supply, including the Compound; and

(C) conduct manufacturing and process development activities, including manufacturing scale up and start up process development, and analytical and quality assurance and control method development, and activities related to the foregoing, for the Compound; and

(D) conduct manufacturing and process development activities, including manufacturing scale up and start up process development, and analytical and quality assurance and control method development, and activities related to the foregoing, for the Product (excluding the Compound) for use in the Field in the Territory; and

(ii) manufacture or have manufactured adequate supplies of the Product for use in the Field in the Territory.

(b) Strata shall use its Commercially Reasonable Efforts to resolve any shelf-life, regulatory and other manufacturing issues respecting the Product.

(c) Strata agrees that: (i) Micrologix and its Representatives shall be entitled to contract directly with any Third Party with whom Strata has entered into such definitive agreement(s) under Section 5.3(a) and (ii) such definitive agreement(s) shall not contain any contractual provision that would prohibit Micrologix and its Representatives from contracting directly or otherwise having access to any such Third Party(ies) as part of either manufacturing any product for use outside the Territory or any product for use inside the Territory, but outside the Field. Strata further agrees that, if there is any Strata Intellectual Property developed by Strata or such Third Party(ies) in the course of the activities described in Section 5.3(a), Micrologix shall have a non-exclusive, royalty free license to use such Strata Intellectual Property as part of either manufacturing any product for use outside the Territory or any product for use inside the Territory, but outside the Field. Strata will use Commercially Reasonable Efforts not to limit or restrict Strata's ability to grant Micrologix such license as provided for herein without violating the terms of any agreement or other arrangement with any such Third Party. The Parties acknowledge that if Strata is required to pay material license fees or royalties to any such Third Party(ies) in order to grant Micrologix such license to use the Strata Intellectual Property, then Strata shall in a timely fashion offer to Micrologix in writing a license or sublicense to such Strata Intellectual Property. Within a reasonable period of time (but not to exceed [***] after receipt of Strata's offer), Micrologix shall either accept the license or sublicense of same and pay to Strata the amount of such material licensing fees or royalties, or advise Strata that Micrologix does not wish to obtain such rights.

(d) In the event that:

(i) Strata, using Commercially Reasonable Efforts, fails to obtain the ability to grant a license or sublicense as provided for in Section 5.3(c) without violating the terms of any such agreement or other arrangement, then Strata shall have no obligation to grant such license to Micrologix under Section 5.3(c); or

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(ii) Micrologix advises Strata that Micrologix does not wish to obtain the rights referred to in Section 5.3(c), or if Micrologix fails to notify Strata within a reasonable period of time (not to exceed [***] as noted above) that it accepts such license or sublicense, then Strata shall have no obligation to grant such license or sublicense to Micrologix under Section 5.3(c); or

(iii) Micrologix advises Strata that Micrologix does wish to obtain the rights referred to in Section 5.3(c) within a reasonable period of time (not to exceed [***] as noted above) and pays such licensing fees or royalties then Strata shall be deemed to have granted such license or sublicense to Micrologix under Section 5.3(c) without further formality.

(e) If Strata manufactures the Product itself, rather than through Third Part(ies), Strata will provide reasonable technical assistance, at Micrologix's cost and expense to provide Micrologix and its Representatives the technology and Know How necessary to permit Micrologix or its Representatives to manufacture or have manufactured any product for use outside the Territory or any product for use inside the Territory, but outside the Field.

(f) Strata and Micrologix shall share in the manufacturing development costs for the Compound. Strata shall recover such costs from Micrologix as set forth in Section 4.7(k) for [***] of Strata's documented out-of-pocket costs of conducting the activities set out in Section 5.3(a)(i)(C) up to a maximum of [***] (the "**Manufacturing Development Costs**").

(g) **Transfer of Micrologix Compound and Product Inventory**.

(i) Subject to Section 5.3(g)(vi), at the request of Strata, such request to be made within six (6) months after the Effective Date, Micrologix shall make available to Strata at Micrologix's documented out-of-pocket cost, all or any part of Micrologix's inventory of "MBI 226 – GMP Inventory" as set out in Exhibit "C" conforming to the specifications mutually agreed upon by the Parties to the extent such inventory has not been used or dedicated for use by Micrologix for other purposes.

(ii) Subject to Section 5.3(g)(vi), at the request of Strata, such request to be made within six (6) months after the Effective Date, Micrologix shall make available to Strata at [***] of Micrologix's documented out-of-pocket cost, all or any part of Micrologix's inventory of "MBI 266 Reference Standard" as set out in Exhibit "C" to the extent such inventory has not been used or dedicated for use by Micrologix for other purposes.

(iii) At the request(s) of Strata, such request(s) to be made within twelve (12) months after the Effective Date, Micrologix shall make available to Strata

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at [***] of Micrologix's documented out-of-pocket cost, all or any part of Micrologix's inventory of "MBI 226 non-GMP Inventory", all for use as contemplated hereunder, as set out in Exhibit "C".

(iv) As soon as practical, and in any event before the expiry of three (3) months from after the Effective Date, Micrologix shall transfer to Strata at [***], all of Micrologix's inventory of "MBI 266 1.0% Gel Inventory", on an "as is" basis, all for use as contemplated hereunder, as set out in Exhibit "C".

(v) Pursuant to Micrologix making Compound available to Strata in Section 5.3(g)(i), Micrologix shall cause its Representative to release or re-release such Compound to Strata with all release documentation including all certificates of analyses confirming the identity, strength, quality and purity of the lots of Compound, certificates of compliance confirming that the same lots of Compound were manufactured, tested, stored and supplied in compliance with cGMPs and all Applicable Laws, each such certificate signed by an authorized signatory of Micrologix's Representative, any deviation or discrepancy reports pertaining to Compound relating to deviations that may require reporting to the FDA, and all such other documentation and information as is reasonably required by Strata.

(vi) With respect to the inventories that are made available by Micrologix pursuant to Section 5.3(g)(i) and Section 5.3(g)(ii), until the expiry of three (3) months from the Effective Date, Micrologix will not use or dedicate for use any of such inventory. Thereafter, until the expiry of six (6) months from the Effective Date, Micrologix will not use or dedicate for use any of such inventory without first giving Strata ten (10) days prior written notice of same. If Strata gives notice in writing within such period of its intention to purchase such inventory, Micrologix shall sell such inventory to Strata and same shall not be used or dedicated for use by Micrologix. If Strata gives notice in writing within such period that it does not intend to purchase such inventory, or if Strata fails to give notice within such period, Micrologix may use or dedicate such inventory, and same shall not be sold to Strata.

(h) **Co-negotiation for Commercial Supply of the Compound**. In the event that both Parties require commercial supplies of the Compound and it is in the best interests of each Party to obtain a single source of supply for both Parties, the Parties acknowledge that they intend to approach jointly and co-negotiate with Third Party suppliers for the manufacture of commercial supplies of the Compound. Any such co-negotiation shall be under the oversight of the JDMC. The Parties acknowledge and agree that any benefits from any economies of scale recognized from such co-negotiation for commercial supplies of the Compound shall be shared by the Parties. Nothing in this Section will oblige either Party to enter into any agreement with any Third Party, or restrict either Party's ability to enter into any agreement with a Third Party without the other Party.

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Section 5.4 Patent Marking.

Each Party shall use Commercially Reasonable Efforts to ensure that where permissible under Applicable Law(s) and provided there is adequate space available on any such packaging, such Party shall identify by number any applicable Micrologix Patent Rights and applicable patent rights within the Strata Intellectual Property with any reasonable patent marking notification(s).

ARTICLE 6
REGULATORY COMPLIANCE

Section 6.1 Ownership and Maintenance of Governmental Approvals.

(a) Strata will own all Marketing Authorizations for each country in the Territory for use in the Field. Without limiting the generality of the foregoing, Strata shall prepare and submit in its own name and at its expense the NDA with the FDA in the U.S. and any other equivalent application with the Competent Authorities in other countries in the Territory. Without acting as a limitation to any other provision under this Agreement, Strata shall maintain a current and valid DMF on the Compound and the Product, whether as an independent document or as part of the NDA, which it shall keep up to date at all times during the Term and shall cause any Subcontractor to similarly maintain the same or grant the Subcontractor reference rights to Strata's DMF for the Product.

(b) Other than those required to be maintained by Micrologix under Section 6.7(b), Strata shall secure and maintain in good standing, at its sole cost and expense, any and all Governmental Approvals (including, Marketing Authorizations, licenses, permits and consents, facility licenses and permits required by Applicable Laws or by the applicable Competent Authorities) necessary and/or required for Strata to perform its obligations under this Agreement and use Commercially Reasonable Efforts at its cost and expense to secure and maintain any variations and renewals thereof.

(c) Excluding Marketing Authorizations and subject to Section 6.7(b), Micrologix shall secure and maintain, at its sole cost and expense, any and all Governmental Approvals (including, licenses, permits and consents, facility licenses and permits required by Applicable Laws or by the applicable Competent Authorities) necessary and/or required for Micrologix to perform its obligations under this Agreement and any Development Subcontract and use Commercially Reasonable Efforts, at its cost and expense to secure and maintain any variations or renewals thereof.

Section 6.2 Rights of Reference.

(a) For the Products in the Field in the Territory, Micrologix shall grant and hereby grants to Strata and its Representatives (subject to the terms of Section 3.5), a free-of-charge right to reference and use and have full access to all Governmental Approvals and all other regulatory documents owned or Controlled by Micrologix to the extent relating to the Compound, the Product, and MBI 594AN, including any IND, any NDA and any DMF (whether as an independent document or as

part of any NDA, and all chemistry, manufacturing and controls information), and any supplements, amendments or updates to the foregoing.

(b) For use outside the Territory, or for any Product for use inside the Territory but outside the Field, Strata shall grant and hereby grants to Micrologix and its Representatives a free-of-charge right to reference and use and have full access to all Governmental Approvals and all regulatory documents owned or Controlled by Strata to the extent relating to the Compound or the Product, including any NDA and DMF (whether as an independent document or as part of any NDA, and all chemistry, manufacturing and controls information), and any supplements, amendments or updates to the foregoing.

(c) For the Products in the Field in the Territory, Micrologix shall make Commercially Reasonable Efforts to grant or have granted to Strata (subject to the terms of Section 3.5), a free-of-charge right of reference and use and have full access to all Governmental Approvals and all other regulatory documents owned or Controlled by Fujisawa Healthcare, Inc. or by any Third Party licensee of Micrologix to the extent related to the Compound, the Product, and MBI 594AN, including any IND, any NDA and any DMF (whether as an independent document or as part of any NDA, and all chemistry, manufacturing and controls information), and any supplements, amendments or updates to the foregoing.

(d) For use outside the Territory, or for any Product for use inside the Territory but outside the Field, Strata shall make Commercially Reasonable Efforts to grant or have granted to Micrologix and its Representatives a free-of-charge right of reference and use and have full access to all Governmental Approvals and all other regulatory documents owned or Controlled by any Third Party licensee of Strata to the extent related to the Compound or the Product, including any IND, any NDA and any DMF (whether as an independent document or as part of any NDA, and all chemistry, manufacturing and controls information), and any supplements, amendments or updates to the foregoing. Such rights of reference, use and access shall survive termination of this Agreement.

(e) For avoidance of doubt, no transfer by a Party of Control in respect of any Governmental Approvals or other regulatory documents referred to in this Section shall limit the rights of the other Party to the most current version of same up to the time of such transfer.

Section 6.3 Adverse Drug Event Reporting and Post Marketing Surveillance.

(a) Each Party, on behalf of itself, its Affiliates and any permitted sublicensees, shall advise the other Party, by telephone or facsimile, promptly but in no event later than seventy-two (72) hours or such shorter time period as may be required by a Competent Authority after a Party, its Affiliates and/or sublicensees becomes aware of any serious adverse drug event (as defined in 21 CFR Section 312.32(a) or its equivalent under Applicable Law(s) as the same may be amended, supplemented or replaced from time to time) (a "**SADE**") involving the Product or the Compound. Such advising Party shall provide the other Party with a written report delivered by confirmed facsimile of any SADE, stating the full

facts known to such Party, including customer name, address, telephone number, batch, lot and serial numbers, and other information as required by Applicable Laws. After receipt by the Parties of an Approval Letter in any country, Strata shall have full responsibility in such country for: (i) monitoring such SADEs; (ii) data collection activities that occur between Strata and the patient or medical professional, as appropriate, including any follow-up inquiries which Strata deems necessary or appropriate; and (iii) meeting the requirements of the Competent Authorities, including the submission of SADE individual reports and periodic reports as necessary. As the holder of the Marketing Authorizations, any reporting (and follow-up thereto) to the Competent Authorities relating to the Compound and the Product in the Field in the Territory shall remain the responsibility of Strata.

(b) In the event either Party requires information regarding SADEs with respect to reports required to be filed by it in order to comply with Applicable Laws, including obligations to report SADEs to the Competent Authorities, each Party agrees to provide such information to the other in sufficient time to enable each Party to report such SADEs to the Competent Authorities in accordance with Applicable Laws.

(c) If the report of an SADE causes a Competent Authority to request a Labelling revision and/or any other corrective action, or if Strata believes it is necessary to have a Labelling revision or conduct a post marketing surveillance program as a result of an SADE, then Strata shall determine all of the material terms and conditions of such Labelling revision, corrective action or post marketing surveillance program in consultation with the applicable Competent Authority. Upon Strata's request, Micrologix will cooperate with Strata with respect to any of the foregoing. The costs of such Labelling revision, corrective action or post marketing surveillance program shall be borne one hundred percent (100%) by Strata. Notwithstanding the foregoing, however, the Parties agree that if any such Labelling revision or corrective action or post marketing surveillance program is due to the negligence or willful misconduct in the conduct by Micrologix and/or its Representatives of the pre-clinical and clinical research and development activities in connection with the Product prior to and after the Effective Date, then, in such event, the costs of any such Labelling revision, corrective action, or post marketing surveillance program, as the case may be, shall be borne one hundred percent (100%) by Micrologix. Subject to Section 5.3 and Section 6.2, the Parties agree that Strata shall own the results and underlying data from any Phase IV Study.

(d) Within thirty (30) days of the filing of each report with the FDA on drug related adverse events associated with the Compound as may be required under Applicable Laws, each Party will provide to the other Party particulars of such adverse events.

Section 6.4 Post Marketing Commitments. If the FDA or other Competent Authority requires a Post Marketing Commitment for the Product, then Strata shall use Commercially Reasonable Efforts to implement such Post Marketing Commitment at Strata's expense.

Section 6.5 Assistance**.**

Each Party shall provide reasonable assistance to the other at the other's request, in connection with their obligations pursuant to this Article 6, the requesting Party shall reimburse all of the other Party's reasonable documented out-of-pocket costs of such assistance, subject to the allocation of costs determined pursuant to this Article 6.

Section 6.6 Compliance**.**

Subject to the other terms and conditions of this Agreement, the Parties agree to the following general compliance provisions:

(a) Strata shall be responsible for compliance in all material respects with Applicable Laws and the Governmental Approvals relating to its activities under the Development, the making, manufacturing, marketing, advertising, promoting, selling, distributing, and commercializing the Product, including the maintenance of the Marketing Authorizations and other requirements of a Competent Authority applicable thereto, obtaining and holding all necessary permits and any other requirements relating to its activities under the Development, the making, manufacture, import, export, storage, sale and distribution of the Product. Any and all Labelling, packaging and artwork and any and all proposed change to any such Labelling, packaging and/or artwork shall be determined by Strata, which shall have the sole right and decision-making authority with respect thereto. Strata shall have the sole right and decision making authority with respect to any and all advertising, sales and marketing materials (collectively the "**Promotional Material(s)**") and shall be responsible for all interactions with the Competent Authorities in connection with such Promotional Materials. Strata shall submit any required changes to the Labelling, packaging and/or artwork to the Competent Authorities in a timely fashion at Strata's expense.

(b) Micrologix shall be responsible for compliance in all material respects with Applicable Laws and Governmental Approvals relating to Development to be conducted by Micrologix pursuant to any Development Subcontract. Strata shall be responsible for compliance in all material respects with Applicable Laws and Governmental Approvals relating to the Development to be conducted by Strata. Each Party shall cause their respective Subcontractors to comply with this Section 6.6(b).

(c) As provided in this Agreement with regard to each Party's obligations hereunder, Strata and Micrologix (as the case may be) shall each comply in all material respects with all Applicable Laws within the Territory, including the provision of information by Strata and Micrologix to each other necessary for Micrologix and Strata, as the case may be, to comply with any applicable reporting requirements and Governmental Approvals required; and maintaining any and all licenses, permits and consents necessary and/or required for complying with such Party's

obligations under this Agreement. During the Term, each Party agrees to execute and deliver to the other Party any certifications that may be required by Applicable Laws, including any debarment certification.

(d) Each Party shall promptly notify the other Party of any written or oral notices received from, or inspections by, the FDA, or other Competent Authority, which materially impact the Product, the Development and/or the Marketing Authorizations, and shall promptly inform the other Party of any responses to such written notices or inspections and the resolution of any issue raised by the FDA or other Competent Authority.

Section 6.7 General Regulatory Matters.

(a) Subject to Micrologix's obligations under Section 6.7(b) and Applicable Laws during the period in which it is the IND holder, Strata shall have all regulatory responsibility with respect to and relative to the Product and has the sole right and decision making authority with respect to all such regulatory matters, including without limitation reaching agreement on all regulatory matters with the FDA and/or any other Competent Authority.

(b) The Parties acknowledge that Micrologix, as of the Effective Date, owns and holds certain Governmental Approvals in connection with the research and development of the Product, including without limitation the IND listed in Exhibit "D". Micrologix shall be responsible for the filing and maintenance in good standing of all such Governmental Approvals, with costs and expenses associated therewith to be included in Reimbursable Costs. During the time that Micrologix is the holder of the IND, Micrologix shall comply with all Applicable Laws applicable to the holder of the IND, including, without limitation, process, track and report all IND Safety Reports (as defined by the FDA). Upon Strata's request, such request to be made as soon as reasonably possible, Micrologix shall transfer to Strata, without any additional consideration, those Governmental Approvals (including without limitation the IND) requested by Strata.

(c) During the time that Micrologix is the holder of such Governmental Approvals, Strata shall be entitled to attend any and all meetings and participate in telephone calls with the Competent Authorities, including without limitation any meeting preparation, meeting co-ordination, preparation of minutes and pre-NDA meeting with the FDA. During such time as Micrologix is the holder of such Governmental Approvals, subject to Micrologix's obligations under Section 6.7(b) and Applicable Laws during the period of time in which it is the IND holder:

(i) Strata has the sole right and decision making authority for all regulatory matters with respect to or relative to the Product.

(ii) While it is still the holder of the IND in the United States, Micrologix shall give Strata no less than three (3) business days notice following the scheduling of any such meeting and/or telephone call with the FDA and/or other Competent Authority (or such shorter period of time, if the meeting

and/or telephone call is scheduled within such three (3) business days and in such event such notice shall be in sufficient time so that Strata shall be able to attend and/or participate in such meeting and/or telephone call).

(iii) Micrologix shall provide Strata copies of any materials relating to any regulatory matter prior to their presentation to the FDA or other Competent Authority during the Development, so that Strata shall have an opportunity to review and comment thereon.

(iv) The JDMC shall approve all such materials prior to presentation.

ARTICLE 7
PATENTS

Section 7.1 Maintenance of Patents or Marks.

(a) Micrologix shall, at Micrologix's expense and on a timely basis in each country in the Territory: (i) use Commercially Reasonable Efforts to obtain Micrologix Patent Rights in all countries in the Territory; (ii) pay all fees and file all documentation and other materials required by any Competent Authority in each applicable country to maintain and/or renew Micrologix Patent Rights; and (iii) shall use Commercially Reasonable Efforts to otherwise maintain the Micrologix Patent Rights in all countries in which Strata has the right and elects to exercise any or all of its rights hereunder related to the Product; provided however, that upon written request by Micrologix, Strata shall, at no cost or expense to Strata, provide such reasonable assistance as may be necessary to enable Micrologix to comply with the administrative formalities necessary to register or maintain any Micrologix Patent Rights.

(b) In the event Micrologix intends to abandon the prosecution or maintenance of all or any part of Micrologix Patent Rights claiming the Product or the Compound (which it shall only be permitted to do in the event it has a bona fide belief that obtaining or maintaining rights are not possible using Commercially Reasonable Efforts), Micrologix shall notify Strata no less than [***] (or such shorter period of time if there is a shorter period of time required by a Competent Authority) prior to the date it intends to abandon the prosecution or maintenance, as applicable, of any such Micrologix Patent Rights.

(c) In the event Micrologix notifies Strata within the period provided in Section 7.1(b), Strata has the right but not the obligation to assume such prosecution and/or maintenance and shall notify Micrologix if, and when, Strata wishes to assume the responsibility for prosecuting and maintaining such Micrologix Patent Rights, as applicable, whereupon Micrologix shall permit Strata, at Strata's expense, to take over such prosecution and/or maintenance, as applicable, and Micrologix shall cooperate in any such transfer of responsibilities and rights as

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necessary or prudent for the benefit of Strata to prosecute and/or maintain the foregoing rights. Thereafter, Strata shall have the right but not the obligation to prosecute or maintain any such Micrologix Patent Right, as the case may be, at its expense; provided that Strata keep Micrologix reasonably informed of the progress of any such prosecution. Micrologix shall have the right to review all such pending applications and other proceedings and make recommendations to Strata concerning them and their conduct, but the final decision with respect thereto shall rest with Strata, provided that Strata acts reasonably.

(d) Each Party shall make available to the other Party or its authorized attorneys, agents or representatives, its employees, agents or consultants necessary or appropriate to enable the other Party to file, prosecute and maintain its patent applications covering the Product for a reasonable period of time sufficient for the other Party to obtain the assistance it needs from such personnel. Micrologix shall provide Strata with copies of all material correspondence, documentation and/or submissions provided to, and received from, U.S. PTO and comparable Competent Authorities that may materially affect Strata's rights under this Agreement.

Section 7.2 Cooperation and Procedures Relative to Actions Brought Under Section 7.3 and Section 7.4.

(a) The Parties shall reasonably cooperate with each other with respect to any litigation, action, suit, claim or other proceeding under Section 7.3 or Section 7.4 (an "**Article 7 Proceeding**"). Without limiting the generality of the foregoing, the "Non-Litigating Party" (as hereinafter defined) agrees to cooperate reasonably in any Article 7 Proceeding, as may be requested by or necessary to the "Litigating Party" (as hereinafter defined) including, joining any Article 7 Proceeding as a party, executing all necessary documents, supplying essential documentary evidence and making available essential witnesses then in its employment or engaged as a consultant.

(b) The Party prosecuting any Article 7 Proceeding under Section 7.3 or controlling the defence of any Article 7 Proceeding under Section 7.4 shall be referred to in this context, as the "**Litigating Party**"). The other Party in this context shall be referred to as the "**Non-Litigating Party**". Except as provided in Section 7.2(e) or Section 7.4(b), the Litigating Party shall have the right to control any Article 7 Proceeding. In addition, the Litigating Party shall have the right to control the settlement or compromise of any Article 7 Proceeding and may so settle or compromise without the Non-Litigating Party's prior written consent, provided that the terms of any such settlement or compromise: (i) does not materially impair the Non-Litigating Party's rights hereunder (including each Party's rights in the Micrologix Technology or the validity or enforceability thereof); (ii) would not require the Non-Litigating Party to be subject to an injunction or to make a monetary payment or would restrict the claims in or admit any invalidity or unenforceability of the Micrologix Patent Rights; (iii) provide for the unconditional release of the Non-Litigating Party; and (iv) expressly state that neither the fact of settlement, nor the settlement agreement shall constitute or be construed or interpreted, as, an admission by the Non-Litigating Party of any

issue, fact, allegation or any other aspect of the claim being settled. In all other cases, the Litigating Party may not settle any Article 7 Proceeding without the prior written consent of the Non-Litigating Party, which consent shall not be unreasonably withheld or delayed. The Non-Litigating Party may not pay or voluntarily permit the determination of any liability which is subject to any such Article 7 Proceeding while the Litigating Party is negotiating the settlement thereof or contesting the matter, except with the prior written consent of the Non-Litigating Party, which consent shall not be unreasonably withheld or delayed.

(c) Upon learning of any actual, contemplated or threatened Article 7 Proceeding involving any of the Micrologix Patent Rights that claims the Product or the Compound, each Party shall promptly notify the other Party of such and shall, upon request, provide to the other Party an assessment of the status of any such proceeding.

(d) To the extent any cooperation provided by Micrologix hereunder requires Micrologix to disclose information that would be deemed Micrologix Confidential Information (other than any information which shall become the property and right of Strata under Section 3.4), Strata shall treat such information in accordance with Section 8.1.

(e) The Parties acknowledge and agree that circumstances may arise in which a Party hereto may desire to protect its interests by joining or intervening in litigation or other proceeding involving the Micrologix Patent Rights, which proceeding has neither been brought by that Party nor levied against that Party. Accordingly, neither Party shall object or oppose any effort by the other Party, at its own expense, to join or intervene in such litigation or other proceedings involving the Micrologix patent Rights. In the event the Non-Litigating Party seeks to join or intervene in any litigation or other proceeding where such joining or intervention is neither requested by nor necessary to the Litigating Party, then (i) the Litigating Party's right to control the litigation under Section 7.3 or Section 7.4 (as the case may be) shall not be extended to the conduct of the Non-Litigating Party after intervention or joining; and (ii) notwithstanding anything to the contrary contained in Section 7.3 and Section 7.4, the Non-Litigating Party shall bear its own costs associated with its involvement in any such litigation or other proceeding after intervening or joining.

Section 7.3 Prosecution of Infringement.

(a) During the Term, each Party shall give prompt notice to the other of any Third Party act which may infringe one or more claims of the Micrologix Patent Rights that claims the Product or the Compound.

(b) **Infringement within the Field.**

(i) Strata may (but shall have no obligation to do so) prosecute any Article 7 Proceeding under this Section 7.3 against such Third Party infringement of any claims of Micrologix Patent Rights where such infringement primarily relates to such Third Party activities in the Field in the Territory in

accordance with the terms of Section 7.2 and this Section 7.3 and in such event Strata shall become the Litigating Party.

(ii) In the event Strata fails to institute any Article 7 Proceeding and terminate any Third Party infringement of the claims of Micrologix Patent Rights that the claim the Product or the Compound within thirty (30) days of the later of: (i) receiving notification from Micrologix of any such infringement or (ii) sending notice to Micrologix of such action, Micrologix may take (but shall have no obligation to do so) such action as it deems appropriate, including the filing of a lawsuit against such Third Party. In such event Micrologix shall promptly notify Strata of any such Article 7 Proceeding and shall become the Litigating Party.

(c) **Infringement outside the Field.**

(i) Micrologix may (but shall have no obligation to do so) prosecute any Article 7 Proceeding under this Section 7.3 against such Third Party infringement of any claims of Micrologix Patent Rights where such infringement does not primarily relate to such Third Party activities in the Field in the Territory in accordance with the terms of Section 7.2 and this Section 7.3 and in such event Micrologix shall become the Litigating Party.

(ii) In the event Micrologix fails to institute any Article 7 Proceeding and terminate any Third Party infringement of the claims of Micrologix Patent Rights that claim the Product or the Compound within thirty (30) days of the later of: (i) receiving notification from Strata of any such infringement or (ii) sending notice to Strata of such action, Strata may take (but shall have no obligation to do so) such action as it deems appropriate, including the filing of a lawsuit against such Third Party. In such event Strata shall promptly notify Micrologix of any such Article 7 Proceeding and shall become the Litigating Party.

(d) Micrologix and Strata shall share all Costs in connection with any Article 7 Proceeding under this Section 7.3, on the basis of [***]% paid by the Litigating Party and [***]% paid by the Non-Litigating Party, provided that Micrologix and Strata shall first recover their respective actual documented out-of-pocket Costs, or equitable proportions thereof, associated with any Article 7 Proceeding under this Section 7.3, or settlement thereof from any recovery made by the Litigating Party. Any excess amount recovered by the Litigating Party shall be shared between Strata and Micrologix on the basis of [***]% to the Litigating Party and [***]% to the Non-Litigating Party. In the event there is no recovery from a Third Party or if any such recovery does not cover all of the Costs of the Litigating and/or Non-Litigating Party, as the case may be, then the Parties agree to share any such unrecovered Costs on the basis of [***]% to the Litigating Party and

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[***]% to the Non-Litigating Party. If Strata is the Litigating Party, Strata shall recover such amounts by [***].

Section 7.4 Infringement Claimed by Third Parties.

(a) In the event a Third Party commences, or threatens to commence, any Article 7 Proceeding against a Party to this Agreement alleging infringement of a Third Party's intellectual property rights by the making, manufacture, use, sale, offer for sale, export and/or import by Strata, its Affiliates or sublicensees of the Product, the Party against whom such proceeding is threatened or commenced shall give prompt notice to the other Party ("**Infringement Notice**").

(b) Strata shall control the defense and settlement of any such Article 7 Proceeding under this Section 7.4 in accordance with the terms of Section 7.2 and this Section 7.4 and shall become the Litigating Party; provided that, in the event that the validity and enforceability of the claims of Micrologix Patent Rights are in issue in any such Article 7 Proceeding under this Section 7.4, Micrologix may (but shall have no obligation to do so) control the defense and settlement of any such Article 7 Proceeding under this Section 7.4 in accordance with the terms of Section 7.2 and this Section 7.4 solely to the extent that such defense and settlement relates to validity and enforceability of the claims of the Micrologix Patent Rights.

(c) Micrologix shall be liable for its own Costs in connection with any Article 7 Proceeding under this Section 7.4.

Section 7.5 Co-operation with Other Licensees.

Strata acknowledges that Micrologix may grant to licensees rights in the Micrologix Technology in the Territory in respect of fields outside the Field, and may grant to other licensees rights outside the Territory. If Micrologix grants such rights to other licensees, in the event of any litigation in respect of:

(a) fields outside of the Field that may reasonably affect Strata's use of the Micrologix Technology in the Field or the use or sale of Products by Strata; or

(b) the Field that may reasonably affect Micrologix or one or more of Micrologix's licensee's use of the Micrologix Technology outside the Field or the making, manufacture, use or sale of products outside the Field by Micrologix or one or more other such licensee(s);

then Micrologix, Strata and such other licensee(s) will use good faith efforts to determine jointly the course of action, if any, necessary or appropriate to prosecute or defend the litigation. Micrologix will use Commercially Reasonable Efforts to include in its other license agreements, provisions that allow the participation of Strata as contemplated herein. If Micrologix is unable to include in any such other license agreement such provisions, then with respect to the licensee under such other license agreement, Strata shall not be bound by the terms and conditions of this Section 7.5.

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ARTICLE 8
CONFIDENTIALITY

Section 8.1 Confidentiality.

(a) During the Term and for a period of five (5) years thereafter, each Party shall maintain all Confidential Information of the other Party as confidential and shall not disclose any such Confidential Information to any Third Party or use any such Confidential Information for any purpose, except (i) as expressly authorized by this Agreement or with the prior written consent of the other Party, which consent shall not be unreasonably withheld or delayed, (ii) as required by Applicable Laws or court order of a court of competent jurisdiction (provided that the disclosing Party shall first notify the other Party to afford the other Party, for a period of ten (10) business days or such lesser period as may be provided by Applicable Law, an opportunity to seek whatever protective relief it deems appropriate, and the disclosing Party shall use Commercially Reasonable Efforts to obtain confidential treatment of any such information required to be disclosed), (iii) to its Representatives to accomplish the purposes of this Agreement, so long as such Representatives are under an obligation of confidentiality no less stringent than as set forth herein, (iv) to bona fide potential investors and their respective advisors during financing or an acquisition, merger or other like reorganization, so long as such investors and advisors are under an obligation of confidentiality no less stringent than as set forth herein, except as otherwise provided herein, and (v) as is required to exercise its rights and perform its obligations under this Agreement, so long as the recipients of such information are under an obligation of confidentiality no less stringent than as set forth herein. Each Party may use such Confidential Information only to the extent required to accomplish the purposes of this Agreement.

(b) Notwithstanding any provision to the contrary herein or in any confidentiality or nondisclosure agreement between the Parties, from time to time, either Party may disclose to bona fide potential investors and their respective advisors during financing or an acquisition, merger or other like reorganization the following Confidential Information:

(i) [***];

(ii) [***];

(iii) [***];

(iv) [***];

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(v) [***];

(vi) [***];

(vii) [***];

(viii) this Agreement, in the form as redacted and filed with the SEC and available for disclosure, as may be modified by SEC filings, press releases or other public disclosures, or if not filed with the SEC, as executed with the financial particulars in Article 4 redacted to the extent not publicly disclosed; and

(ix) such additional information and materials as may be agreed-to by the Parties;

all without obtaining written agreement of confidence and non-use from the recipient. The disclosing Party remains liable to the other Party for any use or disclosure made of such information by such investors and advisors, as if such investors and advisors were bound by the terms of this Article 8. No information disclosed pursuant to this Section 8.1(b) that becomes generally known or available, directly or indirectly as a result of a disclosure permitted by this Section, shall be excluded from the definition of Confidential Information pursuant to the exclusion set out in Section 1.14(a).

(c) Each Party shall use at least the same standard of care as it uses to protect its own Confidential Information to ensure that it and its Affiliates and Representatives do not disclose or make any unauthorized use of the other Party's Confidential Information. Each Party shall be responsible for any breach of this Agreement by its Representatives. Each Party shall promptly notify the other Party upon discovery of any unauthorized use or disclosure of the other Party's Confidential Information.

(d) Micrologix acknowledges and agrees that the Micrologix Know-How licensed to Strata has value to Strata in being maintained as confidential. Therefore, Micrologix shall keep the Micrologix Know-How confidential as if it were Confidential Information of Strata as set forth in this Article 8.

Section 8.2 Publicity Review.

The Parties agree that the public announcement of the execution of this Agreement shall be in the form of a press release to be mutually agreed upon by the Parties on or before the Effective Date and thereafter each Party shall be entitled to make or publish any public statement consistent with the contents thereof. Thereafter, except as allowed in the preceding sentence, the Parties will jointly discuss and agree, based on the principles of this Section 8.2, on any statement to the public regarding this Agreement or any aspect of this Agreement, and the results of clinical studies conducted as part of the Development, subject in each case to disclosure otherwise required by Applicable Laws. When a Party elects to make any such statement or disclosure required under Applicable Law, it will give the other Party at least five (5) business days notice to review and comment on such statement, unless the applicable Competent Authority requires disclosure such that a Party is prohibited by Applicable Law to provide such advance review by the other Party (in which case it shall be disclosed according to such requirement and notice will

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be provided as soon as possible). The terms of this Agreement may also be disclosed to Competent Authorities, including the United States Securities and Exchange Commission or any other exchange or securities commission having authority over a Party, where required by Applicable Law, with redaction of financial information not otherwise required to be disclosed under Applicable Laws in which event the disclosing Party shall provide in advance of submission to the other Party for review and comment a copy of such redactions made to this Agreement.

ARTICLE 9
REPRESENTATIONS, WARRANTIES AND COVENANTS

Section 9.1 Corporate Power.

Each Party hereby represents, warrants and covenants that such Party is, and will remain through the Term, duly organized and validly existing under the laws of the state of its incorporation and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof.

Section 9.2 Due Authorization.

Each Party hereby represents and warrants that such Party is duly authorized to execute and deliver this Agreement and covenants to perform its obligations hereunder.

Section 9.3 Binding Obligation/No Conflict.

Each Party hereby represents, warrants and covenants that: (i) this Agreement is a legal and valid obligation binding upon it and is enforceable in accordance with its terms; and (ii) the execution, delivery and performance of this Agreement by such Party does not, and will not during the Term, conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it may be bound, nor to the best knowledge of each Party as of the Effective Date, violate any Applicable Laws.

Section 9.4 Ownership of Micrologix Technology.

Micrologix represents, warrants, and covenants, as the case may be, that:

(a) as of the Effective Date and during the Term, it is and shall remain the sole owner of all right, title and interest in and to the Micrologix Technology, subject to Micrologix's ability to license and assign as permitted hereunder; and, to the best of the knowledge of Micrologix as of the Effective Date, no Representative of Micrologix or any Third Party has any rights to the Micrologix Technology;

(b) as of the Effective Date, it has not granted and will not grant after the Effective Date any license under the Micrologix Technology for any product in the Territory for use in the Field to any Third Party, and is under no obligation to grant any such license, except to Strata, and there are, and will be, no rights granted to any Third Party and/or no agreements, either written or oral, regarding either the Micrologix Technology which are inconsistent or in conflict with this Agreement;

(c) as of the Effective Date, there are no outstanding liens, judgments, injunctions, decrees, rulings, security interests, or other encumbrances on the Micrologix Technology, and through the Term, there shall be no liens, judgments, injunctions, decrees, rulings, security interests, or any other encumbrances (other than security interests filed by Micrologix's lender(s) and licensee(s) in the ordinary course of business) on the Micrologix Technology which could materially affect Strata's interests in the Micrologix Technology;

(d) as of the Effective Date and during the Term, it has taken and will take Commercially Reasonable Efforts to ensure that all Micrologix Know-How has been and will continue to be fully protected and maintained in accordance with appropriate procedures for its protection;

(e) (i) as of the Effective Date, Micrologix has made available to Strata all material information in its possession or Control relating to the Product in the Field; and (ii) as of the Effective Date, to the best of Micrologix's knowledge, all art that Micrologix believes to be material to the patentability of any claims within the Micrologix Patent Rights claiming the Product or the Compound has been cited by Micrologix to the U.S. PTO for U.S. patent rights or to the comparable Competent Authority in such other jurisdictions in the Territory that require disclosure of material information in possession or Control of the patentee; and

(f) Exhibit "B" is a true, complete and current listing of the Micrologix Patents as of the Effective Date.

Section 9.5 Patent and Other Intellectual Property Rights Proceedings.

As of the Effective Date, Micrologix represents and warrants that:

(a) to the best of its knowledge, no patent within the Micrologix Patent Rights, or patent application with regard to the Micrologix Patent Rights, as the case may be, is the subject of any pending interference, opposition, cancellation or other protest proceeding, or judicial proceeding;

(b) to the best of its knowledge, the Micrologix Technology and any process, procedure or method used to manufacture the Compound and the Product do not infringe, interfere with, or misappropriate the intellectual property rights of any Third Party;

(c) to the best of its knowledge, the practice of the Micrologix Patent Rights and any process, procedure or method used to manufacture the Compound and the Product in the Territory do not and will not infringe, interfere with, or misappropriate any intellectual property rights of any Third Party;

(d) there has been no lapse of any claims within the Micrologix Patents in the Territory;

(e) Micrologix has not received any: (i) notices or communications that the development, making, manufacture, use, marketing, advertising, promoting,

distributing, offer for sale, selling, importation or exportation of the Compound or the Product or use of the Micrologix Technology would infringe or misappropriate any intellectual property rights of any Third Party; or (ii) allegation regarding the legality, enforceability, or validity of the Micrologix Technology, other than those made by the U.S. PTO or other comparable Competent Authorities in other countries in the prosecution of the Micrologix Patent Rights and previously disclosed to Strata;

(f) Micrologix is not aware of any Third Party having infringed or misappropriated the Micrologix Technology and has not sent any notices or communications to any Third Party that the activities of such Third Party infringe or misappropriate the Micrologix Technology.

Section 9.6 Micrologix's Additional Warranties.

As of the Effective Date, Micrologix represents and warrants that:

(a) Exhibit "D" is a true, complete and current listing of the regulatory filings relating to Product or Compound owned or Controlled by Micrologix as of the Effective Date, including, all INDs; and

(b) Micrologix has not deliberately withheld any material information or data known to Micrologix relating to:

(i) the results of preclinical and clinical studies of the Compound and the Product conducted by or on behalf of Micrologix;

(ii) Micrologix's ongoing clinical development activities in the United States for the Product, including the status of all such studies; and

(iii) the manufacturing, testing and release of the Compound and Product, including CMC information therefor.

Section 9.7 Strata's Additional Warranties.

As of the Effective Date, Strata represents and warrants that upon completion of transactions related to this Agreement, which transactions are conditional only upon the execution and delivery of this Agreement, Strata shall be entitled to receive proceeds of a financing of not less than $5 million.

Section 9.8 Pre-Clinical and Clinical Studies Prior to Effective Date.

Micrologix represents and warrants that all of the pre-clinical and clinical trials related to the Product prior to the Effective Date have been conducted in accordance with Applicable Laws.

Section 9.9 Debarment.

During the Term, neither of the Parties shall knowingly utilize any employee, representative, agent, assistant or associate who has been debarred by the FDA pursuant to 21 U.S.C. Section 335a (a) or (b) of the Act in connection with any of the activities to be carried out under this

Agreement. Micrologix further represents and warrants that, as of the Effective Date, to the best of its knowledge, none of the entities, laboratories or clinical sites participating in the clinical studies prior to the Effective Date had been debarred at the relevant time.

Section 9.10 Limitation on Warranties.

(a) EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT:

(i) NOTHING HEREIN SHALL BE CONSTRUED AS A REPRESENTATION OR WARRANTY BY MICROLOGIX TO STRATA THAT THE MICROLOGIX TECHNOLOGY IS NOT INFRINGED BY ANY THIRD PARTY, OR THAT THE PRACTICE OF SUCH RIGHTS DOES NOT INFRINGE ANY PUBLISHED INTELLECTUAL PROPERTY RIGHTS OF ANY THIRD PARTY.

(ii) NEITHER PARTY MAKES ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR ANY OTHER WARRANTY, EXPRESS OR IMPLIED, WITH RESPECT TO THE PRODUCT.

(b) NEITHER PARTY MAKES ANY OTHER WARRANTIES HEREUNDER, EXPRESS OR IMPLIED, INCLUDING WARRANTIES CONCERNING THE SUCCESS OF THE DEVELOPMENT PROGRAM, THE SUCCESS OF THE MARKETING AND COMMERCIALIZATION OF THE PRODUCT OR THE COMMERCIAL UTILITY OF THE PRODUCT.

ARTICLE 10
INDEMNIFICATION AND INSURANCE

Section 10.1 Strata Indemnified by Micrologix.

(a) Micrologix shall indemnify, defend and hold Strata, and its Representatives (in respect of each Party, its "**Indemnitees**"), harmless from and against any Third Party liabilities, obligations, damages, losses, claims, encumbrances, costs or expenses (including attorneys' fees) (any or all of the foregoing herein referred to as "**Loss**") insofar as a Loss or actions in respect thereof, occurred subsequent to the Effective Date (except as provided in Section 10.1(a)(iii) below), and arises out of or is based upon:

(i) any breach by Micrologix of its representations, warranties, covenants, obligations or agreements under this Agreement; or

(ii) the negligence or willful misconduct of Micrologix and/or any of Micrologix's Indemnitees, including violation of Applicable Laws in their performance under this Agreement; or

(iii) Micrologix's (or any Subcontractor's) conduct of the pre-clinical and clinical research and development activities in connection with the Product prior to and after the Effective Date; provided however, Micrologix's duty to indemnify under this Section 10.1(a)(iii) shall not

include product liability claims unless Micrologix's liability for same arises pursuant to Section 10.1(a)(i) or Section 10.1(a)(ii).

(b) Micrologix's obligations to indemnify Strata hereunder shall not apply to the extent any such Loss arises out of or is based on the:

(i) inactions or actions of Strata or its Indemnitees for which Strata is obligated to indemnify Micrologix under Section 10.2; or

(ii) negligence or willful misconduct of Strata and/or its Indemnitees.

Section 10.2 Micrologix Indemnified by Strata.

(a) Strata shall indemnify, defend and hold harmless Micrologix and its Indemnitees from and against any Loss insofar as such Loss or actions in respect thereof occurred subsequent to the Effective Date, and arises out of or is based upon:

(i) any breach by Strata of its representations, warranties, covenants, obligations or agreements under this Agreement; or

(ii) the negligence or willful misconduct of Strata and/or any of Strata's Indemnitees, including any violation of Applicable Law in their performance under this Agreement; or

(iii) Strata's or its Indemnitees' making, manufacture, marketing, sale, distribution, storage or promotion of the Product, including any injury or death to any person or damage to any property caused by any Product provided by Strata or its Indemnitees, whether by reason of breach of warranty, negligence, product defect or otherwise, and regardless of the form in which any such claim is made.

(b) Strata's obligations to indemnify Micrologix hereunder shall not apply to the extent any such Loss arises out of or is based on the:

(i) inactions or actions of Micrologix or its Indemnitees for which Micrologix is obligated to indemnify Strata under Section 10.1; or

(ii) the negligence or willful misconduct of Micrologix and/or its Indemnitees.

Section 10.3 Prompt Notice Required.

No claim for indemnification hereunder shall be valid unless notice of the matter which may give rise to such claim is given in writing by the Party seeking indemnification (the "**Indemnified Party**") to the persons against whom indemnification may be sought (the "**Indemnitor**") as soon as reasonably practicable after such Indemnified Party becomes aware of such claim. Such notice shall state that the Indemnitor is required to indemnify the Indemnified Party and its Indemnitees for a Loss and shall specify the amount of Loss, if available, and relevant details thereof. The Indemnitor shall notify Indemnified Party no later than thirty (30) days from such notice of its intention to assume the defense of any such claim. Failure of the Indemnified Party to notify Indemnitor within such notice period shall not relieve Indemnitor of any liability

hereunder, except to the extent the Indemnitor reasonably demonstrates that the defense of such Third Party claim is prejudiced by such failure.

Section 10.4 Indemnitor May Settle.

The Indemnitor shall, at its expense, have the right to settle and defend any action which may be brought in connection with all matters for which indemnification is available. In such event the Indemnified Party shall cooperate with the Indemnitor as reasonably requested by the Indemnitor in connection with such action; provided that the Indemnified Party shall have the right to fully participate in such defence at its own expense. The defence by the Indemnitor of any such actions shall not be deemed a waiver by the Indemnitor of its right to assert a claim with respect to the responsibility of the Indemnified Party with respect to the Loss in question. The Indemnitor shall have the right to settle or compromise any claim against the Indemnified Party without the consent of the Indemnified Party provided that the terms of any settlement or compromise: (a) does not materially impair the Indemnified Party's rights hereunder (including each Party's rights in the Micrologix Technology); (b) would not require the Indemnified Party to be subject to an injunction or to make a monetary payment or would restrict the claims in or admit any invalidity or unenforceability of the Micrologix Patent Rights; (c) provide for the unconditional release of the Indemnified Party; and (d) expressly state that neither the fact of settlement nor the settlement agreement shall constitute, or be construed or interpreted as, an admission by the Indemnified Party of any issue, fact, allegation or any other aspect of the claim being settled. In all other cases, the Indemnitor may not settle any such action without the prior written consent of the Indemnified Party, which consent shall not be unreasonably withheld or delayed. No Indemnified Party shall pay or voluntarily permit the determination of any liability which is subject to any such action while the Indemnitor is negotiating the settlement thereof or contesting the matter, except with the prior written consent of the Indemnitor, which consent shall not be unreasonably withheld or delayed. If the Indemnitor fails to give Indemnified Party notice of its intention to defend any such action as provided herein, the Indemnified Party involved shall have the right to assume the defence thereof with counsel of its choice and defend, settle or otherwise dispose of such action. If Strata is the Indemnified Party in such case, Strata shall recover its Costs by deducting its Costs from any royalty payments or any other amounts payable to Micrologix hereunder in accordance with Section 4.7(c).

Section 10.5 Insurance.

Each Party shall, at its sole cost and expense, obtain and keep in force during the Term and for a period of not less than three (3) years after termination, cancellation or expiration of this Agreement the following insurance: (a) general liability insurance, including blanket contractual liability coverage with bodily injury, death and property damage with limits of $[***] per occurrence and $[***] in the aggregate within six months after the Effective Date; and (b) clinical studies and product liability insurance with bodily injury death and property damage limits of not less than $[***] per occurrence and $[***] in the aggregate; provided, however, each Party's obligation to maintain such product liability insurance shall not commence until

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immediately prior to the First Commercial Sale of the Product in the first country in the Territory and each Party's obligation to maintain such clinical studies insurance shall not commence until immediately prior to the first human dosing by such Party. Upon execution of this Agreement, and upon the other Party's request thereafter, each Party shall furnish the other with a certificate of insurance signed by an authorized representative of such Party's insurance underwriter evidencing the insurance coverage required by this Agreement and providing for at least thirty (30) days prior written notice to the other Party of any cancellation, termination or reduction of such insurance coverage. Each Party shall use its Commercially Reasonable Efforts to cause Third Parties engaged by a Party to perform its obligations under this Agreement to maintain such types of insurance coverages and for such period of time as are customary for such Third Parties given the nature of the services to be provided.

ARTICLE 11
ADDITIONAL COVENANTS OF THE PARTIES

Section 11.1 Micrologix Covenant Not To Compete.

Micrologix hereby covenants and agrees, and shall cause its Affiliates to agree, not to, in whole or in part, develop, in-license, market, make, manufacture or have manufactured, sell, promote, distribute or have marketed, have sold or have distributed any product in the Territory in the Field (in this Section, a "**Section 11.1 Competitive Product**") during the Term and for a period of [***] thereafter. Notwithstanding the foregoing, if Micrologix acquires an entity or all or substantially all of the assets of an entity during such period of time and such entity distributes or such assets include a Section 11.1 Competitive Product, Micrologix or its Affiliate shall have [***] in which to divest itself of such Section 11.1 Competitive Product or to otherwise cease distribution of such Section 11.1 Competitive Product, and Micrologix shall not be in breach of this Section 11.1 if it so divests or ceases distribution within such [***] period. Strata and Micrologix hereby agree that the covenants set forth in this Section 11.1 are a material and substantial part of the transactions contemplated by this Agreement.

Section 11.2 Launch of Competitive Product by Strata.

Strata hereby agrees that in the event Strata and/or its Affiliates develop, in-license, market, sell, promote, distribute or have marketed, or have sold any product in the Field in a particular country in the Territory that is not a Product hereunder (in this Section, a "**Competitive Product**") during the Term, directly for themselves or by a Third Party, licensee or sublicensee on behalf of Strata and/or its Affiliates, then pursuant to Section 13.4, Strata's rights with respect to such country under this Agreement shall terminate and revert to Micrologix. No termination pursuant to this Section shall terminate this Agreement with respect to any other country in the Territory. Notwithstanding the foregoing, if Strata or an Affiliate acquires an entity or all or substantially all of the assets of an entity during such period of time and such entity distributes or such assets include a Competitive Product, Strata, or its Affiliate(s), shall have [***] in which to divest itself of such Competitive Product or to otherwise cease distribution of such Competitive Product, and Strata shall not be in violation of this Section 11.2 if it so divests or ceases distribution within such [***] period. The Parties mutually agree that Strata's (or Affiliates')

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commercialization, as described above, of any Competitive Product shall not be deemed a breach of this Agreement, and Micrologix sole recourse for such an event shall be that as described in this Section 11.2 only.

Section 11.3 Limitation To The Territory.

Strata hereby covenants that it will not directly or indirectly, without the prior written authorization of Micrologix: (i) promote or actively solicit the sale of the Product or advertise the Product, outside of the Territory; (ii) purchase or cause to be purchased Product which Strata has represented, directly or indirectly, as being for the purpose of sale in a specific country in the Territory for sale in any other country outside the Territory; (iii) contact any of Micrologix's suppliers or vendors of the Product or element thereof for the purpose of causing the Product to be sold outside the Territory; (iv) knowingly sell or distribute for resale the Product purchased hereunder to a Third Party who intends to sell the Product outside of the Territory; and (vi) knowingly sell or distribute for resale Product purchased from a Third Party outside the Territory for resale in the Territory.

Section 11.4 Records and Audits.

(a) Each Party shall keep or cause to be kept true, accurate and complete Books and Records as are required to determine, in a manner consistent with accrual method of accounting in accordance with GAAP, any sums or credits due under this Agreement during the Term and for a period of three years thereafter or as otherwise required to comply with Applicable Laws. Without limiting the generality of the foregoing, the Parties agree that such Books and Records shall include the following:

(i) Strata shall keep such Books and Records to permit Micrologix to confirm the completeness and accuracy of (A) the information presented in each Royalty Statement and all payments due hereunder; (B) the calculation of Net Sales; (C) any payments due Micrologix under this Agreement; and (D) any other payment obligations of Strata hereunder.

(ii) Micrologix shall keep such Books and Records to permit Strata to confirm the completeness and accuracy of (A) Reimbursable Costs; (B) any payments due Strata under this Agreement; and (C) any other obligations of Micrologix hereunder.

(b) With regard to sums or credits due or related reports, at the request (and expense) of the requesting Party, the other Party shall permit the requesting Party and/or such requesting Party's independent certified public accountant selected by such Party and reasonably acceptable to the other Party to audit and/or inspect only those Books and Records of the other Party as may be necessary to determine, with respect to any calendar year ending no more than three years prior to such Party's request, the completeness and accuracy of any reports made and/or any sums or credits due under this Agreement. Any such independent accounting firm shall be subject to the confidentiality provisions of this Agreement. Such inspection shall be conducted during the Party's normal business hours, no more than once in any twelve (12) month period and upon at least thirty (30) days prior

written notice by the requesting Party. If such requesting Party concludes that such payments were underpaid during the periods reviewed by such requesting Party and/or its accountants, the other Party shall pay the requesting Party the amount of any such underpayments, plus interest at a rate equal to the Prime Rate of Interest, within thirty (30) days of the date the requesting Party delivers to the other Party the report so concluding that such payments were underpaid. If such requesting Party and/or its accounting firm concludes that such payments were overpaid during such period, the Party shall pay to the other Party the amount of any such overpayments, without interest, within thirty (30) days of the date the requesting Party delivers to the other Party the report so concluding that such payments were overpaid. The requesting Party shall bear the full cost of such audit unless such audit discloses an underpayment by more than [***] *** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions. of the amount due during such period. In such case, the other Party shall bear the full cost of such audit.

(c) In the event the non-requesting Party does not agree with the conclusions of such report under Section 11.4(b), (whether such payments were underpaid or overpaid), then such Party shall notify the other Party within thirty (30) days after receipt of such report. Thereafter, the Parties shall in good faith try and resolve such differences. If the Parties are unable to reach a mutual agreement within fifteen (15) days after the date of notice then independent auditors of each Party shall meet and select an independent accounting firm (being an accounting firm not used by either Party) to make the final determination within fifteen (15) days thereafter. The determination of such independent accounting firm shall be binding and conclusive on the Parties, and the cost of such firm shall be borne by the Party against whom the determination by such firm is made.

(d) Micrologix shall, upon prior, reasonable notice by Strata and during normal business hours, allow Strata or its Representative to inspect and audit Micrologix's facilities, equipment, personnel and operating procedures (and of any Subcontractor, as applicable) used to develop the Product and any Books and Records related thereto to confirm compliance with the terms and conditions of this Agreement, including compliance with Applicable Laws and Governmental Approvals; provided that Strata shall use Commercially Reasonable Efforts to ensure that such inspection and audit shall not interfere with Micrologix's (or its Subcontractor's, as applicable) normal operations. However, notwithstanding the foregoing, Strata shall be permitted to inspect and audit as provided above immediately on notice in the event of a bona fide belief that (i) an Applicable Law is being, or may be, violated or (ii) there is, or may be, an SADE or imminent and otherwise material harm to the public due to the Product. Without limiting anything else under this Agreement, if any of the obligations of Micrologix is performed by a Subcontractor, then Micrologix shall cause any such Subcontractor to comply with the terms and conditions of this Section 11.4(d). If any inspection or audit hereunder reveals that Micrologix (or its Subcontractor(s) or other Representatives) is not in compliance in all material respects with the

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terms and conditions of this Agreement, Applicable Laws, or/and applicable Governmental Approvals, Micrologix, at its sole cost, shall use Commercially Reasonable Efforts to promptly correct (and, as applicable, cause its Subcontractor(s) to use Commercially Reasonable Efforts to promptly correct) any such deficiencies to ensure compliance as required hereunder. Micrologix shall keep Strata informed on a regular, on-going and periodic basis as to the status of any such deficiencies and such corrections.

Section 11.5 Marketing Expenses.

Strata covenants and agrees that, except as otherwise specified in this Agreement, Strata shall be solely responsible for the cost and implementation of any and all marketing, sales, promotional and related activities concerning or related to the marketing, sale, distribution and promotion of the Product under this Agreement.

Section 11.6 Further Actions.

Upon the terms and subject to the conditions hereof, each of the Parties shall use its Commercially Reasonable Efforts to take, or cause to be taken, all appropriate action and do, or cause to be done, all things necessary or advisable under Applicable Laws or otherwise to consummate and make effective the transactions contemplated by this Agreement.

ARTICLE 12
PRODUCT RECALL

Section 12.1 Product Recalls or Withdrawal.

If at any time or from time to time during the Term: (a) any Competent Authority of any country in the Territory requests Strata to recall or withdraw the Product; (b) a court of competent jurisdiction issues an order or directive for the Product to be recalled or withdrawn; or (c) if a voluntary recall or withdrawal of the Product is contemplated by Strata (individually or collectively, a "**Recall**"), then Strata shall carry out any Recall in the Territory in as expeditious a manner as reasonably possible to preserve the goodwill and reputation of the Product and the goodwill and reputation of the Parties. Strata shall in all events be responsible for conducting any Recall in the Territory, market withdrawals or corrections with respect to the Product in the Territory. Strata shall maintain records of all sales and distribution of Product and customers sufficient to adequately administer a Recall for the period required by Applicable Law. Micrologix shall cooperate as reasonably requested by Strata in connection with any such Recall. Strata will be responsible for complying with all Applicable Laws and Governmental Approvals during the Recall and will be responsible for all interactions with appropriate Competent Authorities, including, the FDA Office of Compliance in the U.S. and the appropriate FDA local district office(s) in the U.S. Strata shall be responsible for preparing and timely submitting any reports any other documentation required by the Competent Authorities in connection with any such Recall.

Section 12.2 Recall Costs.

Strata shall be responsible for conducting any Recall of the Product in the Territory and the cost and expense therefor shall be paid by Strata, unless such Recall is due to, prior to or during the

Development: (i) any breach by Micrologix of its representations, warranties, covenants, obligations or agreements under this Agreement; or (ii) the negligence or willful misconduct of Micrologix and/or any of Micrologix's Representatives under this Agreement, including violation of Applicable Laws in their performance under this Agreement; in which case all such costs and expenses, to the extent same are reasonable, shall be borne and paid solely by Micrologix. In such event, Micrologix will reimburse Strata for any such costs and expenses paid by Strata within thirty (30) days of its receipt of a reasonably detailed invoice(s) for such costs and expenses from Strata.

Section 12.3 Notification Of Complaints.

During the Term and for a period of four (4) years after the termination, expiration or cancellation of this Agreement or for such longer period as may be required by Applicable Law(s), each Party agrees to (a) notify the other Party immediately of all available material information concerning any complaint, product defect reports, and similar notices received by either Party with respect to the Product, whether or not determined to be attributable to the Product and (b) with respect to an SADE, comply with the provisions of Section 6.6. Strata shall define and implement appropriate and necessary regulatory compliance procedures for product defect reporting, including action plans and an SOP and will handle all product complaints in the Territory. In connection with any such product complaint Micrologix shall cooperate as reasonably requested by Strata. Strata, at its sole cost and expense, will have the responsibility for preparing and submitting any reports to the Competent Authorities, including FDA field alerts.

Section 12.4 Notification Of Threatened Action.

During the Term and, for a period of four years after the termination, expiration or cancellation of this Agreement or for such longer period as may be required by Applicable Law(s), each Party agrees to immediately notify the other Party of any information it receives regarding any threatened or pending action, inspection or communication by or from a concerned Competent Authority which may affect the safety or efficacy claims of the Product or the continued marketing or distribution of the Product. Upon receipt of such information, the Parties shall consult with each other in an effort to arrive at a mutually acceptable procedure for taking appropriate action, provided that, subject to Micrologix's obligation under Section 6.1 and Applicable Laws during the Period Micrologix is the IND holder, Strata shall have the final decision making authority with respect thereto.

ARTICLE 13
TERM AND TERMINATION

Section 13.1 Term.

This Agreement shall become effective on the Effective Date and shall expire on the date of the expiration of the last to expire Royalty Term in any country in the Territory (the "**Term**"), unless earlier terminated as provided in Section 13.2, Section 13.3 or Section 13.4.

Section 13.2 Termination by Either Party.

Either Party may terminate this Agreement (in its entirety or on a country by country basis as hereinafter provided) prior to the expiration of the Term upon the occurrence of any of the following:

(a) upon or after the cessation of operations of the other Party or the bankruptcy, dissolution or winding up of the other Party (other than dissolution or winding up for the purposes or reconstruction or amalgamation which includes an assignment permitted by this Agreement) or the filing of any involuntary petition for bankruptcy, dissolution, liquidation or winding up of the affairs of the other Party which is not dismissed within ninety (90) days after the date on which it is filed or commenced, and in the case of any of the foregoing events, the non-defaulting Party may terminate the Agreement in its entirety; or

(b) upon or after the breach of any material provision of this Agreement by the allegedly breaching Party if the allegedly breaching Party has not cured such breach within sixty (60) days after written notice thereof by the non-breaching Party, the non-breaching Party may, at its sole option, terminate this Agreement with respect to the particular country in the Territory that is the subject of such breach, and this Agreement shall remain in effect as it applies to all other countries; provided, however, that if such breach and failure to cure occurred in the United States, the non-breaching Party may terminate this Agreement in its entirety, and if such breach and failure to cure occurred in a Major European Market Country, the non-breaching Party may terminate this Agreement in respect of the whole of Europe. For the avoidance of doubt, performance of the development and commercialization obligations required to be performed in accordance with Commercially Reasonable Efforts hereunder are evaluated based upon the Territory as a whole as set out in Section 1.10.

Section 13.3 Termination by Strata.

Strata may terminate this Agreement in its entirety, or on a country-by-country basis prior to the expiration of the Term as follows:

(a) subject to Section 2.3(d), prior to issuance of a Marketing Authorization in the US, at any time on written notice to Micrologix if it is determined by Strata in good faith, acting reasonably and in accordance with prudent scientific and business judgment and otherwise in accordance with generally accepted practices in the pharmaceutical industry, that the Product is not reasonably expected to demonstrate safety or efficacy; or

(b) if the Second Phase III Study is commenced, at any time on written notice to Micrologix if Strata exercises its right to terminate such study pursuant to Section 2.3(d); or

(c) if the Second Phase III Study is not commenced, or after the completion of the Second Phase III Study, at any time upon one hundred twenty (120) days prior written notice to Micrologix.

Section 13.4 Termination by Micrologix.

Micrologix may terminate this Agreement in its entirety or on a country by country basis prior to the expiration of the Term upon thirty (30) days prior written notice if Strata conducts any of the activities respecting a Competitive Product in a particular country as set forth in Section 11.2.

Section 13.5 Effect of Termination.

(a) **Payment Obligations**. If this Agreement is terminated by either Party pursuant to Section 13.2, Section 13.3 or Section 13.4, subject to the rights and obligations of Strata related to selling off Product inventory as provided in Section 13.5(b)(ii) and Section 13.5(b)(iii) and to pay Reimbursable Costs and certain wind down costs as set forth in Sections Section 13.5(b)(iv)(A), Strata shall not be obligated to pay any other wind down costs, milestone payments and/or other monies to Micrologix under this Agreement, other than payments due and owing prior to the effective date of termination.

(b) **Termination by Either Party**. Upon the early termination of this Agreement by either Party pursuant to Section 13.2, Section 13.3 or Section 13.4, the following shall occur:

(i) Subject to Section 13.7, Strata, its sublicensees and Affiliates (as the case may be) shall have no right to practice within the Micrologix Patent Rights or use any of the Micrologix Technology, and all rights, title or interest in, or other incidents of ownership under, the Micrologix Technology shall revert to and become the sole property of Micrologix, and the licenses granted to Strata under Section 3.1 shall automatically terminate.

(ii) Notwithstanding Section 13.5(b)(i), provided that this Agreement is terminated other than: (A) by Micrologix due to the breach of Strata pursuant to Section 13.2 or Section 13.4; or (B) by Strata pursuant to Section 13.3; Strata may, in its sole discretion, elect to sell-off or distribute, as applicable, its existing inventory of Product to which the termination pertains in accordance with the terms set forth in Section 13.5(b)(iii), after the effective date of termination, by notifying Micrologix of its decision within thirty (30) days after the date it receives a notice of termination by Micrologix or the date it provides a notice of termination to Micrologix, as the case may be.

(iii) If Strata elects pursuant to Section 13.5(b)(ii) to sell-off or distribute, as applicable, its existing inventory, it shall not, either directly or indirectly, use or permit the use of the Product except as set forth under this Section 13.5(b)(iii) and shall proceed as follows:

(A) continue to comply with its royalty obligations for the Product to Micrologix under Article 4;

(B) continue to sell off or distribute, as applicable, existing inventory of Product until such time as the inventory is depleted but in no

event more than six (6) months after the applicable notice of termination. At the expiration of such period, Strata shall sell all existing inventory of Product to Micrologix. In such case, Micrologix shall pay to Strata the full amount of the actual cost paid by Strata, or Strata's documented out-of-pocket costs, as applicable, for such remaining inventory of Product;

(C) if Strata does not elect pursuant to Section 13.5(b)(ii) to sell-off or distribute, as applicable, any existing inventory of Product, or if this Agreement is terminated by Micrologix under Section 13.2 or Section 13.4 for Strata's breach, or by Strata pursuant to Section 13.3, Strata shall, at Micrologix's election, either:

(1) sell all existing inventory of Product to Micrologix at Strata's actual cost of acquisition, or Strata's documented out-of-pocket costs, as applicable; or

(2) destroy all remaining inventory of Product in accordance with Applicable Laws and provide Micrologix with written proof of destruction sufficient to comply with Applicable Laws.

In either case, Micrologix shall pay to Strata the actual cost paid by Strata for such remaining inventory of Product;

(D) if Strata sells any inventory of Product to Micrologix pursuant to this Section 13.5(b)(iii), it shall warrant that such inventory of Product has been stored in material compliance with the applicable specifications therefor, Governmental Approvals and all Applicable Laws, has not been adulterated within the meaning of Applicable Laws and has otherwise been maintained by Strata according to such specifications, Governmental Approvals and Applicable Laws; and

(E) any sales of Product made by Strata to Micrologix pursuant to this Section 13.5(b)(iii) shall be made by Strata within thirty (30) days after the date it becomes obligated to do so and shall be shipped to Micrologix appropriately packaged and stored. All transportation costs in connection with such sale, including insurance, freight and duties, and all reasonable costs of re-working the Product so that such Product is in saleable form, shall be shared equally by Strata and Micrologix. Amounts owed by either Party to the other pursuant to this Section 13.5(b)(iii) for the Product shall be paid by such Party within ten (10) days after receipt by a Party of a reasonably detailed invoice from the other Party for the amount so owing to it by the other Party under this Section 13.5(b)(iii).

(iv) if this Agreement is terminated prior to the completion of the Development and the payment therefor:

(A) by Micrologix pursuant to Section 13.2 for Strata's breach or pursuant to Section 13.4, or by Strata pursuant to Section 13.3(a) or Section 13.3(b), Strata shall, at Micrologix's election, pay Micrologix's reasonable, wind-down costs under any Development Subcontract provided that Micrologix uses Commercially Reasonable Efforts to minimize, or if possible eliminate, such costs.

(B) by Strata pursuant to Section 13.2 due to the breach of Micrologix, Strata shall have no obligation to pay for any wind-down costs, milestone payments and/or any other monies due and owing from and after the effective date of such termination under this Agreement.

(v) if this Agreement is terminated by Micrologix pursuant to Section 13.2 for Strata's breach or pursuant to Section 13.4, or by Strata pursuant to Section 13.3(a) or Section 13.3(b), to the extent of its legal right to do so, Strata shall immediately assign or transfer to Micrologix any Governmental Approvals and trademarks for the Product held in the name of or Controlled by Strata, if any, in any country in the Territory.

(vi) to the extent of its legal right to do so, Strata shall, at Micrologix's request, grant Micrologix a worldwide royalty-bearing, license under any Strata Work Product necessary to use, market, advertise, promote, distribute, offer for sale, sell, make, manufacture, have manufactured, export and import, and develop Products with the right to sublicense and assign the foregoing, in consideration of such reasonable royalties on net sales by Micrologix or Product to be negotiated in good faith between Micrologix and Strata at such time, and if the Parties cannot agree on such license and royalties, either Party may refer the matter to arbitration pursuant to Article 14. Nothing in this Section shall cause a royalty to be payable in respect of rights obtained by Micrologix pursuant to Section 5.3 or Section 6.2.

(vii) if this Agreement is terminated by Strata pursuant to Section 13.2 due to the breach of Micrologix, to the extent of its legal right to do so, Strata shall immediately assign or transfer to Micrologix any Governmental Approvals and trademarks for the Product held in the name of or Controlled by Strata, if any, in any country in the Territory, in consideration of such reasonable royalties on net sales by Micrologix of Product to be negotiated in good faith between Micrologix and Strata at such time, and if the Parties cannot agree on such license and royalties, either Party may refer the matter to arbitration pursuant to Article 14. Nothing in this Section shall cause a royalty to be payable in respect of rights obtained by Micrologix pursuant to Section 6.2.

(viii) at the sole option and request of Micrologix, which request shall be made no more than sixty (60) days after the effective date of termination, if Micrologix chooses to permit Third Party sublicenses related to the

Product to survive termination of this Agreement, Strata will cooperate reasonably to facilitate the transfer of Third Party sublicenses from Strata to Micrologix or its designee.

(ix) except as otherwise provided in this Agreement, expiration or termination of this Agreement shall not relieve the Parties of any obligation accruing prior to such expiration or termination. Except as set forth below or elsewhere in this Agreement, the obligations and rights of the Parties under Article 1 (as needed), Section 3.4, Section 4.7(b)(ii), Section 4.7(c), Section 5.3(c), Section 5.3(e) (for a one year period after expiration or termination of this Agreement, in respect of the manufacture of Product for use in the Field in the Territory), Section 6.2(b), Section 7.2, Section 7.4, Article 8, Article 9, Article 10, Article 12, Article 13, Article 14 and Article 15, and any other that by its terms is intended to survive, shall survive expiration or termination of this Agreement.

(x) subject to the provision of Section 13.7, within thirty (30) days following the expiration or termination of this Agreement, each Party shall return to the other Party, or destroy, upon the written request of the other Party, any and all Confidential Information of the other Party in its possession and upon a Party's request, such destruction (or delivery) shall be confirmed in writing to such Party by a responsible officer of the other Party, except for such Confidential Information which the receiving Party is required to keep under Applicable Laws, in which event such Confidential Information shall be held subject to the terms and conditions of Article VIII.

(c) **Termination on a Country-by-Country Basis**. In the event any termination under this Agreement relates solely to one or more countries in the Territory as permitted herein, then this Agreement and the license contained in Section 3.1 shall only be terminated to the extent it applies to such country or countries in the Territory and this Agreement shall remain in effect as it applies to all other countries in the Territory.

(d) **Bankruptcy Rights**. In the event this Agreement is terminated or rejected by a Party or its receiver or trustee under applicable bankruptcy laws due to such Party's bankruptcy, then all rights and licenses granted under or pursuant to this Agreement by such Party to the other Party are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the Bankruptcy Code in the United States and other comparable Applicable Law in any other country in the Territory (collectively "**Other Bankruptcy Laws**"), licenses of rights to "intellectual property" as defined under Section 101(52) of the United State Bankruptcy Code. The Parties agree that all intellectual property rights licensed hereunder, including any patents or patent applications of a Party in any country covered by the license grants under this Agreement, are part of the "intellectual property" as defined in Section 101(52) of the United States Bankruptcy Code, subject to protections afforded the non-terminating Party under Section 365(n) of United States Bankruptcy Code or Other Bankruptcy Laws.

Section 13.6 Remedies.

All of the non-breaching Party's remedies shall be cumulative, and the exercise of one remedy hereunder by the non-defaulting Party shall not be deemed to be an election of remedies. These remedies shall include the non-breaching Party's other rights of recovery for such breach with or without terminating this Agreement.

Section 13.7 License Following Expiration.

Upon expiration of each of the applicable Royalty Terms in each country in the Territory, Strata shall thereafter have an irrevocable, non-exclusive, royalty-free license in such country, with the right to sublicense, to use, develop, market, advertise, promote, distribute, make, manufacture, have manufactured, offer for sale, sell, export and import the Product for use in the Field in the Territory. Upon request by Strata, Micrologix shall continue to allow Strata to manufacture and sell the Product under the Micrologix Technology pursuant to a separate agreement to be negotiated in good faith between the Parties.

ARTICLE 14
DISPUTE RESOLUTION/DAMAGES

Section 14.1 Disputes.

The Parties recognize that disputes as to certain matters may from time to time arise during the Term which relate to either Party's rights and/or obligations hereunder or to the interpretation, performance, breach, or termination of this Agreement, (a "**Dispute**"). It is the objective of the Parties to establish procedures to facilitate the resolution of a Dispute in an expedient manner by mutual cooperation and without resort to litigation. To accomplish this objective, the Parties agree to follow the procedures set forth in this Article 14 if and when a Dispute arises under this Agreement. The Parties acknowledge and agree that nothing under this Article 14 shall in any way affect, alter, negate or modify Strata's tie-breaking vote in the JDMC under Section 2.4(d).

Subject to Section 11.4(c), a Dispute among the Parties will be resolved as recited in this Article 14. Any Disputes relating to this Agreement shall be promptly presented to the Chief Executive Officers of Micrologix and Strata, or their respective designees (who must be members of a Party's senior management) for resolution. From the date of referral of a Dispute to the Chief Executive Officers or their designees of the Parties and until such time as any matter has been resolved by the Parties or has been finally settled by arbitration hereunder, the running of the cure periods (if any) as to which a Party must cure a breach that is part of the subject matter of any Dispute shall be suspended. In the event that the Chief Executive Officers of Micrologix and Strata, or their respective designees, cannot after good faith negotiations resolve the Dispute within 10 days (or such other period of time as mutually agreed to by the Parties in writing) of being requested by a Party to resolve a Dispute, the Parties agree that such Dispute shall be resolved by binding arbitration in accordance with this Section 14.1.

If a Party intends to begin arbitration to resolve such Dispute, such Party shall provide written notice (the "**Arbitration Notice**") to the other Party informing such other Party of such intention and the issues to be resolved. Any arbitration hereunder shall be conducted pursuant to the Commercial Arbitration Rules of the American Arbitration Association ("**AAA**"), including the Supplementary Procedures for Large Complex Disputes (the "**AAA Rule**") except as modified

herein. The arbitration shall be conducted by a panel of three (3) arbitrators (the "**Panel**") to be mutually agreed upon by the Parties and appointed by the AAA. The arbitrators shall be industry experts experienced in the issues comprising the Dispute and shall have no past, present or anticipated future affiliation with either Party. If the Parties are unable to agree upon all or any number of the three (3) mutually acceptable arbitrators within thirty (30) days after the filing of the Arbitration Notice, the AAA shall promptly appoint the arbitrator(s) to complete the Panel in accordance with the criteria set forth in this Section 14.1. The arbitration shall take place in Denver, Colorado. The Panel shall apply the laws of the State of Delaware, without regard to its conflicts of laws provisions. The Panel shall issue appropriate protective orders to protect each Party's Confidential Information. If a Party can demonstrate to the Panel that the complexity of the issue or other reasons warrant the extension of one or more timetables in the AAA Rules, the Panel may extend such timetables but in no event shall the proceeding extend more than twelve (12) months from the date of filing of the Arbitration Notice with the AAA. The Panel's decision shall be in writing. The Panel shall have the authority to award any remedy allowed by law or in equity, including compensatory damages, pre-judgment interest and to grant final, complete, interim, or interlocutory relief, including specific performance, injunctions and other equitable relief, but not punitive or other damages set forth in Section 14.5 and each Party shall be deemed to have waived any right to such excluded damages. Each Party shall bear its own costs, fees and expenses in the arbitration and shall share equally the Panel's fees, unless the Panel determines that its fees are to be paid by the non-prevailing Party.

Section 14.2 Performance to Continue.

Each Party shall continue to perform its obligations under this Agreement pending final resolution of any Dispute arising out of or related to this Agreement; including continuing the Development, provided, however, that a Party may suspend performance of its obligations during any period in which the other Party fails or refuses to perform its obligations.

Section 14.3 Determination of Patents and Other Intellectual Property.

Notwithstanding the foregoing, any dispute relating to the determination of validity of claims, infringement or claim interpretation relating to Micrologix's Patents shall be submitted exclusively to the federal courts.

Section 14.4 Injunctive Relief.

Nothing in this Agreement shall prevent either Party from seeking a temporary restraining order or injunction against the other Party as required to prevent such other Party's misuse of the intellectual property or Confidential Information of the other Party seeking such temporary restraining order or injunction. In addition nothing in this Agreement shall prevent Strata from seeking a temporary restraining order or injunction against Micrologix to prevent any breach by Micrologix under Section 11.1. The Parties understand and agree that because of the difficulty in measuring economic losses to the non breaching Party as a result of a breach of the covenants set forth in this Agreement respecting intellectual property and Confidential Information and because of the immediate and irreparable damage that may be caused to the non breaching Party for which monetary damages would not be a sufficient remedy, the Parties agree that the non breaching Party will be entitled to seek specific performance, temporary and permanent injunctive relief, and such other equitable remedies to which it may then be entitled against the

breaching Party. This Section 14.4 shall not limit any other legal or equitable remedies that the non breaching Party may have against the breaching Party.

Section 14.5 No Consequential Damages.

EXCEPT WITH REGARD TO DAMAGES ARISING UNDER SECTION 8.1(B) AND EACH PARTY'S DUTY TO INDEMNIFY THE OTHER FOR INDIRECT, INCIDENTAL, SPECIAL, CONSEQUENTIAL OR PUNITIVE DAMAGES RECOVERED BY A THIRD PARTY AS PROVIDED UNDER ARTICLE 10, IN NO EVENT SHALL EITHER PARTY BE LIABLE TO THE OTHER FOR ANY INDIRECT, INCIDENTAL, SPECIAL, CONSEQUENTIAL OR PUNITIVE DAMAGES INCURRED BY EITHER PARTY UNDER THIS AGREEMENT OR OTHERWISE.

Section 14.6 Attorney's Fees.

In the event of any claim hereunder related to either Party's infringement of the intellectual property rights of the other Party or the misuse of Confidential Information of the other Party, the prevailing party in any such dispute shall pay the reasonable legal fees and costs related thereto.

ARTICLE 15
MISCELLANEOUS

Section 15.1 No Solicitation.

Neither Party nor its Affiliates (collectively, the "**Initiating Group**") shall, directly or through its representatives, solicit for employment any officer, director, employee or consultant of the other Party or its subsidiaries or Affiliates (collectively, the "**Other Group**") with whom the Initiating Group has contact in connection with, or who otherwise is known by the Initiating Group to participate in, the transactions contemplated by this Agreement for a period of [***]. The Initiating Group shall not be precluded from hiring any such person who has been terminated by the Other Group prior to commencement of employment discussions between such person and the Initiating Group or its representatives. "**Solicitation**" shall not include any generalized public advertisement or any other solicitation by the Initiating Group or its representatives that is not specifically directed toward any such employee of the Other Group or toward any group of such employees of the Other Group.

Section 15.2 Assignment; Binding Effect.

Except as otherwise provided in this Agreement, neither this Agreement nor any of the rights, interests or obligations hereunder shall be assigned by any of the Parties hereto (whether by operation of Applicable Laws or otherwise) without the prior written consent of the other Party, which consent shall not be unreasonably withheld or delayed. Notwithstanding the foregoing, either Party may sell, transfer or assign its rights under this Agreement to any Third Party, as part of a sale or transfer of substantially all of a Party's assets; provided that such Third Party agrees

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in writing to be bound by the terms and conditions of this Agreement. Subject to the preceding sentence, this Agreement shall be binding upon and shall inure to the benefit of the Parties hereto and their respective permitted successors and assigns. Notwithstanding anything contained in this Agreement to the contrary, nothing herein, expressed or implied, is intended to confer on any person other than the Parties hereto or their Representatives, respective heirs, successors, executors, administrators and assigns any rights, remedies, obligations or liabilities under or by reason of this Agreement. Any purported assignment, sale, transfer, delegation or other disposition by a Party, except as permitted herein, shall be null and void.

Section 15.3 Force Majeure.

Neither Party shall be held liable or responsible to the other Party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected Party, including fire, flood, embargo, war, act of war (whether war be declared or not), act of terrorism, failure of supplier, insurrection, riot, civil commotion, strike, lockout or other labour disturbance, act of God (a "**Force Majeure**"); provided that the Party whose performance is delayed or prevented shall provide prompt notice of the Force Majeure to the other Party. Performance shall be excused so long as the condition constituting Force Majeure continues and the non-performing Party uses good faith diligent efforts to mitigate, avoid or end such delay of failure in performance as soon as practicable.

Section 15.4 Governing Law.

This Agreement shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, except that no conflict of laws provision shall be applied to make the laws of any other jurisdiction applicable to this Agreement.

Section 15.5 Waiver.

Except as specifically provided for herein, the waiver from time to time by either of the Parties of any of their rights or their failure to exercise any remedy shall not operate or be construed as a continuing waiver of same or of any other of such Party's rights or remedies provided in this Agreement.

Section 15.6 Severability.

In case any provision of this Agreement shall be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not in any way be affected or impaired thereby.

Section 15.7 No Right to Use Names.

Except as otherwise provided herein, no right, express or implied, is granted by the Agreement to use in any manner the name "Micrologix," "Strata" or any other trade name or trademark of the other Party or its Affiliates in connection with the performance of the Agreement.

Section 15.8 Notices.

All notices and other communications provided for hereunder shall be in writing and shall be mailed by first-class, registered or certified mail, postage paid, or delivered personally, by overnight delivery service or by facsimile, computer mail or other electronic means, with confirmation of receipt, addressed as follows:

If to Micrologix:	Micrologix Biotech Inc. BC Research Complex 3650 Wesbrook Mall Vancouver, BC Canada V6S 2L2 Attention: President
With a copy to:	Farris, Vaughan, Wills & Murphy 2600 — 700 West Georgia Street Vancouver, BC Canada V7Y 1B3 Attention: James Hatton
If to Strata:	Strata Pharmaceuticals, Inc. 10923 Cloverhurst Way San Diego, California 92130 Attention: CEO
With copies to:	Morrison & Foerster LLP 3811 Valley Centre Drive, Suite 500 San Diego, California 92130-2332 Attention: Jay de Groot

Notice so given shall be deemed given and received (a) if by mail on the fourth day after posting; (b) by cable, telegram, telex or personal delivery on the date of actual transmission, with evidence of transmission acceptance, or (as the case may be) personal or other delivery; and (c) if by overnight delivery courier, on the next business day following the day such notice is delivered to the overnight delivery courier service.

Section 15.9 Independent Contractors.

The activities and resources of each Party shall be managed by such Party, acting independently and in its individual capacity. It is expressly agreed that Micrologix and Strata shall be independent contractors and that the relationship between the two Parties shall not constitute a partnership or agency of any kind. Neither Micrologix nor Strata shall have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on the other Party, without the prior written consent of the other Party.

Section 15.10 Rules of Construction.

The Parties hereto agree that they have been represented by counsel during the negotiation and execution of this Agreement and, therefore, waive the application of any law, regulation, holding or rule of construction providing that ambiguities in an agreement or other document will be construed against the Party drafting such agreement or document.

Section 15.11 Entire Agreement; Amendment.

This Agreement (including the Exhibits attached hereto) sets forth all of the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto with respect to the subject matter hereof and supersedes and terminates all prior agreements and understandings between the Parties, including the Letter Agreement. There are no covenants, promises, agreements, warranties, representations conditions or understandings, either oral or written, between the Parties other than as set forth herein. No subsequent alteration, amendment, change or addition to this Agreement shall be binding upon the Parties hereto unless reduced to writing and signed by the respective authorized officers of the Parties. Purchase orders, purchase order releases, confirmations, acceptances and similar documents submitted by a Party in conducting the activities contemplated under this Agreement are for administrative purposes only and shall not add to or modify the terms of the Agreement. To the extent of any conflict or inconsistency between this Agreement and any such document, the terms of this Agreement shall govern.

Section 15.12 Counterparts; Facsimile.

This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement may be signed and delivered to the other Party by facsimile signature; such transmission will be deemed a valid signature.

Section 15.13 Interpretation.

The Section headings contained in this Agreement are for reference purposes only and shall not affect the meaning or interpretation of this Agreement. Except where the context clearly requires to the contrary: (i) each reference in this Agreement to a designated "Section" or "Exhibit" is to the corresponding Section or Exhibit of or to this Agreement; (ii) instances of gender or entity-specific usage (e.g., "his" "her" "its" "person" or "individual") shall not be interpreted to preclude the application of any provision of this Agreement to any individual or entity; (iii) "including" shall mean "including, without limitation"; (iv) references to Applicable Laws shall mean such Applicable Laws in effect during the Term (taking into account any amendments thereto effective at such time without regard to whether such amendments were enacted or adopted after the Effective Date); (v) references to "$" or "dollars" shall mean the lawful currency of the United States; (vi) references to "Federal" or "federal" shall be to laws, agencies or other attributes of the United States (and not to any State or locality thereof); (vii) references to "days" shall mean calendar days, unless it is expressly stated as "business days"; and (viii) the English language version of this Agreement shall govern all questions of interpretation relating to this Agreement, notwithstanding that this Agreement may have been translated into, and executed in, other languages.

IN WITNESS WHEREOF, the Parties hereto have caused this Agreement to be executed by their duly authorized officers as of the Effective Date.

Micrologix Biotech Inc.

By: /s/ James DeMesa
Name: James DeMesa
Title: President and CEO

Strata Pharmaceuticals, Inc.

By: /s/ Theodore R. Schroeder
Name: Theodore R. Schroeder
Title: President and Chief Executive Officer

EXHIBIT A

DEVELOPMENT PLANS

Please refer to the following documents:

- Strata Pharmaceuticals Inc. Development Plan, Timeline and Budget for NDA for LCSI Based on Second Phase III Study, dated July___, 2004; and
- Strata Pharmaceuticals Inc. Development Plan, Timeline and budget for NDA for CRBSI Based on First Phase III Study, dated July ___, 2004.

EXHIBIT B

PATENTS

Country	Application or Patent No.
USA	[***]
USA	[***]
USA	[***]
USA	[***]
USA	[***]
PCT	[***]
Canada	[***]
Europe	[***]
Belgium	[***]
Switzerland	[***]
Germany	[***]
Spain	[***]
France	[***]
Great Britain	[***]
Hong Kong	[***]
Ireland	[***]
Italy	[***]
Europe	[***]
Hong Kong	[***]

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Country	Application or Patent No.
USA	[***]
USA	[***]
USA	[***]
USA	[***]
PCT	[***]
Canada	[***]
Europe	[***]
Hong Kong	[***]
USA	[***]
USA	[***]
PCT	[***]
CA	[***]
Europe	[***]

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EXHIBIT C

INVENTORY

[***]

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EXHIBIT D

REGULATORY FILINGS

[***]

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Exhibit 10.11

CERTAIN MATERIAL (INDICATED BY AN ASTERISK) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

IV APAP AGREEMENT
(US and Canada)

by and between

BRISTOL-MYERS SQUIBB COMPANY

and

CADENCE PHARMACEUTICALS, INC.

February 21, 2006

TABLE OF CONTENTS

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INDEX OF DEFINED TERMS

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IV APAP AGREEMENT

(US and Canada)

This IV APAP Agreement (US and Canada) (the "**Agreement**") is entered into as of February 21, 2006 (the "**Execution Date**"), by and between Bristol-Myers Squibb Company, a Delaware corporation having an address at 345 Park Avenue, New York, New York 10154 ("**BMS**"), and Cadence Pharmaceuticals, Inc., a Delaware corporation having an address at 12730 High Bluff Drive, San Diego, California 92130 ("**Cadence**"), effective as of March 29, 2006 (the "**Effective Date**"). Cadence and BMS are sometimes collectively referred to herein as the "**Parties**" and each individually as a "**Party**."

BACKGROUND

1. BMS has licensed from SCR Pharmatop, a civil law partnership organized under the laws of France, having its head office's address at 10, Square St. Florentin, 78150 Le Chesnay, France, recorded with the Register of Commerce and Companies of Versailles under No. 407552702 ("**Pharmatop**"), rights under certain patents and patent applications relating to parenteral paracetamol (also referred to in the United States as "acetaminophen") formulations in the United States, Canada and Mexico.

2. The License Agreement dated as of December 23, 2002, between Pharmatop and BMS (the "**Pharmatop License Agreement**") sets forth such rights.

3. BMS desires to sublicense to Cadence BMS's intellectual property rights and related obligations under the Pharmatop License Agreement to Cadence with respect to the Territory (as defined below) upon the terms and conditions set forth in this Agreement and to provide for certain other matters.

AGREEMENT

THEREFORE, the Parties, intending to be legally bound, agree as follows:

ARTICLE I – DEFINITIONS

1.1 Defined Terms. As used in this Agreement, the following terms shall have the following meanings:

"**Adverse Event**" means any untoward medical occurrence in a patient or clinical investigation subject administered any Product, and which does not necessarily have a causal relationship with such product. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example),

symptom or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. For the avoidance of doubt, in the U.S. an Adverse Event shall include an adverse experience or test result in connection with the use of the Product

that requires a written IND safety report in accordance with 21 CFR Part 312.32(c), as amended or superseded from time to time.

"**Affiliated Company**" of a Party means any corporation, firm, partnership or other entity that directly or indirectly Controls, is Controlled by or is under common Control with such Party at any time during the term of this Agreement, but only for so long as such entity directly or indirectly Controls, is Controlled by or is under common Control with such Party.

"**Agreement**" has the meaning given to such term in the introductory paragraph hereof.

"**Annual Operating Plan**" has the meaning given to such term in Section 3.1 hereof.

"[***]" has the meaning given to such term in Section 3.2 hereof.

"**Applicable Law**" means any applicable federal, state, local or foreign statute, law, ordinance, rule or regulation, judicial order, or industry standard imposed by regulation or law, including the laws of the United States and Canada, and regulations promulgated by any other applicable Governmental Entity or Drug Regulatory Authority.

"**Approval**" means, with respect to any Product in any regulatory jurisdiction, approval from the applicable Drug Regulatory Authority sufficient for the importation, manufacture, distribution, use and sale of the Product in such jurisdiction in accordance with Applicable Law, including receipt of pricing and reimbursement approvals, where applicable.

"**Available** [[***]" has the meaning set forth in Section 2.24(a).

"**Balance Sheet**" has the meaning given to such term in Section 6.2(b) hereof.

"**Balance Sheet Date**" has the meaning given to such term in Section 6.2(b) hereof.

"**Bankruptcy**" means with respect to a Party the first to occur of:

(i) such Party shall have (A) voluntarily commenced any proceeding or filed any petition seeking relief under Title 11 of the United States Code, or any other bankruptcy, insolvency or similar law or any law for the protection of creditors of the United States, any state thereof, or any other applicable jurisdiction, (B) applied for or consented to the appointment of a receiver, trustee, custodian, sequestrator, conciliator, administrator or similar official for it or a substantial part of its property, (C) filed an answer admitting the material allegations of a petition filed against or in respect of it in any such proceeding, (D) made a general assignment for the benefit of creditors, (E) admitted in writing its inability, to pay its debts as they become due or (F) taken corporate action for the purpose of effecting any of the foregoing; or

(ii) an involuntary proceeding shall have been commenced or any involuntary petition shall have been filed in a court of competent jurisdiction seeking (A) relief in respect of such Party or of a substantial part of its or their property, under Title 11 of the

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United States Code, or any other bankruptcy, insolvency or similar law of the United States, any state thereof or any other applicable jurisdiction, (B) the appointment of a receiver, trustee, custodian, sequestrator, conciliator, administrator or similar official for such Party or all or substantially all of its property or (C) the winding-up or liquidation of such Party; and such proceeding or petition shall have continued undismissed for 60 days or an order or decree approving or ordering any of the foregoing shall have continued unstayed and in effect for 30 days.

"**BMS**" has the meaning given to such term in the introductory paragraph hereof.

"[***]" means (i) [***]and (ii) [***].

"**BMS Indemnitees**" has the meaning given to such term in Section 7.2 hereof.

"**BMS Know-How**" means formulation and manufacturing know-how that is used by BMS and its Affiliated Companies as of the Execution Date or during the Supply Term (as defined in the Clinical Supply Agreement) to make or formulate the Product or the Clinical Testing Products (as defined in the Clinical Supply Agreement) in the European Union.

"**BMS Patent Product**" means any Product for which the manufacture, use, import, sale or offer for sale in the United States would otherwise infringe a Valid Claim of any of the BMS Patents but for the license rights granted by BMS in Article 2 hereof.

"**BMS Patent Royalty Term**" means the date commencing upon the expiration of the Pharmatop Royalty Term in the United States and terminating upon the date that the manufacture, use, import, sale or offer for sale of BMS Patent Products in the United States is no longer covered by any Valid Claim of a BMS Patent (including any patent term extensions, such as pediatric exclusivity extensions, as may be available under Applicable Law) or covered by any data or regulatory exclusivity.

"**BMS Patents**" means the Patents listed on Schedule 1.1.

"**BMS Rights**" means (i) BMS's rights under the Pharmatop Patents and Pharmatop Know-How with respect to the Products in the Territory licensed to BMS under the Pharmatop License Agreement during the term of this Agreement, subject to the limitations, terms and conditions set forth in the Pharmatop License Agreement and (ii) the right granted to BMS in Section 2.1 of the Pharmatop License Agreement to make and have made the Products outside the Territory for use within the Territory.

"**Business Day**" means any day other than a Saturday, a Sunday or a United States Federal holiday.

"**Cadence**" has the meaning given to such term in the introductory paragraph hereof.

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"**Cadence Claims**" has the meaning given to such term in Section 6.2(d) hereof.

"**Cadence Indemnitees**" has the meaning given to such term in Section 7.3 hereof.

"**Calendar Quarter**" means each of the periods of time from (a) January 1 through March 31; (b) April 1 through June 30; (c) July 1 through September 30; and (d) October 1 through December 31.

"**Calendar Year**" means a year that begins on January 1 and ends on December 31.

"[***]" has the meaning set forth in Section 2.1(c)(i).

"[***]" has the meaning set forth in Section 2.24(d).

"[***]" has the meaning set forth in Section 2.24(a).

"[***]" has the meaning set forth in Section 3.2(f).

"**Clinical Study Countries**" means the countries set forth on a list of such countries that has been Previously Disclosed, as such list is amended from time to time in accordance with the last paragraph of Section 3.6.

"**Clinical Supply Agreement**" means the Clinical Supply Agreement dated as of the Execution Date between Lawrence Laboratories and Cadence (and BMS, as guarantor).

"**Clinical Testing Product**" has the meaning set forth in the Clinical Supply Agreement.

"**Confidential Information**" means (a) with respect to a Party and its Affiliated Companies (collectively, the "**Receiving Party**"), all information, Technology and confidential or proprietary materials which are disclosed by the other Party and its Affiliated Companies (collectively, the "**Disclosing Party**") to the Receiving Party hereunder or under the Clinical Supply Agreement or that has previously been disclosed under the Mutual Confidential Disclosure Agreement between the Parties dated July 6, 2005, as amended, or to any of its employees, consultants, Affiliated Companies or sublicensees and any information that is considered Confidential Information for purposes of the Clinical Supply Agreement, (b) the Product Data, which shall be Confidential Information of BMS to the extent resulting from work, trials or studies conducted by or on behalf of BMS and which shall be Confidential Information of Cadence to the extent resulting from work, trials or studies conducted by or on behalf of Cadence, (c) correspondence with Drug Regulatory Authorities, which shall be Confidential Information of the Party that conducted such correspondence, and (d) all reports (including any development, commercialization and/or financial reports), plans (including the Development Plan and the Annual Operating Plan) and other documents and budgets provided by Cadence and/or its Affiliated Companies to BMS pursuant to this Agreement, all of which shall be considered Confidential Information of Cadence except, in each of (a), (b),(c) or (d), to the extent that any such information (i) as of the date of disclosure is known to the Receiving Party

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or its Affiliated Companies, as demonstrated by credible written documentation existing and in the possession of the Receiving Party prior to the date of disclosure, other than by virtue of a prior confidential disclosure to such Receiving Party; (ii) as of the date of disclosure is in, or subsequently enters, the public domain, through no fault or omission of the Receiving Party; (iii) is obtained without restriction from a Third Party having a lawful right to make such disclosure free from any obligation of confidentiality to the Disclosing Party; or (iv) is independently developed by or for the Receiving Party without reference to or reliance upon any Confidential Information of the Disclosing Party as demonstrated by credible written documentation. The amount of the payments made to BMS under this Agreement shall be Confidential Information of both BMS and Cadence. A Party's Affiliated Company that has disclosed Confidential Information to a Receiving Party shall continue to be considered a Disclosing Party even after it ceases to be an Affiliated Company of such Party. A Party's Affiliated Company that has received Confidential Information from a Disclosing Party shall continue to be considered a Receiving Party even after it ceases to be an Affiliated Company of such Party.

"**Consent**" has the meaning given to such term in Section 6.1(d) hereof.

"**Contract Research Organization**" means a reputable Third Party research or development organization one of whose principal businesses is the provision of contract research or development services to unrelated Persons.

"**Contracts**" means all contracts, agreements, commitments and other legally binding arrangements, whether oral or written.

"**Control**" means (a) with respect to any intellectual property (including any Patents or Technology), the possession by a Party of the ability to grant a license or sublicense of such intellectual property without violating the terms of, or requiring a consent under, any agreement or arrangement between such Party and any Third Party and (b) when used with respect to any Person means the power to direct or cause the direction of the management or policies of such Person, directly or indirectly, whether through the ownership of voting securities, by contract, or otherwise. "**Controlled**" and "**Controlling**" shall have correlative meanings.

"**Covenant Termination Date**" has the meaning set forth in Section 2.24(c).

"**Derivative**" of paracetamol means any compound whose chemical structure is derived from the chemical structure for paracetamol through structural modifications and/or chemical changes that retain those portions of paracetamol's chemical

structure that are known to contribute materially to the activity, specificity and selectivity of paracetamol.

"**Development Plan**" has the meaning given to such term in Section 3.3 hereof.

"**Disclosing Party**" has the meaning given to such term in the definition of "Confidential Information" herein.

"**Dispute**" has the meaning given to such term in Section 7.6 hereof.

"**Dollar**" or "**$** " means United States dollars, the lawful currency of the United States.

"**Drug Regulatory Authority**" means any Governmental Entity with responsibility for granting any licenses, approvals or authorizations or granting pricing and/or reimbursement approvals necessary for the marketing and sale of pharmaceutical products in any regulatory jurisdiction.

"**Effective Date**" has the meaning given to such term in the introductory paragraph hereof.

"**Exchange Act**" means the Securities Exchange Act of 1934, as amended from time to time.

"[***] **Date**" means [***] on which (i) [***], (ii) [***] or (iii) [***]; provided that (A) [***] and (B) [***].

"[***] **Period**" means the [***] not include any period during which [***].

"[***] **Date**" has the meaning given to such term in Section 2.1(c).

"**Execution Date**" has the meaning given to such term in the introductory paragraph hereof.

"**FDA**" means the United States Food and Drug Administration or any successor agency.

"**FDCA**" means the Federal Food, Drug & Cosmetics Act, 21 U.S.C. 321 et seq., any amendments or supplements thereto, or any regulations promulgated or adopted thereunder or any successor act thereof.

"**Financial Statements**" has the meaning given to such term in Section 6.2(a) hereof.

"**Force Majeure**" has the meaning given to such term in Section 9.6(b) hereof."**Governmental Entity**" means any Federal, state, local or foreign government or any court of competent jurisdiction, regulatory or administrative agency or commission or other governmental authority or instrumentality, domestic or foreign.

"**HSR Act**" means the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended.

"**ICC**" has the meaning given to such term in Section 7.6(a) hereof.

"**Improvement**" means any adaptation, improvement, enhancement or upgrade with respect to the formulation and/or manufacture of the Products, whether such Improvement can be protected by patent or not.

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"**In Accordance With GAAP**" has the meaning given to such term in Section 6.2(a) hereof.

"**IND**" means an Investigational New Drug Application (as defined in 21 CFR Part 312.3, as amended or superseded from time to time) that is required to be filed with the FDA before beginning clinical testing of a Product in human subjects in the United States, or any successor application or procedure.

"**Indemnified Party**" has the meaning given to such term in Section 7.4 hereof.

"**Indemnifying Party**" has the meaning given to such term in Section 7.1 hereof.

"**Indemnitees**" has the meaning given to such term in Section 7.1 hereof.

"**Judgments**" has the meaning given to such term in Section 6.1(d) hereof.

"**License**" has the meaning given to such term in Section 2.1(a) hereof.

"**Lien**" means any pledge, encumbrance, mortgage, security interest, purchase option, call or similar right.

"**Loan Agreement**" has the meaning given to such term in Section 6.2(b) hereof.

"**Losses**" has the meaning given to such term in Section 7.1 hereof.

"**Material Adverse Effect**" means, with respect to any applicable representation and warranty of a Party or to any other matter to which such phrase is applied, a material adverse change in or effect on (i) such Party's (and its subsidiaries') business, operations, assets, condition (financial or otherwise) taken as a whole or (ii) such Party's ability to perform its obligations under any Transaction Document to which it is a party.

"**NDA**" means a new drug application or an abbreviated new drug application (as described in 21 CFR 314.50), including any amendments or supplements thereto, filed with the FDA pursuant to the FDCA and includes any Common Technical Document for the Registration of Pharmaceuticals for Human Use filed with the FDA or any Drug Regulatory Authority in Canada.

"**NDA Acceptance**" means the earlier of (i) the date Cadence receives written notice from the FDA of acceptance by the FDA of an NDA filed by or on behalf of Cadence or its licensees with respect to any Product in the United States, or (ii) sixty (60) days following filing of such NDA with the FDA, provided that Cadence has not received a "Notice of Refusal to File" from the FDA with respect to such NDA.

"**Net Sales**" means the total revenue invoiced by Cadence, its Affiliated Companies, sublicensees, co-promotion and co-marketing partners and any other Person selling or promoting Products on behalf of any such Person from the sale of a Product to independent Third Parties in the Territory less the following amounts: (a) credits, allowances and rebates to, and chargebacks from the account of, such customers for spoiled, damaged, out-dated and returned Product;

(b) trade discounts, cash discounts, quantity discounts, rebates and other price reduction programs, and other charge back payments; (c) sales, value-added and other similar taxes (including duties or other governmental charges levied on, absorbed or otherwise imposed on the sales of Products including governmental charges otherwise measured by the billing amount); (d) customs duties, surcharges and other governmental charges incurred in connection with the exportation or importation of the Product; and (e) bad debts on Product sales written off in accordance with generally accepted accounting principles, consistently applied. For the purposes of this definition, samples distributed by Cadence, its Affiliated Companies, sublicensees, co-promotion and co-marketing partners and any other Person selling or promoting Products on behalf of any such Person to their customers free of charge, and any Product used or provided for clinical or research purposes, shall not be included in Net Sales.

When Products are sold for monies other than Dollars, the monies due will first be determined in the foreign currency of the country in which such Products were sold and then converted into equivalent Dollars, on a monthly basis, using the applicable U.S. Federal Reserve rate in effect on the last business day of each calendar month.

In the event that Cadence makes sales of Products to an Affiliated Company, sublicensee, co-promotion or co-marketing partner or any other person selling or promoting Products on behalf of any such Person, the calculation of Net Sales shall be based on the greater of (x) the revenue received by Cadence from its sale of Products to the Affiliated Company, sublicensee, co-promotion or co-marketing partner or other person selling or promoting Products on behalf of any such Person, as the case may be, and (y) the revenue received by the Affiliated Company, sublicensee, co-promotion or co-marketing partner or other person selling or promoting Products on behalf of any such Person from its sale of Products to Third Parties.

"[***] **Date**" has the meaning set forth in Section 2.1(c).

"[***] **Date**" has the meaning set forth in Section 2.24(d).

"**Organizational Documents**" means, with respect to any Person at any time, such Person's certificate or articles of incorporation, by-laws, memorandum and articles of association, certificate of formation of limited liability company,

limited liability company agreement, and other similar organizational or constituent documents, as applicable, in effect at such time.

"**Other Chemical Entity**" means any chemical entity that is not parenteral paracetamol or a Derivative thereof.

"**Other Reportable Information**" has the meaning set forth in Section 2.15(e).

"**Parties**" has the meaning given to such term in the introductory paragraph hereof.

"**Party**" has the meaning given to such term in the introductory paragraph hereof.

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"**Patents**" means, to the extent that they have been or are filed or issued in the Territory: (a) patents and patent applications existing as of the Execution Date and/or at any time thereafter; and (b) any divisionals, continuations, substitutions, continuations-in-part, extensions, renewals, re-examinations or reissues of such patents and/or applications as of the Execution Date and/or at any time thereafter.

"**Person**" means any individual, firm, corporation, partnership, limited liability company, trust, joint venture, governmental authority or other entity.

"**Pharmatop**" has the meaning given to such term in Background.

"**Pharmatop Know-How**" means the Know-How (as such term is defined in the Pharmatop License Agreement) licensed to BMS under the Pharmatop License Agreement.

"**Pharmatop License Agreement**" has the meaning given to such term in Background.

"**Pharmatop Patent Challenge**" has the meaning given to such term in Section 2.16(a).

"**Pharmatop Patents**" means the Licensed Patents (as such term is defined in the Pharmatop License Agreement) filed or issued in the Territory and licensed to BMS under the Pharmatop License Agreement.

"**Pharmatop Royalty Term**" means, with respect to each country in the Territory on a country-by-country basis, the date commencing with the date of first commercial sale of a Product in such country, and terminating upon the latest of (a) the date that is ten (10) years after such first commercial sale in such country, (b) the date that the manufacture, use and sale of a Product in such country is no longer covered by any Valid Claim of a Pharmatop Patent in such country (including any patent term extensions, such as pediatric exclusivity extensions, as may be available under Applicable Law) or (c) the date that the obligation of BMS to pay royalties to Pharmatop (or any successor licensor), pursuant to the Pharmatop License Agreement, terminates.

"**Previously Disclosed**" means with respect to any document or information, a document or information set forth in a mutually agreed letter or memorandum delivered by Cadence or BMS to the other contemporaneously with the execution of this Agreement which identifies such document or information as "Previously Disclosed" for purposes of this Agreement.

"**Proceedings**" has the meaning given to such term in Section 6.1(e) hereof.

"**Product**" means (i) any parenterally administered dosage form containing paracetamol (or any Derivative thereof) alone or in combination with one or more other drugs (as defined, as of December 23, 2002, in Section 201 of the FDCA), and for which the manufacture, use or sale in a country in the Territory (x) would otherwise infringe any of the Pharmatop Patents or BMS Patents but for the license rights granted by BMS in Article 2 hereof, and/or (y) incorporates or uses to any material extent any Pharmatop Know-How and/or (ii) any parenterally administered dosage form containing paracetamol (or any Derivative thereof) alone or in combination with

one or more other drugs (as defined, as of December 23, 2002, in Section 201 of the FDCA) that is manufactured by a process that incorporates or uses to any material extent any BMS Know-How. When used with respect to any jurisdiction outside the Territory, "Product" shall refer to any parenterally administered dosage form containing paracetamol (or any Derivative thereof) alone or in combination with one or more other drugs (as defined, as of December 23, 2002, in Section 201 of the FDCA).

"**Product Data**" means data, information and conclusions resulting from any analytical, galenical, stability, toxicology or pharmacokinetic work and/or clinical studies and/or clinical trials relating to, or conducted by or on behalf of BMS or Cadence and filed in support of, Approval of Products in the United States.

"**Qualifying** [***]" means a [***], with respect to which [***].

"**Qualifying [***]**" means any [***] (i) [***], (ii) [***], and (iii) [***].

"**Receiving Party**" has the meaning given to such term in the definition of "Confidential Information" herein.

"**Registrational Information**" has the meaning set forth in the Pharmatop License Agreement.

"**Regulatory Filings**" means, collectively, any and all INDs, NDAs or any other filings (including any foreign equivalents) as may be required by any Drug Regulatory Authority for the development, manufacture or commercialization of Products, as applicable.

"[***] **Product**" has the meaning given to such term in Section 2.24(b) hereof.

"**Royalties**" has the meaning given to such term in Section 4.1(h) hereof.

"**Rules**" has the meaning given to such term in Section 7.6(a) hereof.

"[***]" has the meaning given to such term in Section 2.24(a).

"[***]" has the meaning set forth in Section 2.24(a).

"**Specified Number of Days**" has the meaning given to such term in Section 8.3.

"**Sublicense**" has the meaning given to such term in Section 2.1(a) hereof.

"**Tax**" means all taxes, charges, fees, levies or other assessments, and all estimated payments thereof, including income, excise, license, severance, stamp, occupation, premium, profits, windfall profits, customs duties, capital stock, employment, disability, registration, alternative or add-on minimum, property, sales, use, value added, environmental, franchise, payroll, transfer, gross receipts, withholding, social security or similar unemployment taxes, and any other tax of any kind whatsoever, imposed by any federal, state, local or foreign

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governmental authority, including any interest, penalties and additions to tax relating to such taxes, charges, fees, levies or other assessments.

"**Tech Transfer Period**" has the meaning given to such term in Section 2.12 hereof.

"**Tech Transfer Plan**" has the meaning given to such term in Section 2.10 hereof.

"**Technology**" means and includes all inventions, discoveries, Improvements, trade secrets, know-how, processes, procedures, research records, records of inventions, test information, market surveys and other similar proprietary methods, materials or property, whether or not patentable, relating to Products, including (a) samples of, methods of production or use of, and structural and functional information pertaining to, chemical compounds, proteins or other biological substances, (b) data, formulations, techniques and know-how (including any negative results), and (c) rights under patents, patent applications and copyrights.

"**Technology Documentation**" means a written description of the BMS Know-How.

"**Territory**" means the United States (including Puerto Rico and all U.S. possessions and territories) and Canada.

"**Third Party**" means any Person other than Cadence, BMS and their respective Affiliated Companies.

"**Title 11**" has the meaning given to such term in Section 8.10 hereof.

"**Transaction Documents**" means this Agreement and the Clinical Supply Agreement.

"**Transfer Taxes**" means taxes and assessments imposed upon the transfer, such as transfer, sales, value added, and stamp taxes, and not Taxes measured by income or gain, but including any interest, penalties or other additions thereto.

"[***]" has the meaning set forth in Section 2.24(a).

"[***]" has the meaning set forth in Section 2.24(a).

"**Valid Claim**" means a claim in any unexpired issued Pharmatop Patent or BMS Patent that has not been held invalid or unenforceable by a non-appealed or unappealable decision by a court or other appropriate body of competent jurisdiction, and which is not admitted to be invalid through disclaimer, dedication to the public, and which has not been cancelled or abandoned in accordance with and as permitted by (i) both the terms of this Agreement and the Pharmatop License Agreement in the case of the Pharmatop Patents, or (ii) the terms of this Agreement in the case of the BMS Patents.

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ARTICLE II – GRANT OF U.S. AND CANADIAN RIGHTS AND RELATED TRANSFERS

2.1 Grant of Sublicense and License .

(a) Effective as of the Effective Date and subject to Section 3.4 and the reservation of rights set forth in Section 2.2 and subject to early termination as provided in Article VIII, BMS hereby grants to Cadence on behalf of itself and its Affiliated Companies:

(i) subject to the terms, conditions and limitations set forth in the Pharmatop License Agreement and subject to Section 2.1(c):

(A) an exclusive (even as to BMS), royalty-bearing sublicense under the BMS Rights with the right to sublicense as provided in Section 2.4, to import, use, sell and offer for sale Products in the Territory;

(B) an exclusive (even as to BMS) sublicense under the BMS Rights, with the right to sublicense as provided in Section 2.4, to make and have made the Products in the Territory solely for (1) import, use, sale and offer for sale within the Territory or (2) import and use in clinical trials in the Clinical Study Countries as permitted by Section 3.6; and

(C) an exclusive (even as to BMS) sublicense under the BMS Rights, with the right to sublicense as provided in Section 2.4, to make and have made the Products anywhere in the world solely for (1) import, use, sale and offer for sale within the Territory, subject to the limitations set forth in Section 2.1 of the Pharmatop License Agreement (other than the consent of UPSA S.A., which has been obtained as of the Effective Date) and subject to Section 3.8, or (2) import or use in Cadence's clinical trials in the Clinical Study Countries as permitted by Section 3.6 hereof;

(ii) a non-exclusive license under the BMS Patents, with the right to sublicense as provided in Section 2.4, to import, use, sell and offer for sale Products in the Territory; provided, however, that the license granted in this paragraph shall not grant any right to the composition of matter of any Other Chemical Entity, or the right to import, use, sell or offer for sale any Other Chemical Entity or to any use not claimed by the BMS Patents;

(iii) a non-exclusive license under the BMS Patents, with the right to sublicense as provided in Section 2.4, to make and have made the Products in the Territory solely for import, use, sale and offer for sale within the Territory; *provided*, *however*, that the license granted in this paragraph shall not grant any right to the composition of matter of any Other Chemical Entity, or the right to make or have made any Other Chemical Entity or to any use not claimed by the BMS Patents;

(iv) a non-exclusive license under the BMS Know-How, with the right to sublicense as provided in Section 2.4, to make and have made the Products anywhere in the world solely for (1) use and sale within the Territory and (2) import and use in clinical trials in the Clinical Study Countries as permitted by Section 3.6; and.

(v) a non-exclusive right to use, copy, translate, display and distribute (subject to any confidentiality obligations), improve and make derivative works of the BMS Technology Documentation for the purpose of making and having made the Products consistent with the license set forth above with respect to the BMS Know-How.

The sublicenses granted in Section 2.1(a)(i) are referred to herein collectively as the "**Sublicense**"), and the licenses granted in Sections 2.1(a)(ii), (iii), (iv) and (v) are referred to herein collectively as the "**License**").

The Sublicense granted to Cadence hereby shall only permit Cadence to sell Products that are packaged, finished products ready for use, and the Sublicense shall not extend to any sales in bulk or of semi-finished products except to permitted sublicensee(s) of Cadence. Except as may be otherwise agreed in writing by BMS in its sole discretion, the License granted to Cadence hereby shall only permit Cadence to sell Products that are packaged, finished products ready for use, and the License shall not extend to any sales in bulk or of semi-finished products except to permitted sublicensee(s) of Cadence.

(b) Cadence hereby (i) accepts such Sublicense and License, (ii) acknowledges that the Sublicense rights granted hereunder are subject and subordinate to the rights of Pharmatop under, and all the terms and conditions of, the Pharmatop License Agreement and (iii) agrees to comply with all the restrictions of the Pharmatop License Agreement that relate to the exercise of the rights sublicensed to Cadence hereunder.

(c) If on the [***], then [***]; provided that:

(i) [***] (A) Cadence may [***] and (B) such [***]. Cadence shall provide to BMS evidence reasonably satisfactory to BMS of the accuracy of such report. Notwithstanding the foregoing, [***] (A) [***] or (B) [***]. In the event [***] as provided in this Section 2.1(c).

(ii) Such [***].

(iii) Such [***].

Each date, if any, as of which such [***].

(d) Any Affiliated Companies on whose behalf BMS has made any of the foregoing license grants that hereafter ceases to be an Affiliated Company of BMS shall nevertheless continue to be obligated under such license grants in accordance with the terms of this Agreement.

2.2 No Implied Licenses; Reservation of Rights.

(a) Cadence shall have no licenses or other rights other than those expressly granted in this Agreement, and, in particular and without limiting the foregoing, nothing in this

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Agreement shall be construed to grant Cadence any licenses or other rights in any intellectual property rights, information or data (i) owned or Controlled by BMS or any of its Affiliated Companies, except as expressly set forth in this Agreement or (ii) owned or Controlled by Pharmatop or any of its Affiliated Companies that is not licensed by Pharmatop to BMS under the Pharmatop License Agreement.

(b) Cadence acknowledges that BMS or one or more of its Affiliated Companies holds certain license rights from Pharmatop (whether under the Pharmatop License Agreement or otherwise) relating to countries outside the Territory, and, except for the right of cross-reference provided for in Section 2.8(d), the rights granted to Cadence under this Agreement do not include any license or other rights with respect to such other rights of BMS and its Affiliated Companies, all of which are expressly reserved to BMS and its Affiliated Companies.

(c) Notwithstanding the exclusivity of any rights granted under Section 2.1, BMS hereby reserves the non-exclusive, sublicensable right under the BMS Rights, BMS Patents and BMS Know-How (i) to make and have made the Products in the Territory for supply to Cadence, or to the extent otherwise necessary or appropriate for BMS or any of its Affiliated Companies or sublicensees to perform its obligations, under the Clinical Supply Agreement, (ii) to make and have made the Products anywhere in the world for import, use, sale and offer for sale outside the Territory and (iii) to import, make, have made and use Products in the Territory for any non-clinical or clinical research purpose of BMS and its Affiliated Companies (subject, to the extent applicable, to Section 3.7) or in support of any Regulatory Filings or other activities outside the Territory (subject, to the extent applicable, to Section 3.7); *provided* that the rights reserved pursuant to clause (iii) above shall not be sublicensable.

(d) BMS is not sublicensing or granting to Cadence, and Cadence acknowledges and agrees that it is not receiving any rights under Section 2.10 or the proviso of the last sentence of Section 2.3 of the Pharmatop License Agreement, all of which are reserved to BMS.

(e) BMS shall have no licenses or other rights other than those expressly granted in this Agreement, and, in particular and without limiting the foregoing, nothing in this Agreement shall be construed to grant BMS any licenses or other rights in any intellectual property rights, information or data owned or Controlled by Cadence or any of its Affiliated Companies, except as expressly set forth in this Agreement.

2.3 Rights of Pharmatop.

(a) Nothing in this Agreement shall reduce or limit any of Pharmatop's rights under the Pharmatop License Agreement.

(b) Pharmatop shall have the same right to supervise the activities of Cadence hereunder as Pharmatop has with respect to BMS's activities under the Pharmatop License Agreement.

(c) Pharmatop shall have the same rights to audit Cadence's (and any of its sublicensee's) activities relevant to this Agreement, and to inspect Cadence's (and any

sublicensee's) facilities involved in the manufacture of Products, in the same manner as Pharmatop has with respect to BMS's activities and facilities under the Pharmatop License Agreement.

2.4 Further Sublicenses.

(a) Except as set forth in Section 2.5, the rights licensed to Cadence under Section 2.1 shall be sublicensable to a Third Party [***] (except to the extent otherwise agreed to by BMS in writing in its sole discretion, which writing shall, to the extent applicable, specifically waive compliance with this Section 2.4(a)): (i) such sublicense shall refer to this Agreement and shall be subject and subordinate to this Agreement and, with respect to the Sublicense, the Pharmatop License Agreement, (ii) the sublicensee shall assume and agree in writing to be bound by and comply with the terms and conditions of this Agreement in the same manner as Cadence, and without limiting the generality of the foregoing to maintain insurance coverage at the same levels and on the same terms and conditions as set forth in Section 7.5, provide sales reports pursuant to Section 4.7 hereof and keep books and records and permit BMS to review such books and records pursuant to Section 4.8 hereof, (iii) BMS shall be made an express third party beneficiary of the sublicensee's obligations under such sublicense that relate to compliance with the terms and conditions of this Agreement with the express right to enforce the same directly against the sublicensee, (iv) a copy of the proposed sublicense (except that any confidential financial terms may be redacted) shall be provided to BMS at the time Cadence seeks BMS's consent to such sublicense as aforesaid, (v) an executed copy of the sublicense (except that any confidential financial terms may be redacted) shall be provided to BMS promptly after execution, (vi) each sublicense or other right granted by Cadence with respect to any right licensed to it hereunder shall terminate immediately upon the termination of the Sublicense or License from BMS to Cadence with respect to such right; and (vii) such sublicensees shall not have the right to grant further sublicenses or otherwise transfer any rights sublicensed to them with respect to the Products except in accordance with and subject to this Section 2.4 and all of the other terms and conditions of this Agreement. The foregoing shall also apply in the event of any subsequent amendment or modification of such sublicense agreement. In the event Cadence desires to effect any such sublicense, it shall provide BMS with such information concerning the proposed arrangement as BMS may reasonably request. BMS shall use reasonable efforts to provide its response within [***] ([***])[***] (or, if BMS so requests, [***] ([***])[***]) after receiving such information. The failure of BMS to consent to or disapprove of such proposed sublicense within such [***] period shall not constitute a consent to such sublicense.

(b) Cadence may grant sublicenses to its Affiliated Companies under the Sublicense and the License [***], subject, in the case of a sublicense of rights licensed to Cadence pursuant to the Sublicense, to compliance with the Pharmatop License, and then shall be sublicensable only as follows (except to the extent otherwise agreed to by BMS in writing in its sole discretion, which writing shall, to the extent applicable, specifically waive compliance with this Section 2.4(a)): (i) such sublicense shall be subject and subordinate to this Agreement and, with respect to the Sublicense, the Pharmatop License Agreement, (ii) such sublicense shall

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terminate immediately in the event such Affiliated Company ceases to be an Affiliated Company of Cadence, (iii) an executed copy of the sublicense shall be provided to BMS promptly after execution, (iv) each sublicense or other right granted by Cadence with respect to any right licensed to it hereunder shall terminate immediately upon the termination of the Sublicense or License from BMS to Cadence with respect to such right and (v) such sublicensees shall not have the right to grant further sublicenses or otherwise transfer any rights sublicensed to them with respect to the Products except in accordance with and subject to this Section 2.4 and all of the other terms and conditions of this Agreement. The foregoing shall also apply in the event of any subsequent amendment or modification of such sublicense agreement. Without limiting any of Cadence's responsibilities under Section 2.4(c), Cadence shall cause its Affiliated Company to comply with the terms and conditions of this Agreement in the same manner as Cadence.

(c) Cadence shall be primarily responsible for all payments due and the making of reports under this Agreement by its sublicensees and for compliance with all applicable terms of this Agreement, and Cadence shall remain jointly and severally liable with each of its sublicensees (whether or not such sublicensee is an Affiliated Company of Cadence) for any failure by such sublicensee to perform, observe or comply with the terms and conditions of this Agreement or the Pharmatop License Agreement.

(d) Any purported sublicense hereunder not entered into in compliance with this Section 2.4 shall be null and void and without effect.

(e) Cadence or its Affiliated Companies may engage a Third Party, including a contractor, consultant, or Contract Research Organization, to perform research or development activities with respect to Products on behalf of Cadence or its Affiliated Companies and such activities shall not be deemed a sublicense if no rights under the BMS Rights, BMS Patents or BMS Know-How are licensed or granted; *provided*, that (i) none of the rights of BMS hereunder are diminished or otherwise adversely affected as a result of such engagement, (ii) any such Third Party shall enter into an appropriate written agreement obligating such Third Party to be bound by obligations of confidentiality and restrictions on use of Confidential Information that are no less restrictive than the obligations in this Agreement; and (iii) Cadence shall at all times be responsible for the performance of such Third Party. Cadence shall use all reasonable efforts to cause such Third Party to agree in writing to assign to Cadence inventions made by such Third Party in performing such services for Cadence.

2.5 Delegation of Manufacturing. Subject to the scope of the rights granted to Cadence in the Sublicense and the License and subject to Section 3.8, Cadence may arrange by written agreement to have the Products manufactured by a Third Party manufacturer without the prior consent of BMS but subject to compliance with the Pharmatop License Agreement with respect to sublicensing, if applicable, and subject to clauses (i), (iii), (v), (vi) and (vii) of Section 2.4(a) and the provision to BMS of a copy of the agreement or agreements relating to such manufacturing arrangement (subject to redaction of confidential financial terms) promptly after the execution thereof. If the Products are manufactured by a Third Party manufacturer (other than pursuant to the Clinical Supply Agreement), Cadence shall notify BMS and Pharmatop and shall provide BMS and Pharmatop with the identity of each such manufacturer and provide proof to BMS and Pharmatop that (a) each such manufacturer has been informed in writing that the products to be made are subject to the Licensed Patents (as defined in the

Pharmatop License Agreement) held by Pharmatop and (b) each such manufacturer has agreed to manufacture the Products only pursuant to a written agreement with Cadence and solely for the benefit of Cadence and its sublicensees. In addition Cadence shall use reasonable efforts to have such Third Party agree in writing to assign or license to Cadence Improvements made by such Third Party with respect to the manufacture of the Products, which license if obtained by Cadence shall include the right to sublicense such rights to BMS and Pharmatop as contemplated by Section 2.7. The above restrictions do not apply to raw materials, packaging items or other incidental articles from outside suppliers, or to the performance of packing operations in accordance with customary practices in the pharmaceutical industry.

2.6 Development and Commercialization Arrangements. Cadence shall not enter into any co-development or other development collaboration with any Third Party with respect to the Products without the prior written consent of BMS. The engagement of a Contract Research Organization to perform research or development services on behalf of Cadence or its Affiliated Companies, which research is funded entirely by Cadence and its Affiliated Companies (and not indirectly by a Third Party through Cadence or any of its Affiliated Companies), shall not constitute a co-development or other development collaboration that requires the consent of BMS. In the event Cadence enters into any co-promotion or co-marketing arrangement with any Third Party with respect to the Products or any other arrangement with a Third Party whereby such Third Party would distribute or commercialize any Product, Cadence shall include in the quarterly reports provided to BMS pursuant to Section 3.2 information concerning the activities of the other party to such co-promotion, co-marketing, distribution or commercialization arrangement. In connection with any arrangement with a Third Party whereby such Third Party would distribute, co-promote, co-market or otherwise develop or commercialize any Product (or collaborate with Cadence in the development or commercialization of any Product), Cadence shall comply, and shall cause such Third Party to comply, with all applicable terms and conditions of this Agreement and the Pharmatop License Agreement. Cadence shall remain jointly and severally liable with any such Third Party for any failure by such Third Party to perform, observe or comply with the terms and conditions of this Agreement or the Pharmatop License Agreement.

2.7 Improvements.

(a) BMS shall inform Cadence in a timely manner of any Improvements made by Pharmatop (or any Third Party sublicensees of Pharmatop) as to which BMS receives notice pursuant to Section 2.2 or Article 8 of the Pharmatop License Agreement. If requested by Cadence, BMS will request that Pharmatop license such Improvements to BMS and, upon receipt of such license, shall sublicense such Improvements to Cadence on a non-exclusive, [***] basis ([***]), consistent with the license thereof from Pharmatop and the Pharmatop License Agreement, to the extent not already covered by the Sublicense.

(b) BMS shall notify Cadence in writing of any Improvements made in whole or in part by its (and its Affiliated Companies') employees, agents, sublicensees and Third Party manufacturers after the Effective Date and Controlled and implemented by BMS and its

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Affiliated Companies. Upon the request of Cadence, BMS shall grant Cadence a non-exclusive, [***] license to practice and use such Improvements, including the right to grant sublicenses, anywhere in the world to make and have made Products solely (i) to import, use, sale and offer for sale within the Territory and (ii) to import and use in clinical trials in the Clinical Study Countries as permitted by Section 3.6. BMS shall provide Cadence with such information in BMS's possession as may be reasonably requested by Cadence in order to practice such Improvements.

(c) Cadence shall notify BMS and Pharmatop in writing of any Improvements made in whole or in part by its (and its Affiliated Companies') employees, agents, sublicensees and Third Party manufacturers after the Effective Date and Controlled and implemented by Cadence and its Affiliated Companies, and Cadence shall license such Improvements to Pharmatop on the basis described in Article 8 of the Pharmatop License Agreement. In addition, upon the request of BMS, Cadence shall grant BMS a non-exclusive [***] license to practice and use such Improvements, including the right to grant sublicenses, anywhere in the world (i) to make and have made the Products in the Territory for supply to Cadence, or to the extent otherwise necessary or appropriate for BMS or any of its Affiliated Companies or sublicensees to perform its obligations, under the Clinical Supply Agreement, (ii) to make and have made the Products anywhere in the world for import, use, sale and offer for sale outside the Territory and (iii) to import, make, have made and use Products in the Territory for any non-clinical or clinical research purpose of BMS and its Affiliated Companies (subject, to the extent applicable, to Section 3.7) or in support of any Regulatory Filings or other activities outside the Territory (subject, to the extent applicable, to Section 3.7); *provided* that the rights granted pursuant to clause (iii) above shall not be sublicensable. Cadence shall provide BMS with such information in Cadence's possession as may be reasonably requested by BMS in order to practice such Improvements.

2.8 Transfer of Regulatory Filings; Communications with Regulatory Authorities.

(a) As of the Effective Date, BMS hereby cedes and assigns to Cadence all right, title and interest in and to the Regulatory Filings with Drug Regulatory Authorities in the Territory relating to the Products and shall use reasonable efforts to take any actions with the applicable Drug Regulatory Authority in the Territory that are necessary to transfer ownership and control of such Regulatory Filings to Cadence not later than five (5) days after the Effective Date.

(b) During the [***]([***])[***] period following the Effective Date, BMS shall transfer to Cadence copies of all Regulatory Filings with Drug Regulatory Authorities in the Territory relating to Products and shall provide Cadence with copies of all material correspondence with Drug Regulatory Authorities in the Territory relating to Products. Following the Effective Date, Cadence shall have sole responsibility for (i) communicating with Drug Regulatory Authorities in the Territory with respect to Products, including responsibility for all Regulatory Filings in the Territory and all associated official correspondence and informal communications, and (ii) subject to Section 2.15, reporting to Drug Regulatory Authorities in the Territory any Adverse Event relating to Products in compliance with the requirements of Applicable Law in the Territory. If BMS maintains such Regulatory Filings and correspondence

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in electronic form, BMS shall provide such copies to Cadence in electronic form, but BMS shall have no obligation to reformat or otherwise alter or modify any materials or to create or recreate any such materials in electronic form in order to provide them to Cadence.

(c) BMS and its Affiliated Companies and licensees and, subject to the terms of Sections 3.1 and 3.3 of the Pharmatop License Agreement, Pharmatop shall have a right to cross-reference, file or incorporate by reference any Regulatory Filings in the Territory transferred hereunder or subsequently made by Cadence and its Affiliated Companies and sublicensees with respect to Products in the Territory (and any data contained therein) to support Regulatory Filings by BMS and its Affiliated Companies and licensees for Products outside the Territory.

(d) Cadence and its Affiliated Companies and licensees shall have a right to cross-reference, file or incorporate by reference any Regulatory Filings made by BMS and its Affiliated Companies and sublicensees of the BMS Rights with respect to Products outside the Territory (and any data contained therein) to support Regulatory Filings by Cadence and its Affiliated Companies and licensees in the Territory (or Regulatory Filings in such additional jurisdictions where Cadence may in the future acquire rights).

2.9 Transfer of Data and Transition Arrangements. Following the Effective Date:

(a) During the [***] ([***])[***] period following the Effective Date, BMS shall provide to Cadence a copy of (i) all Product Data, (ii) other written information, data and reports in BMS's possession that relate exclusively to the Products to the extent such information, data and reports are necessary (in the reasonable judgment of both BMS and Cadence) to the development of the Products in the Territory, and (iii) the full Marketing Authorization dossier submitted to Drug Regulatory Authorities in the EU with respect to the Products (in non-Common Technical Document format) and the variation dossiers submitted to Drug Regulatory Authorities in the EU with respect to the Products after the initial Approval, including (1) with respect to Perfalgan (A) copies of the applicable clinical study reports (and the appendices, tables, listings and graphs therein), (B) copies of the raw data from the applicable clinical studies included in the Marketing Authorization Application, (C) to the extent available, rendered PDF copies of such clinical study reports (and such appendices, tables, listings and graphs) and (D) to the extent available, SAS data sets containing such raw data and (2) with respect to ProDafalgan, to the extent they exist, (A) copies of the applicable clinical study reports (and the appendices, tables, listings and graphs therein), (B) copies of the raw data from the applicable clinical studies included in the Marketing Authorization Application, (C) rendered PDF copies of such clinical study reports (and such appendices, tables, listings and graphs) and (D) SAS data sets containing such raw data, but only to the extent such information, data and reports described in clauses (i), (ii) and (iii) above are reasonably available to BMS or its Affiliated Companies without undue searching (the information, data and reports described in clauses (ii) and (iii) above being referred to herein as "**Other Product Data**"); *provided*, *however*, that the foregoing shall in no event require BMS or its Affiliated Companies to provide copies of laboratory notebooks or manufacturing run records required to be maintained by BMS or its Affiliated Companies under Applicable Law. If BMS or its Affiliated Company maintains

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such Product Data or Other Product Data in electronic form, BMS shall provide such copies to Cadence in electronic form, but BMS shall have no obligation to reformat or otherwise alter or modify any materials or to create or recreate any such materials in electronic form in order to provide them to Cadence. BMS shall retain ownership of such Product Data and Other Product Data, may retain a copy of the Product Data and Other Product Data and retains the right to use and reference such Product Data and Other Product Data for any purpose to the extent consistent with BMS's other retained rights and the rights granted to Cadence hereunder, including the right to cross-reference, file or incorporate by reference such Product Data and Other Product Data and to assign, transfer or license to other Persons any or all of such rights of use and reference. Cadence shall have the right to use such Product Data and Other Product Data for any purpose in connection with the exercise of the rights granted to Cadence under this Agreement. In the event that any such Regulatory Filing is supplemented or modified, BMS shall notify Cadence that supplements or modifications have been made not later than [***] ([***])[***] after such supplementation or modification, and BMS shall provide Cadence with copies thereof upon Cadence's request.

(b) Cadence shall notify BMS in writing of the completion of any additional registrational clinical trials or studies (Phase I – Phase III) or large-scale safety studies performed by or on behalf of Cadence relating to Products within [***]([***])[***] after the final study report relating to such trial or study has been completed and received all necessary internal Cadence approvals in accordance with Cadence's customary procedures. Cadence shall provide BMS semi-annually with copies of any such final study reports and copies of the final study reports relating to any non-registrational clinical trials or studies performed by or on behalf of Cadence relating to Products that have received all necessary internal Cadence approvals in accordance with Cadence's customary procedures, in each case that have received such necessary approvals in the preceding semi-annual period, and BMS and its Affiliated Companies and licensees shall have a right to cross-reference, file or incorporate by reference such final study reports and any existing or future Regulatory Filings (and any data contained therein) made or maintained by Cadence and its Affiliated Companies for Products in the Territory (including the foreign equivalent of any NDA relating to Products) to support Regulatory Filings by BMS and its Affiliated Companies and licensees for Products outside the Territory and to use such final study reports, Regulatory Filings and data for other commercially reasonable uses to support commercialization activities outside the Territory. In the event that any such Regulatory Filing is supplemented or modified, Cadence shall notify BMS that supplements or modifications have been made not later than [***]([***])[***] after such supplementation or modification, and Cadence shall provide BMS with copies thereof upon Cadence's request.

(c) BMS shall notify Cadence in writing of the completion of any additional registrational clinical trials or studies (Phase I — Phase III) or large-scale safety studies done within the then existing label performed by or on behalf of BMS relating to Products within [***]([***])[***] after the final study report relating to such trial or study has been completed and received all necessary internal BMS approvals in accordance with BMS's customary procedures. BMS shall provide Cadence semi-annually with copies of any such final study reports and copies of the final study reports relating to any non-registrational clinical trials or

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studies performed by or on behalf of BMS relating to Products that have received all necessary internal BMS approvals in accordance with BMS's customary procedures, in each case that have received such necessary approvals in the preceding semi-annual period, and Cadence and its Affiliated Companies and licensees shall have a right to cross-reference, file or incorporate by reference such final study reports and any existing or future Regulatory Filings (and any data contained therein) made or maintained by BMS and its Affiliated Companies for Products outside the Territory (including the foreign equivalent of any NDA relating to Products) to support Regulatory Filings by Cadence and its Affiliated Companies and licensees for Products in the Territory and to use such final study reports, Regulatory Filings and data for other commercially reasonable uses to support commercialization activities in the Territory.

(d) BMS shall provide Cadence with prompt written notice of any Registrational Information of Pharmatop made available to BMS pursuant to Article III of the Pharmatop License Agreement. To the extent permitted by the Pharmatop License Agreement, Cadence and its Affiliated Companies and licensees shall have a right to cross-reference, file or incorporate by reference any such Registrational Information to support Regulatory Filings by Cadence and its Affiliated Companies and licensees for Products in the Territory, *provided* [***] reimburses [***] directly (or indirectly through payment to [***]) [***] ([***]) of the [***] to develop or obtain such Pharmatop Registrational Information consistent with Sections 3.1 and 3.3 of the Pharmatop License Agreement.

2.10 Tech Transfer Plan. Within [***]([***])[***] of the Effective Date, the Parties shall meet to develop a technology transfer plan (the **"Tech Transfer Plan"**) containing a plan and schedule for transferring and otherwise providing Cadence access to the BMS Know-How and Technology Documentation.

2.11 Technology Documentation. Pursuant to the Tech Transfer Plan, BMS shall provide Cadence with one (1) copy (which may be in paper or electronic form as provided below) of the Technology Documentation to which BMS or its Affiliated Companies have access to without undue searching (unless such documents are material to the manufacture of the Products or Clinical Testing Products in which case BMS shall use all reasonable commercial efforts to locate such Technology Documentation); *provided*, *however*, that the foregoing shall in no event require BMS to provide copies of laboratory notebooks or manufacturing run records required to be maintained by BMS under Applicable Law (other than one blank batch record which shall be provided to Cadence). If BMS maintains such Technology Documentation in electronic form, BMS shall provide such Technology Documentation to Cadence in electronic form. Otherwise, BMS may provide such Technology Documentation in paper form. All Technology Documentation shall be in the English language, reasonably comprehendible and, if any Technology Documentation requires translation, authenticated translation shall be provided by BMS at no cost to Cadence. BMS shall not have any obligation to translate any documentation relating to the Pharmatop Know-How. The Technology Documentation at the time provided to Cadence shall be written with sufficient detail and clarity for Cadence, a Cadence Affiliated Company or a Third Party sublicensee or supplier of Cadence to practice and/or otherwise utilize the manufacturing processes disclosed thereunder. The Technology

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Documentation shall not be used by Cadence for any purpose other than to manufacture the Products and Clinical Testing Products as permitted under this Agreement and the Clinical Supply Agreement. The Technology Documentation shall be Confidential Information of BMS, and Cadence shall have full responsibility and liability to BMS for any unauthorized use or disclosure of such Confidential Information; *provided* that Cadence shall have the right to disclose and otherwise provide such Technology Documentation to one or more Third Party manufacturers and/or suppliers so long as such Third Parties agree to maintain the confidentiality of such information. BMS shall be responsible for the cost of providing one (1) set of copies only; *provided*, *however*, that BMS shall have no obligation to reformat or otherwise alter or modify any such materials to the extent provided consistent with this Section 2.11, or to create materials in electronic form, in order to provide them to Cadence.

2.12 Technical Assistance. During the period commencing on the Effective Date and ending on [***] (the "**Tech Transfer Period**"), BMS shall provide the technical assistance provided for in this Section 2.12. During the Tech Transfer Period, BMS shall provide Cadence with the assistance of up to [***] of BMS employees having knowledge relevant to the Clinical Testing Products, the Technology Documentation and the BMS Know-How to provide Cadence with a reasonable level of technical assistance and consultation in connection with the technology transfer and implementation of the manufacturing processes included in the Technology Documentation for the purpose of assisting Cadence in assuming the responsibility for manufacturing the Products. The first [***]([***])[***] of such technical assistance and consultation shall be without charge to Cadence other than for the reasonable out-of-pocket costs of BMS and its Affiliated Companies. For technical assistance and consultation in excess of [***]([***])[***], Cadence shall pay BMS for such technical assistance and consultation at the rate of [***]. [***]. Cadence shall bear [***] implementing the Technology Documentation, including all costs and expenses it incurs in connection with such technology transfer, process development, manufacturing scale-up, quality control and quality assurance. BMS makes no warranty, express or implied, that Cadence shall be able to successfully implement and use the Technology Documentation. Cadence shall be responsible for ensuring that its personnel who receive such assistance are appropriately qualified and experienced for such purpose. At Cadence's written request, BMS shall, during the Tech Transfer Period and upon reasonable prior notice and subject to BMS's customary rules and restrictions with respect to site visits by non-BMS personnel, permit Cadence's technical personnel to visit the facilities utilized by BMS for the supply of Clinical Testing Products under the Clinical Supply Agreement for the purpose of personally observing the production of the Clinical Testing Products. The time of BMS employees expended in connection with any such visit (but not visits contemplated by the Clinical Supply Agreement) shall be charged against the [***] of technical assistance and consultation to be provided by BMS hereunder and compensated as provided in this Section 2.12. BMS shall not have any obligation to provide any such technical assistance or consultation following the expiration of the Tech Transfer Period.

2.13 Cooperation. The Parties shall cooperate to implement processes to ensure a close, cooperative working relationship between the Parties and their respective technical personnel in order to facilitate the technology transfer assistance contemplated above.

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2.14 Additional Assistance. In the event Cadence desires any additional technical assistance or consultation, Cadence may request such additional technical assistance or consultation from BMS. BMS shall consider such request in good faith, but BMS shall not have any obligation to provide any such additional technical assistance or consultation unless BMS agrees in writing in its sole discretion to provide such additional technical assistance or consultation. In the event BMS agrees in its sole discretion to provide any such additional technical assistance or consultation, Cadence shall pay BMS for such additional technical assistance or consultation at a rate equal to [***].

2.15 Pharmacovigilance; Adverse Event Reporting. Subject to the terms of this Agreement, and within [***] ([***])[***] after the Effective Date of this Agreement, BMS and Cadence (under the guidance of their respective Pharmacovigilance Departments, or equivalent thereof) shall in good faith define and finalize the responsibilities the Parties shall employ to protect patients and promote their well-being in their respective territories. These responsibilities shall include mutually acceptable guidelines and procedures for the receipt, investigation, recordation, communication, and exchange (as between the Parties) of adverse event reports, pregnancy reports, and any other information concerning the safety of the Product. Such guidelines and procedures shall be in accordance with, and enable the Parties and their Affiliated Companies to fulfill, local and international regulatory reporting obligations to government authorities. Furthermore, such agreed procedures shall be consistent with relevant International Council for Harmonization guidelines, except where said guidelines may conflict with existing local regulatory safety reporting requirements, in which case local reporting requirements shall prevail.

Until such guidelines and procedures are set forth in an agreement between the Parties, hereafter referred to as the Safety Data Exchange Agreement, the terms of paragraphs (a) – (d) and (f) below, of this Section, shall apply. Following the execution of the Safety Data Exchange Agreement, paragraphs (a) – (d) and (f) shall have no further force or effect.

(a) Each Party shall notify the other Party as soon as practicable, but not later than [***]([***])[***] after it receives information about the initiation of any investigation, review or inquiry by any Drug Regulatory Authority concerning the safety of the Product.

(b) Individual Case Safety Reports and pregnancy reports which come to the attention of either Party shall be notified to the other Party, in English, in the form of a source document or CIOMS Form by secure email or fax within [***]([***])[***] of receipt.

(c) Each Party is responsible for complying with all applicable investigational and post-marketing safety reporting regulations with respect to the use of the Product in the territory in which its affiliated companies, its sublicensees, its agents, or its contractors promotes the Product, as subject to the terms of this Agreement. This includes the submission of expedited and periodic reports to the appropriate Drug Regulatory Authority(s).

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(d) All information to be reported to a Party under this Section shall be sent as follows (or to such other address, contact person, telephone number, facsimile number or e-mail address as may be specified in writing to the other Party):

(i) To BMS, at:

Bristol-Myers Squibb Company
Global Pharmacovigilance
Adverse Event Processing
311 Pennington-Rocky Hill Road
Mail Stop HW 19-1.01
Pennington, NJ 08534
USA
FAX Number: 609-818-3804
Email: worldwide.safety@bms.com

(ii) To Cadence, at:

Cadence Pharmaceuticals, Inc.
12730 High Bluff Drive, Suite 410
San Diego, CA 92130
Attention: Vice President, Regulatory Affairs and Quality Assurance
Telephone: [***]
Facsimile: 858-436-1401
Email: [***]

(e) A Party's costs incurred in connection with receiving, investigating, recording, reviewing, communicating, and exchanging Adverse Events and Other Reportable Information shall be borne solely by such Party. As used herein, "**Other Reportable Information**" means any communication or other information that questions the purity, identity, potency or quality of the Product and all reports of Product exposure during pregnancy and Product overdose whether or not resulting in an Adverse Event.

(f) If any Drug Regulatory Authority (1) should contact Cadence with respect to the improper development, use, distribution, manufacture or commercialization of any Product, (2) conducts, or gives notice of its intent to conduct, an inspection at Cadence's facilities, or (3) takes, or gives notice of its intent to take, any other regulatory action with respect to any activity of Cadence that could reasonably be expected to adversely affect any development or commercialization activities of any Product under this Agreement, then Cadence shall promptly notify BMS of such contact or notice. Cadence shall provide BMS with copies of all pertinent information and documentation issued by any such Drug Regulatory Authority within two (2) Business Days of receipt and copies of any responses to such Drug Regulatory Authority that pertain to the Products promptly after the submission thereof to such Drug Regulatory Authority.

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2.16 Infringement – Pharmatop Patents.

(a) In the event either Party becomes aware that the Pharmatop Patents (or their inventorship) have become the subject to an administrative or judicial action, suit or challenge by a Third Party (including any reexamination or other proceeding challenging the validity or enforceability of the Pharmatop Patents) with respect to the Territory (to the extent relating to the Territory, a "**Pharmatop Patent Challenge**"), such Party shall promptly notify the other Party and BMS and Cadence shall consult with each other in order to attempt to determine the appropriate response to such Pharmatop Patent Challenge. If Pharmatop undertakes the defense thereof, Cadence shall have the right, to the extent permitted by the Pharmatop License Agreement, to participate and be represented in any such Pharmatop Patent Challenge by its own counsel [***]. To the extent Cadence is not permitted by the Pharmatop License Agreement to participate directly in such Pharmatop Patent Challenge, BMS shall (i) consult with Cadence during the defense of such Pharmatop Patent Challenge and (ii) if requested by Cadence, participate in such Pharmatop Patent Challenge [***] and cooperate with Cadence, [***], to arrange for the interests of the Parties (including Cadence) to be represented in such Pharmatop Patent Challenge.

If Pharmatop does not defend any such Pharmatop Patent Challenge, BMS shall provide written notice to Cadence promptly after receiving notice of Pharmatop's decision not to defend and shall consult with Cadence concerning the defense of such Pharmatop Patent Challenge. BMS shall use reasonable efforts (in light of relevant time and other deadlines) to determine whether it will defend such Pharmatop Patent Challenge and, if BMS elects not to defend such Pharmatop Patent Challenge, shall use reasonable efforts to provide Cadence with sufficient notice to permit Cadence to defend such Pharmatop Patent Challenge as permitted by Section 6.3 of the Pharmatop License Agreement and as set forth in this Section 2.16.

If BMS elects to defend against any such Pharmatop Patent Challenge as permitted by Section 6.3 of the Pharmatop License Agreement, BMS shall consult with Cadence during the defense of such Pharmatop Patent Challenge and BMS shall permit Cadence to participate and be represented in any such Pharmatop Patent Challenge by its own counsel [***].

The Parties shall reasonably assist Pharmatop and the other Party in the defense of any Pharmatop Patent Challenge. In the event the Party defending such Pharmatop Patent Challenge requests the assistance of the other Party, [***] shall reimburse the [***] for its [***] incurred in connection with such assistance. BMS shall not, without the written consent of Cadence, consent to the entry into any such settlement agreement by Pharmatop, that would restrict the scope, or adversely affect the enforceability or validity of, any of the Pharmatop Patents in the Territory.

If neither Pharmatop nor BMS elects to defend against a Pharmatop Patent Challenge, then BMS shall provide written notice to Cadence promptly after the later of BMS receiving notice of such decision by Pharmatop or such decision by BMS (in accordance with the last sentence of the second paragraph of this Section 2.16(a)) and, to the extent permitted by the

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Pharmatop License Agreement, Cadence shall have the right to defend [***] any such Pharmatop Patent Challenge in accordance with Section 6.3(b) of the Pharmatop License Agreement, and BMS shall be entitled to participate and be represented in any such Pharmatop Patent Challenge by its own counsel [***]. Cadence shall not enter into any settlement agreement with respect to such Pharmatop Patent Challenge, without the written consent of Pharmatop to the extent required by the Pharmatop License Agreement, and the written consent of BMS. If Cadence is not permitted by the Pharmatop License Agreement to defend such Pharmatop Patent Challenge, then at the written request of Cadence, BMS shall defend such action, suit or challenge as provided above, at [***].

(b) In the event either Party becomes aware of any infringement of a Valid Claim in the Territory under the Pharmatop Patents, such Party shall promptly notify the other Party and BMS and Cadence shall consult with each other and with Pharmatop in order to attempt to end such infringement, consistent with the Pharmatop License Agreement and shall take all appropriate action to do so. BMS shall have the right in the first instance, but not the obligation, to initiate legal action against an infringing party. Cadence shall reasonably assist BMS and Pharmatop in any action or proceeding prosecuted against the infringing Person by BMS or Pharmatop. If neither Pharmatop nor BMS prosecutes a legal action against the infringing Person (or if Pharmatop or BMS ceases to pursue or withdraws from such action), Cadence may initiate and prosecute such action (or substitute itself for Pharmatop or BMS in such action) at its own expense to the extent permitted by and in accordance with Section 6.5 of the Pharmatop License Agreement. Cadence shall not enter into a settlement agreement concerning such action, suit or challenge without the written consent of BMS.

If neither Pharmatop nor BMS prosecutes a legal action against the infringing Person (or if Pharmatop or BMS ceases to pursue or withdraws from such action) and Cadence is not permitted by Section 6.5 of the Pharmatop License Agreement to initiate and prosecute such action (or substitute itself for Pharmatop or BMS in such action), then at the written request of Cadence, BMS shall initiate and prosecute such action at the expense of Cadence and shall not, without the written consent of Cadence, enter into a settlement agreement with such infringing Person that would restrict the scope, or adversely affect the enforceability or validity of, any of the Pharmatop Patents in the Territory.

(c) Subject to the rights of Pharmatop set forth in the Pharmatop License Agreement, in the event either Party recovers any damages or other sums in such action in relation to any infringement of a Valid Claim under a Pharmatop Patent in the Territory or in settlement thereof, such damages or other sums recovered shall first be applied to all out-of-pocket costs and expenses incurred by the Parties in connection therewith, including attorneys fees, subject to any allocation due to Pharmatop pursuant to the Pharmatop License Agreement. If such recovery (after giving effect to any allocation due to Pharmatop pursuant to the Pharmatop

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License Agreement) is insufficient to cover all such costs and expenses of both Parties, it shall be shared in proportion to the total of such costs and expenses incurred by each Party. If after such reimbursement any funds shall remain from such damages or other sums recovered (after giving effect to any allocation due to Pharmatop pursuant to the Pharmatop License Agreement), such funds shall be shared [***] ([***]) by Cadence and [***] ([***]) by BMS. In the event any such action involves patent rights outside the Territory, Cadence shall be entitled to share only in the portion of any recovery that relates to infringement of any Pharmatop Patents in the Territory and shall not have any right to share in any recovery with respect to rights outside the Territory.

2.17 Infringement – BMS Patents.

(a) In the event the BMS Patents (or their inventorship) become the subject to an administrative or judicial challenge by a Third Party with respect to the Territory, BMS shall notify Cadence of such challenge within [***]([***])[***] of receipt of notice of such challenge. BMS shall have the right, but not the obligation, to defend such action, suit or challenge, and BMS shall notify Cadence of its decision regarding whether or not it will defend such action, suit or challenge. If BMS decides in its sole discretion to enter into any settlement agreement with respect to such action, suit or proceeding, BMS shall notify Cadence of such intent. If such settlement restricts the scope, or adversely affects the license to the BMS Patents granted to Cadence under Section 2.1, Cadence shall have the right, but not the obligation, to enter into discussions with BMS for the purpose of renegotiating the terms of said license in view of such settlement.

(b) If BMS does not defend any such action, suit or challenge and Cadence disagrees with BMS's decision, Cadence shall have the right, but not the obligation, to (i) enter into discussion with BMS for the purpose of renegotiating the terms of the license to the BMS Patents granted to Cadence under Section 2.1 or (ii) notwithstanding Article 8 of this Agreement, terminate the License granted under Sections 2.1(a)(ii) – (v) subject to the confidentiality provisions set forth in Sections 5.2 and 5.3.

2.18 Maintenance of BMS Patents. In the event BMS determines that it no longer desires to maintain any of the BMS Patents, BMS shall notify Cadence in writing of the BMS Patents that it no longer desires to maintain, and Cadence shall have the right to retain counsel of its own choosing to prosecute and maintain such BMS Patents and to make all maintenance and other payments as may be necessary to maintain such BMS Patents in effect.

2.19 Noncontravention. Neither BMS nor Cadence shall be required to take any action pursuant to Section 2.16, 2.17, 2.21 and 2.22 that it determines in its sole judgment and discretion conflicts with or violates any court or government order or decree to which it is then subject.

2.20 Patent Extensions. Subject to applicable terms of the Pharmatop License Agreement, BMS and Cadence shall each cooperate with one another to obtain patent term extensions (including any pediatric exclusivity extensions as may be available) or supplemental protection certificates or their equivalents in any country in the Territory with respect to a BMS Patent or Pharmatop Patent in the Territory.

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2.21 Data Exclusivity and Orange Book Listings. Subject to applicable terms of the Pharmatop License Agreement: (i) with respect to data exclusivity periods in the Territory (such as those periods listed in the FDA's Orange Book (including any available pediatric extensions)) Cadence, as appropriate, shall use commercially reasonable efforts consistent with its obligations under Applicable Law in the Territory to seek, maintain and enforce all such data exclusivity periods available for Products, and (ii) with respect to filings in the FDA Orange Book for issued patents for a Product, the appropriate Party shall, consistent with its obligations under Applicable Law in the Territory, list (and update as appropriate) in a timely manner all applicable Patents required to be filed by it, or that it is permitted to file, under such Applicable Law in connection with such Product. At least [***] ([***])[***] prior to an anticipated deadline for the filing of patent listing information for such Patents, the Party making such filing shall notify in writing and consult with the other Party regarding the content of such filing. In the event of a dispute between the Parties as to whether a particular Patent can be listed and/or the content of the filing for such listing, the Parties shall take expedited steps to resolve the dispute as promptly as possible, including seeking advice of an independent legal counsel to guide their decision. The other Party shall provide, consistent with its obligations under Applicable Law in the Territory, reasonable cooperation to the Party making such listing in filing and maintaining such Orange Book (and foreign equivalent) listings.

2.22 Notification of Patent Certifications. A Party receiving any allegation of patent invalidity, unenforceability or non-infringement of a Pharmatop Patent or a BMS Patent pursuant to a paragraph IV patent certification by a Third Party filing an Abbreviated New Drug Application, an application under §505(b)(2) of the FDCA or other similar patent certification by a Third Party, and/or any foreign equivalent thereof in connection with a Product in the Territory shall notify the other Party and shall provide the other Party with copies of all such allegations. Such notification and copies shall be provided to the other Party within five (5) days after receipt of such certification. If and to the extent such allegation relates to a Pharmatop Patent, and subject to the terms of the Pharmatop License Agreement, Cadence shall have the right (but not the obligation) to contest such patent certification in the Territory and initiate and control actions with respect thereto in accordance with Section 2.16, and upon request by Cadence, BMS shall provide reasonable assistance and cooperation at Cadence's expense in any actions reasonably undertaken by Cadence to contest any such patent certification.

2.23 Audit, Inspection and Review. BMS shall have the right [***] during business hours and upon reasonable prior notice to enter, inspect and evaluate that part of any plant or other facility that is engaged in the production, preparation, processing or storage of the Products for compliance with applicable environmental, health and safety regulations, cGMP and other Applicable Law in the Territory and for compliance with the terms of this Agreement; *provided* that such inspections may not be made more than [***] in any [***]; and *provided*, further, that if material corrective measures are necessary, BMS may [***] verify the implementation of such corrective measures. In addition to the other rights of BMS set forth in this Agreement: (i) BMS shall have the same right to inspect and review the activities of Cadence hereunder as Pharmatop has with respect to BMS under the Pharmatop License Agreement, and (ii) BMS shall have the same rights to audit Cadence's (and any of its sublicensee's) activities relevant to this

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Agreement, and to inspect Cadence's (and any sublicensee's) facilities involved in the manufacture of Products, in the same manner as Pharmatop has with respect to BMS's activities and facilities under the Pharmatop License Agreement. Cadence shall cause its sublicensees, suppliers, toll manufacturers and other Third Parties involved in the production, preparation, processing or storage of the Products to provide such access to BMS and shall include an appropriate provision in the applicable contract with any such Third Party providing for such access and shall cause such sublicensees, suppliers, toll manufacturers and other Third Parties to grant such access to BMS. Cadence shall notify BMS within [***] ([***])[***] after receipt of any notice of any inquiry, inspection or legal action by any Drug Regulatory Authority related to any aspect of the production of the Products. Cadence shall provide to BMS, promptly after receipt by Cadence, a copy of the results of any inspection reports and/or legal actions with or by any Drug Regulatory Authority in the Territory relating to such matters. Cadence shall keep BMS informed on an on-going basis as to any proposed responses regarding corrective or remedial actions to be taken as a result of any such inquiry, inspection or legal action, including actions relating to plants and facilities of Third Parties.

2.24 [***] Covenant; [***] Covenant.

(a) Certain Definitions. As used herein:

"**Available** [***]" means, as of any date, [***] determined In Accordance With GAAP [***].

"[***]" means as of any date, [***] determined In Accordance with GAAP [***]:

(1) (A) [***], or

(B) [***], and

(2) (A) [***], (B) [***] and (C) [***],

but only to the extent any such items are not already included in [***].

"[***]" means, as of any date [***] plus [***], in each case determined In Accordance With GAAP.

"[***]" means, as of any date, the [***].

"[***]" means, as of any date, the [***].

"[***]" means, as of any date, the [***].

(b) [***] Covenant. Provided that neither [***]:

(A) [***]; or

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(B) [***].

The foregoing covenant is referred to herein as the "[***] **Covenant**". [***] shall be entitled to temporary and permanent injunctive relief in order to restrain any violation of this Section 2.24(b).

As used herein, the term "[***] **Product**" means (i) [***] and/or (ii) [***].

(c) Termination of Covenant. If on [***] Covenant shall immediately terminate without any action on the part of [***]. Each such date of such termination is referred to herein as a "**Covenant Termination Date**". In the event [***].

During any period in which [***] shall have the right to (i) [***] and (ii) [***].

(d) Permanent Termination of Covenant; [***]. If [***]

(e) Reinstatement of [***]. As set forth in Section 2.1(c), if and when [***].

ARTICLE III – ADDITIONAL COVENANTS

3.1 Annual Operating Plan. Not later than [***]([***])[***] prior to the beginning of each Calendar Year, Cadence shall provide to BMS a written operating plan (each an "**Annual Operating Plan**") setting forth in reasonable detail Cadence's plans for the continued development (including plans for clinical and other studies and plans for obtaining any necessary Approvals in the Territory) and commercialization of the Products for such Calendar Year, together with the related budgets therefore and the estimated timelines for completion of key activities. The initial Annual Operating Plan for 2006 is as Previously Disclosed. Each subsequent Annual Operating Plan shall include a comparable level of information and detail as set forth in such Previously Disclosed Annual Operating Plan (and following first commercial sale of the Product in the Territory, shall include a line item for advertising and promotional expenses). Cadence shall promptly notify BMS in writing of any material change in any such Annual Operating Plan or of any material deviation from any Annual Operating Plan.

3.2 Development, Commercialization and Financial Reports and Consultations.

(a) Quarterly Development and Commercialization Reports. Cadence shall provide quarterly written reports to BMS, within [***]([***])[***]) following the end of each Calendar Quarter, presenting a summary in reasonable detail of the development and commercialization actions taken by Cadence relating to the Products in the Territory and results obtained through the end of such Calendar Quarter and a summary of any material changes to the Development Plan since the last such quarterly report. The report with respect to commercialization activities shall include, among other things, the number of full-time equivalent sales representatives assigned to each Product by Cadence and any co-promotion or

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co-marketing partner or any Third Party with which Cadence has any other arrangement for such Third Party to market, promote or sell any Product.

(b) [***] Reports. [***]:

(i) [***].

(ii) [***];

(iii) [***].

(c) [***] Statements. If [***] shall be In Accordance With GAAP [***].

(d) Calculations, Notifications and Consultations concerning [***]. If [***]:

(i) [***](A) [***] and (B) [***].

(ii) [***].

(iii) [***].

(e) [***] Reports. If on the [***], if any:

(i) [***], within [***]([***])[***]:

(A) [***],

(B) [***],

(C) [***],

(D) [***],

(E) [***],

(F) [***] Section 3.2(b):

(1) the [***] In Accordance With GAAP.

(2) a [***];

(G) a [***].

(ii) [***]:

(A) within [***]([***])[***]; and

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(B) not later than [***] ([***])[***].

In the event [***].

(f) Standards for Determining [***]. All projections used to determine [***] (i) [***] (A) [***] and (B) [***] and (ii) [***]. If any calculation of [***].

(g) Presentations concerning Development and Commercialization Activities. In addition, on reasonable request by BMS, Cadence shall meet with BMS to make presentations concerning the development and commercialization activities taken relating to the Products and to permit BMS to ask reasonable questions and receive answers from Cadence with respect to such matters (including advertising and promotional expenditures and measures of sales effort); *provided*, *however*, that Cadence shall not be required to make more than [***] in any Calendar Year. [***].

(h) Date of NDA Approval. Cadence shall notify BMS in writing as soon as reasonably practicable of the expected date of approval by the FDA of the NDA with respect to any Product in the United States and shall notify BMS of any such Approval not later than [***]([***])[***] following the date on which Cadence receives written notice of such approval or receives an "approvable letter" from the FDA with respect to any such NDA.

(i) Correspondence with Pharmatop. Each Party shall provide to the other Party copies of all material correspondence and reports provided by it to Pharmatop or by Pharmatop to it after the Effective Date with respect to the Products in the Territory.

3.3 Development Responsibilities and Costs.

(a) Cadence's initial plan (current as of the Execution Date) for the development of the Products, including the clinical and other studies it contemplates as of the date of this Agreement in order to obtain Approval of the Products in the United States and related budgets and timelines as of the Execution Date as the same may be amended from time to time in accordance with Section 3.3(c) (collectively, the "**Development Plan**") has been Previously Disclosed.

(b) Cadence shall have sole responsibility for, and shall bear the cost of the development and commercialization of the Products in the Territory. Cadence shall develop and commercialize the Products in compliance with all Applicable Law. Without limiting the foregoing, Cadence shall cause all Products manufactured, labeled, advertised and sold by it and its Affiliated Companies and sublicensees or on its or their behalf to comply in all material respects with Applicable Law.

(c) Without limiting Cadence's obligations under the Pharmatop License Agreement, Cadence shall use reasonable commercial efforts to pursue, fund and complete the development of the Products as set forth in the Development Plan as modified from time to time in accordance with this Agreement (including obtaining all necessary Approvals in the

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Territory). In the event that the results of clinical or other studies or communications from Drug Regulatory Authorities require a material modification to the Development Plan, Cadence shall consult with BMS concerning such results or communications and potential changes to the Development Plan that would offer a reasonable prospect for obtaining Approvals on a reasonably expeditious basis. Any modification to the Development Plan that involves [***]. No such consent by BMS shall relieve Cadence of any obligation under the Pharmatop License Agreement.

3.4 Obligations in respect of the Pharmatop License Agreement. Notwithstanding any other provision of this Agreement, Cadence (i) hereby unconditionally assumes and agrees during the term of this Agreement to perform as and when due all the obligations of BMS under the Pharmatop License Agreement that relate to the Territory (except (A) to the extent such obligations were required to be performed by BMS prior to the Effective Date and (B) for any obligation to indemnify Pharmatop for any breach by BMS of any such obligations prior to the Effective Date), the BMS Rights or the exercise of the rights sublicensed to Cadence under this Agreement and (ii) shall comply with all the terms and conditions of the Pharmatop License Agreement that relate to the Territory, the BMS Rights or the exercise of the rights sublicensed to Cadence under this Agreement, it being understood that Cadence shall be obligated to perform such obligations and comply with such terms and conditions in respect of its activities under this Agreement and the Pharmatop License Agreement but shall not have any obligation to cause BMS to perform such obligations or to cause BMS to comply with such terms and conditions. Without limiting the foregoing, Cadence shall be obligated to perform and comply, but shall not have any liability with respect to any failure by BMS (but not its own failure) to perform and comply, with Section 4.6(a), Article 10 or Article 12 of the Pharmatop License Agreement. Without limiting any other right or remedy of BMS under this Agreement and in order to prevent, ameliorate, mitigate or cure a breach of the Pharmatop License Agreement, in the event that Cadence fails to perform any of such obligations under the Pharmatop License Agreement (except to the extent that a breach by BMS of its obligations under this Agreement or the Pharmatop License Agreement or any other act or omission by BMS prevents such performance by Cadence or any of its Affiliated Companies, sublicensees, contractors or agents), which failure is not cured within ninety (90) days after written notice from BMS, BMS may perform such obligation on behalf of Cadence at Cadence's expense, and Cadence shall reimburse BMS for its fully burdened costs (including both its out-of-pocket costs and internal costs) in connection with such performance; *provided*, *however*, that this Section 3.4 shall not authorize BMS to control the conduct of any clinical trial or study under the Development Plan. This Agreement sets forth the obligations of the Parties *inter se*, and nothing in this Agreement (including any standard of effort set forth herein) shall limit or modify the obligations of the Parties assumed under the Pharmatop License Agreement.

3.5 Certain Rights and Obligations under the Pharmatop License Agreement.

(a) BMS shall provide Cadence with copies of written communications received by BMS from Pharmatop after the Effective Date pursuant to Section 2.2 of the Pharmatop License Agreement with respect to the results of research and development work

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performed by Pharmatop and concerning any inventions or Know-How (as defined in the Pharmatop License Agreement) made by Pharmatop relating to the Products.

(b) If Pharmatop provides to BMS a copy of any application, filing or request for review and comment by BMS, BMS shall provide a copy of each application, filing or request to Cadence promptly after receipt thereof, and shall give reasonable consideration to any comments of Cadence in any comments provided by BMS to Pharmatop.

(c) If Pharmatop provides to BMS a quarterly written patent report pursuant to Section 5.1(d) of the Pharmatop License Agreement, BMS shall provide a copy of such report to Cadence within a reasonable period of time after receipt thereof, provided that BMS may redact information relating to Patents outside the Territory.

(d) To the extent that Pharmatop is obligated to indemnify sublicensees of BMS pursuant to Section 12.1 of the Pharmatop License Agreement and Cadence desires to assert a claim for indemnification pursuant to such section, Cadence shall have the right, to the extent permitted by the Pharmatop License Agreement, to assert such claim for indemnification against Pharmatop. In the event Cadence is not permitted by the Pharmatop License Agreement to assert such claim directly against Pharmatop, BMS shall cooperate with Cadence (at Cadence's expense and subject to Section 7.7 of this Agreement) to permit Cadence to assert such claim, including, if necessary, allowing Cadence to bring such claim in the name of BMS, unless BMS has a reasonable objection to such procedure; *provided* that Cadence shall give BMS written notice of any proposed settlement with Pharmatop and a reasonable opportunity to review and comment on such proposed settlement, and Cadence shall not enter into any settlement with Pharmatop that could adversely affect the rights of BMS hereunder or under the Pharmatop License Agreement without the prior written consent of BMS in its sole discretion.

(e) To the extent that BMS is permitted to assert against Pharmatop a claim on behalf of Cadence (as BMS's sublicense) for (i) indemnification and defense pursuant to Section 3.2 of the Pharmatop License Agreement based on any use made by Pharmatop, its Affiliated Companies or its or their licensees of the Registrational Information or with respect to the breach of any representation, warranty or covenant of Pharmatop contained in the Pharmatop License Agreement or (ii) for specific performance of any covenant of Pharmatop contained in the Pharmatop License Agreement, BMS shall use reasonable efforts to cooperate with Cadence (at Cadence's expense and subject to Section 7.7 of this Agreement) to permit Cadence to assert such claim or request for specific performance by Pharmatop, including, if necessary, allowing Cadence to bring such claim in the name of BMS, unless BMS has a reasonable objection to such procedure; *provided* that Cadence shall give BMS written notice of any proposed settlement with Pharmatop and a reasonable opportunity to review and comment on such proposed settlement, and Cadence shall not enter into any settlement with Pharmatop that could adversely affect the rights of BMS hereunder or under the Pharmatop License Agreement without the prior written consent of BMS in its sole discretion. BMS makes no representation or warranty as to whether BMS is permitted to assert any such claim on behalf of Cadence.

(f) Whenever Cadence provides any report, notice or other communication to Pharmatop in compliance with of any of the obligations under the Pharmatop License Agreement assumed by Cadence pursuant to Section 3.4 (e.g., the obligation to provide quarterly updates

pursuant to Section 4.3 of the Pharmatop License Agreement), Cadence shall provide a copy of such report or notice to BMS at least [***] ([***])[***] prior to the time such report, notice or communication is provided to Pharmatop or, if it is impracticable to provide such copy at least [***]([***])[***]) ahead of time, Cadence shall provide such copy to BMS as early as practicable prior to the provision thereof to Pharmatop.

(g) BMS agrees that it shall, if reasonably requested by Cadence and at Cadence's expense, take reasonable efforts to enforce the material obligations of Pharmatop under the Pharmatop License Agreement as it relates to the Territory, including obligations under Article 5 of the Pharmatop License Agreement.

(h) BMS covenants that it shall not agree or consent to any amendment, supplement or other modification to the Pharmatop License Agreement or exercise any other right of agreement or consent thereunder, in each case as it relates to the Territory, unless Cadence has consented in its sole discretion in writing to the same.

(i) If Cadence is not in breach of any of its material obligations under this Agreement, BMS shall not terminate the Pharmatop License Agreement (either unilaterally or by mutual agreement with Pharmatop) with respect to any country in the Territory without the prior written consent of Cadence, which consent may be given or withheld in Cadence's sole discretion. If Cadence is in breach of any of its material obligations under this Agreement, BMS may terminate the Pharmatop License Agreement in its sole discretion. If BMS determines to terminate the Pharmatop Agreement, BMS shall consult with Cadence in advance to the extent reasonably practical.

(j) BMS shall not market a Competing Product (as defined in the Pharmatop License Agreement) in any country in the Territory during the Pharmatop Royalty Term for such country without obtaining a written waiver from Pharmatop of the consequences of such marketing under Section 7.4 of the Pharmatop License Agreement.

(k) Cadence shall provide written notice to BMS of any use by Pharmatop of which Cadence is aware of any Registrational Information of Cadence as to which BMS has the right [***] from Pharmatop as contemplated by Sections 3.1 and 3.3 of the Pharmatop License Agreement, and, if requested by Cadence, BMS shall thereafter request from Pharmatop [***] contemplated by Sections 3.1 and 3.3 of the Pharmatop License Agreement. If BMS [***] from Pharmatop for the use by Pharmatop of any Cadence Registrational Information as contemplated by Section 3.1 and 3.3 of the Pharmatop License Agreement, BMS shall [***] over to Cadence within [***]([***])[***] after the receipt thereof.

3.6 Conduct of Clinical Trials of Products by Cadence in Clinical Study Countries. In the event (i) Cadence is unable (or reasonably believes that it will be unable) to recruit in the Territory sufficient clinical study subjects to conduct clinical trials necessary for Approval of the Products in the Territory due to US treatment parameters that would significantly delay or impair Cadence's ability to recruit patients or otherwise complete the study on a timely basis and (ii) Cadence desires to conduct all or a portion of such clinical study in any of the Clinical Study

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Countries where BMS retains rights to commercialize the Product, then Cadence shall notify BMS in writing and provide BMS with a copy of the clinical trial study design and protocol(s) for the conduct of such clinical study in the Clinical Study Countries in which it plans to conduct such study and a statement of the proposed number of patients proposed to be recruited in each city in such Clinical Study Countries. Cadence shall not conduct any such study without the prior written consent of BMS and the license provided for below, which consent and license shall not be unreasonably withheld if: (i) such study design and protocols are reasonably satisfactory to BMS (and its Affiliated Companies in the Clinical Study Countries) and (ii) such study is lawful to conduct in the regulatory jurisdictions where such study will be conducted and meets prevailing ethical standards and guidelines (including BMS internal policies) relating to the conduct of clinical trials and the use of the Product. In the event BMS consents to the conduct of such study in a Clinical Study Country, BMS shall cause its applicable Affiliated Companies to grant a limited license or sublicense to Cadence's Affiliated Company in such Clinical Study Country where the BMS Affiliated Companies have rights to grant such license or sublicense solely for the purpose of permitting such clinical study solely in accordance with such study design and protocol; *provided* that (1) not later than [***] ([***])[***] after [***] during such clinical trial, Cadence shall provide BMS with a written report of the number of vials of Product administered to patients in such clinical study in each country outside the Territory where such study is conducted and [***], and (2) such clinical study shall be subject to such reasonable limitations as may be reasonably satisfactory to BMS to avoid undue concentration of study subjects in a particular city.

Neither BMS nor any of its Affiliated Companies shall have any duties or responsibilities in connection with such clinical trial, other than (to the extent applicable) the supply of Clinical Testing Products pursuant to the Clinical Supply Agreement, except that this provision shall not affect the obligations of BMS and Cadence to exchange safety information as provided in Section 2.15 and the Safety Data Exchange Agreement to be entered into pursuant to Section 2.15.

In the event Cadence desires to conduct all or a portion of such clinical study in [***], then Cadence may request that BMS consent to the inclusion of [***] as an additional Clinical Study Country. In the event (i) Cadence is unable (or reasonably believes that it will be unable) to recruit in the Territory and the Clinical Study Countries sufficient clinical study subjects to conduct clinical trials necessary for Approval of the Products in the Territory due to treatment parameters in the US and the Clinical Study Countries that would significantly delay or impair Cadence's ability to recruit patients or otherwise complete the study on a timely basis and (ii) Cadence desires to conduct all or a portion of such clinical study in any of the other countries where BMS retains rights to commercialize the Product, then Cadence may request that BMS consent to the inclusion of up to [***]([***]) additional countries as Clinical Study Countries; provided that Cadence may not request the inclusion of more [***]([***]) additional countries as Clinical Study Countries, including [***], over the term of this Agreement. In the event Cadence makes such request, BMS shall cause its Alliance Manager to use reasonable efforts to obtain the necessary internal BMS consents and approvals of the applicable BMS Affiliated Company in the applicable country to the inclusion of such country as a Clinical Study Country,

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which consents and approvals may be given or withheld in the sole discretion of such BMS Affiliated Company. In the event such consents and approvals are obtained, the Parties shall amend the list of Clinical Study Countries to include such country.

Cadence acknowledges that as of the Effective Date, BMS does not commercialize, and has not effected the registration of, Products in certain of the Clinical Study Countries and other countries where Cadence may desire to conduct clinical trials or studies. Nothing in this Agreement shall obligate BMS or any of its Affiliated Companies (i) to maintain, retain, obtain or seek any rights in any Clinical Study Country or any other country where Cadence may desire to conduct clinical trials or studies or (ii) to make, maintain, refile, renew or reinstate any Regulatory Filing in any such country.

3.7 Conduct of US or Canadian Clinical Trials of Products by BMS. In the event BMS is unable (or reasonably believes that it will be unable) to recruit outside the Territory sufficient clinical study subjects to conduct clinical trials necessary for Approval of the Products in any jurisdiction outside the Territory due to local treatment parameters that would significantly delay or impair BMS's ability to recruit patients or otherwise complete the study on a timely basis and BMS desires to conduct any clinical trials or studies of Products in the Territory, then BMS shall notify Cadence in writing and provide Cadence with a copy of the clinical trial study design and protocol(s) for the conduct of such clinical trial in the Territory and a statement of the proposed number of patients proposed to be recruited in each city in the Territory. BMS shall not conduct such study without the prior written consent of Cadence, which shall not be unreasonably withheld if: (i) such study design and protocols are reasonably satisfactory to Cadence; and (ii) such study is lawful to conduct in the country in the Territory where such study will be conducted and meets prevailing ethical standards and guidelines (including Cadence internal policies) relating to the conduct of clinical trials and the use of the Product. In the event Cadence consents to the conduct of such study in the Territory, BMS may conduct such study solely in accordance with such study design and protocol; *provided* that:

(A) if such clinical trial or study will take place prior to the launch of the Product by Cadence in the country where BMS proposes to conduct such clinical trial or study, such study is subject to such reasonable limitations designed to avoid impairing Cadence's ability to recruit patients for its own contemporaneous clinical trials; or

(B) if such clinical trial or study will take place after the launch of the Product by Cadence in the country where BMS proposes to conduct such clinical trial or study, then (1) not later than [***] ([***])[***] after [***] during such clinical trial, BMS shall provide Cadence with a written report of the number of vials of Product administered to patients in such clinical study in each country in the Territory where such study is [***], and (2) such clinical study shall be subject to such reasonable limitations as may be reasonably satisfactory to Cadence to avoid undue concentration of study subjects in a particular city in the Territory.

Neither Cadence nor any of its Affiliated Companies shall have any duties or responsibilities in connection with such clinical trial by BMS or its Affiliated Companies, except

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that this provision shall not affect the obligations of BMS and Cadence to exchange safety information as provided in Section 2.15 and the Safety Data Exchange Agreement to be entered into pursuant to Section 2.15.

3.8 Existing BMS Suppliers. [***].

ARTICLE IV – FINANCIAL TERMS

4.1 Payments to BMS. In partial consideration of the rights granted to Cadence hereunder:

(a) On the Effective Date, Cadence shall pay to BMS Twenty-Five Million Dollars ($25,000,000).

(b) Within ten (10) Business Days following the [***], Cadence shall pay to BMS [***]([***]). Such amount shall be paid only once, regardless of [***].

(c) Within ten (10) Business Days after [***], Cadence shall pay to BMS an amount equal to [***]([***])[***]; *provided*, *however*, that such payment shall not exceed [***]([***]).

(d) Not later than [***]([***][***] following the [***] in which the [***], Cadence shall pay to BMS [***]([***]); *provided*, *however*, if [***], Cadence shall pay such amount to BMS not later than [***]([***])[***] following the [***].

(e) In addition to the payment provided for in Section 4.1(d) above, not later than [***]([***][***] following the [***] in which the [***], Cadence shall pay to BMS [***]([***]); *provided*, *however*, if such [***], Cadence shall pay such amount to BMS not later than [***]([***]) [***].

(f) During the Pharmatop Royalty Term, Cadence shall pay to BMS royalties calculated at the rate of:

(i) [***] of that portion of aggregate Net Sales in each Calendar Year that is [***],

(ii) [***] of that portion of aggregate Net Sales in each Calendar Year that is [***] and up to and including Net Sales of [***], and

(iii) [***] of that portion of aggregate Net Sales in each Calendar Year that is [***],

with the aggregate amount of Royalties payable pursuant to clauses (i) – (iii) above [***] by the amount of the [***] and any [***] and [***] of this Agreement and the terms of the Pharmatop License Agreement (which [***] provided for in [***]). In the event the amount of [***] and any [***] with respect to any [***].

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In the event the royalties payable to Pharmatop are reduced in respect of any Combination Product (as defined in the Pharmatop License Agreement) sold by Cadence or its Affiliated Companies or sublicensees in the Territory, the Royalties payable to BMS pursuant to this Section 4.1(f) in respect of such Combination Product shall be reduced (dollar-for-dollar) by the amount of the reduction in such royalties payable to Pharmatop.

[***].

(g) During the BMS Patent Royalty Term, Cadence shall pay to BMS royalties calculated at the rate of:

(i) [***] of that portion of aggregate Net Sales of Products that are BMS Patent Products in each Calendar Year that is [***],

(ii) [***] of that portion of aggregate Net Sales of Products that are BMS Patent Products in each Calendar Year that is in [***] and up to and including Net Sales of such Products of [***], and

(iii) [***] of that portion of aggregate Net Sales of Products that are BMS Patent Products in each Calendar Year that is [***].

[***].

The Royalties payable by Cadence to BMS pursuant to this Section 4.1(g) shall be [***] for any Calendar Quarter if:

(i) [***]

(ii) [***]

(iii) [***]

but only to the extent such Royalties are [***] as of the date of such event.

[***].

(h) The royalties payable pursuant to Section 4.1(f) and Section 4.1(g) are referred to herein as "**Royalties**"). Such Royalties shall be paid quarterly as provided in Section 4.7 of this Agreement.

(i) [***].

4.2 Reduction of Certain Milestone Payments.

(a) If (i) after the Effective Date, a Third Party claim or action challenging the Pharmatop Patents succeeds so as to deprive Pharmatop (and therefore BMS and Cadence) of any of its rights under the Pharmatop Patents in the United States or (ii) after the Effective Date, Pharmatop or BMS is unable to maintain, or a material alteration of the scope or content occurs with respect to, any of the claims under any of the Pharmatop Patents, in the United States, then

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(1) the payment provided for in Section 4.1(b) shall, if not yet earned, be reduced to [[***] ([***]) and (2) the payment provided for in Section 4.1(c) shall, if not yet earned, be reduced by [***].

(b) If a Third Party should market in the United States after the Effective Date a parenterally-administered liquid solution product, in a stable and readily injectible form, that (i) contains paracetamol and one or more other analgesic ingredients, (ii) uses any of the Technology contained within any issued claim of any Pharmatop Patent in such country or any Pharmatop Know-How, and (iii) is not considered to infringe any Pharmatop Patent or BMS Patent in such country (whether by judicial determination or settlement, by joint agreement of either BMS and Pharmatop or BMS and Cadence or by the failure of Pharmatop, BMS and Cadence to prosecute such Third Party for infringement under Section 6.5 of the Pharmatop License Agreement or Section 2.16 of this Agreement), then (1) the payment provided for in Section 4.1(b) shall, if not yet earned, be reduced to [***]([***]) and (2) the payment provided for in Section 4.1(c) shall, if not yet earned, be reduced by [***]; *provided* that (A) during the pendency of any legal action against such Third Party with respect to the possible infringement of a Pharmatop Patent or BMS Patent the amount of such reduction (the "**Retained Sum**") shall be temporarily retained by Cadence until such litigation ends, (B) if the outcome of the litigation is the invalidation of the Pharmatop Patents so that the Third Party is free to sell such product in the United States, [***] and (C) if the outcome of the litigation is not as described in clause (B) above, [***].

(c) The reductions provided for in Sections 4.2(a) and 4.2(b) shall not be [***] and (i) the aggregate amount of the reduction in the payment provided for in Section 4.1(b) shall not exceed [***]([***]) and (ii) the aggregate amount of the reduction in the payment provided for in Section 4.1(c) shall not exceed [***].

(d) Notwithstanding the foregoing Sections 4.2(a) and 4.2(b), if aggregate Net Sales during any Calendar Year [***], then (i) for the [***] such Calendar Year Cadence shall pay to BMS [***]([***]) of the aggregate amount of the reduction [***], (ii) for the [***] such Calendar Year Cadence shall pay to BMS an [***]([***]) of the aggregate [***] and (iii) for the [***] such Calendar Year Cadence shall pay to BMS an [***]([***]) of the aggregate [***]. Such [***] shall be made not later than [***]([***])[***] following the applicable Calendar Year.

4.3 Payments by Cadence to Pharmatop. In partial consideration of the rights granted to Cadence hereunder and without limiting any of the other obligations assumed by Cadence under the Pharmatop License Agreement:

(a) Within ten (10) business days (as such term is used in the Pharmatop License Agreement) following the [***], Cadence shall pay to Pharmatop [***] ([***]) in satisfaction of the obligation set forth in Section 7.1(b) of the Pharmatop License Agreement.

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(b) Cadence shall pay to Pharmatop all royalties payable to Pharmatop pursuant to the Pharmatop License Agreement with respect to the Territory in the manner provided for in such agreement.

(c) If for any period a Guaranteed Payment is due under the Pharmatop License Agreement, Cadence shall pay to Pharmatop the amount of such Guaranteed Payment in the manner provided for in the Pharmatop License Agreement.

(d) Cadence shall provide to BMS evidence reasonably satisfactory to BMS of each such payment.

(e) The amount of the payments made to BMS under this Agreement shall be Confidential Information of BMS and of Cadence. Cadence shall not disclose to Pharmatop in the reports provided by Cadence to Pharmatop pursuant to the Pharmatop License Agreement or otherwise the amount of any payments to BMS hereunder.

4.4 Manner of Payment. All payments to be made to BMS or Cadence hereunder shall be paid in Dollars by wire transfer of immediately available funds to a bank account designated in writing by the payee not less than [***] ([***])[***] prior to the required payment date.

4.5 Interest. Any payment by Cadence to BMS hereunder not made as and when due shall bear interest at the rate of [***]([***]) per annum, compounded daily, from the due date to the date of payment.

4.6 Expenses; Taxes.

(a) *Expenses*. Except as expressly set forth in this Agreement, all costs and expenses incurred in connection with the preparation and negotiation of this Agreement and the other Transaction Documents and the transactions contemplated hereby shall be paid by the Party incurring such expense. Each Party shall bear the fees and expenses of any agent, broker, investment banker, finder or other Person engaged by it or any of its Affiliated Companies in connection with the transactions contemplated by this Agreement and the other Transaction Documents.

(b) *Transfer Taxes*. Any Transfer Tax, if any, applicable to the transactions contemplated by this Agreement shall be borne and paid by Cadence.

(c) *Tax Withholding*. The withholding tax, duties, and other levies (if any) applied by a government of any country of the Territory on payments made by Cadence to BMS hereunder shall be borne by BMS. Cadence, its Affiliated Companies and sublicensees shall cooperate with BMS to enable BMS to claim exemption therefrom under any double taxation or similar agreement in force, shall provide to BMS proper evidence of payments of withholding tax, and shall assist BMS by obtaining or providing in as far as possible the required documentation for the purpose of BMS's tax returns.

4.7 Sales Reports and Royalty and Other Payments. The Royalties payable under Section 4.1 shall be calculated and will be payable quarterly for sales made in each Calendar

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Quarter in the Royalty Term and the BMS Patent Royalty Term, as applicable. Cadence shall prepare and send to BMS within [***] ([***])[***] after the end of each Calendar Quarter ([***]([***])[***] after the last Calendar Quarter in a Calendar Year to allow for additional time to determine any adjustments required to be made on an annual basis) a detailed statement, country by country and by dosage and pharmaceutical form, of the Net Sales (and, during the BMS Patent Royalty Term, the Net Sales of BMS Patent Products), the calculation of the Royalties payable under Section 4.1, the calculation of any amounts payable to Pharmatop pursuant to the Pharmatop License Agreement with respect to the Territory and the calculation of any reduction in the Royalties or other amounts deducted from the payments to BMS as contemplated by Section 4.1 together with a description of any facts or circumstances that Cadence believes entitles it to a reduction in, or deduction from, the Royalties payable under this Agreement as contemplated by Section 4.1 and information reasonably satisfactory to BMS to permit the calculation of any such reduction or deduction, accompanied by payment in accordance with Section 4.4 of the Royalties due BMS. Cadence shall provide to BMS a copy of each statement of Net Sales provided by Cadence to Pharmatop contemporaneously with the provision of such statement to Pharmatop, which statements shall not disclose the Royalties or other amounts payable to BMS under this Agreement.

4.8 Sales Record Audit. Cadence shall keep, and shall cause each of its Affiliated Companies, sublicensees, distributors and agents to keep, full and accurate books of accounting In Accordance With GAAP containing all particulars that may be necessary for the purpose of calculating all Royalties payable to BMS. Such books of accounting (including those of Cadence's Affiliated Companies, sublicensees, distributors and agents) shall be kept at their principal place of business, together with all necessary supporting data. BMS may, on reasonable (but not less than [***]([***])[***]) written notice to Cadence, have the calculation of the Royalties payable under Section 4.1 and any calculation or reconciliation statement provided pursuant to Section 4.7 audited at its own expense by an accounting firm selected by BMS that is reasonably acceptable to Cadence and that is bound by a written agreement of confidentiality to Cadence. The auditor's assignment will be limited to reviewing the accuracy of a calculation or reconciliation statement sent by Cadence, and to disclosing only if there are any errors in payment and, if an error exists, the amount of such error(s) and the calculation thereof, and no additional or any other information. If an audit discloses that the amount of Royalties owed to BMS was understated by more than [***]([***][***], then [***] must reimburse [***] for the cost of the audit, in addition to paying the additional Royalties together with interest on the additional amounts, calculated from the date on which the additional amount should have been paid, as provided in Section 4.5. Such audit rights may be exercised only once in any given Calendar Year, and any such audit shall apply [***].

ARTICLE V – MUTUAL COVENANTS OF THE PARTIES

5.1 Publicity. Neither Party shall issue any public release or announcement concerning this Agreement or the transactions contemplated hereby without the prior consent of the other Party, except to the extent required by Applicable Law or the rules or regulations of any

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United States or foreign securities exchange (or inter-dealer quotation system) or regulatory commission (in which case such Party shall, to the extent practicable, allow the other Party reasonable time to comment on such release or announcement in advance of such issuance); *provided*, *however*, that prior to any such disclosure, such Party shall use reasonable efforts to give advance notice to the other Party of the timing and content of such disclosure. Nothing contained in this Section 5.1 shall prevent either Party from making internal announcements to its and its Affiliated Companies' employees.

5.2 Confidentiality.

(a) *Confidentiality Obligations*. Each Party recognizes that the other Party's Confidential Information constitutes highly valuable and proprietary confidential information and material. Each Party agrees that until the date that is [***]([***])[***] after the date of disclosure to it of any given item of Confidential

Information, it will keep confidential, and will cause its officers, employees, consultants, agents, Affiliated Companies and sublicensees to keep confidential, such Confidential Information disclosed to it by the other Party; *provided* that if the Pharmatop License Agreement requires a longer period of confidentiality with respect to any Confidential Information of Pharmatop disclosed to a Party, such Party shall also observe such longer period of confidentiality in accordance with the Pharmatop License Agreement. Neither BMS nor Cadence nor any of their respective employees, consultants, Affiliated Companies or sublicensees shall use Confidential Information of the other Party for any purpose whatsoever except as otherwise expressly permitted by this Agreement.

(b) *Limited Disclosure*. Each Party agrees that any disclosure of the other Party's Confidential Information to any officer, employee, consultant, agent or Affiliated Company of such Party, shall be made only if and to the extent necessary to carry out its obligations and responsibilities, or to exercise its rights, under this Agreement, shall be limited to the maximum extent possible consistent with such rights and responsibilities, and shall only be made to persons who are bound by their employment (or other) contract (or, in the case of counsel or other licensed professionals, by applicable rules of professional conduct) to maintain the confidentiality thereof and not to use such Confidential Information except as expressly permitted by this Agreement. Each Party further agrees not to disclose or transfer the other Party's Confidential Information to any Third Party under any circumstance without the prior written approval from the other Party (such approval not to be unreasonably withheld, delayed or conditioned if such Confidential Information is appropriately protected by the recipient), except as otherwise required by law, and except as otherwise expressly permitted by this Agreement. Each Party shall take such action, and shall cause its officers, employees, consultants, agents, Affiliated Companies and sublicensees to take such action, to preserve the confidentiality of the other Party's Confidential Information as it would customarily take to preserve the confidentiality of its own Confidential Information, using a level of care that shall not under any circumstances be less than reasonable care. Each of the Receiving Party's Affiliated Companies shall be bound by the confidentiality obligations set forth in this Section 5.2 for the entire period

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set forth in Section 5.2(a), including any entity that becomes an Affiliated Company after the date of the relevant disclosure by the Disclosing Party, whether or not such Affiliated Company ceases to be an Affiliated Company of the Receiving Party during the term of the confidentiality obligations hereunder; and the Receiving Party shall be responsible for any unauthorized disclosure of such Confidential Information by any of its Affiliated Companies to which such Confidential Information is disclosed, including after such company ceases to be an Affiliated Company.

(c) *Authorized Disclosure*. The Receiving Party may disclose Confidential Information belonging to the other Party to the extent (and only to the extent) such disclosure is reasonably necessary in the following instances:

(i) as reasonably necessary for filing or prosecuting Patents as contemplated by this Agreement;

(ii) as reasonably necessary for Regulatory Filings and other communications with Drug Regulatory Authorities as contemplated by this Agreement;

(iii) as reasonably necessary for prosecuting or defending litigation;

(iv) subject to Section 5.2(e) of this Agreement, as reasonably necessary to comply with Applicable Law (including the rules and regulations of the Securities and Exchange Commission or any national securities exchange) and with judicial process, if in the reasonable opinion of the Receiving Party's counsel, such disclosure is necessary for such compliance; and

(v) in connection with the performance of this Agreement and solely on a "reasonable need to know basis", to Affiliated Companies, potential collaborators (including potential co-marketing and co-promotion contractors), sublicensees, potential sublicensees, research collaborators, potential investment bankers, lenders, investors, employees, consultants, medical professionals participating in the conduct of clinical trials, or agents, each of whom prior to disclosure must be bound by similar obligations of confidentiality and non-use at least equivalent in scope to those set forth in this Section 5.2; *provided*, that in the case of disclosure to academic researchers and academic institutions, the confidentiality period hereunder shall be the longest such period as the applicable Party may reasonably negotiate with such researchers or institutions; and *provided*, that the Receiving Party shall remain responsible for any failure by any Person who receives Confidential Information pursuant to this Section 5.2 to treat such Confidential Information as required under this Section 5.2;

provided, however, that nothing in this Agreement shall limit or affect the Parties' confidentiality obligations under the Pharmatop License Agreement.

If and whenever any Confidential Information is disclosed in accordance with this Section 5.2, such disclosure shall not cause any such information to cease to be Confidential Information except to the extent that such disclosure results in a public disclosure of such information (otherwise than by breach of this Agreement). With respect to disclosures under Sections 5.2(c)(iii) and 5.2(c)(iv), where reasonably possible, the Receiving Party shall notify the

Disclosing Party of the Receiving Party's intent to make such disclosure sufficiently prior to making such disclosure so as to allow the Disclosing Party adequate time to take whatever action it may deem appropriate to protect the confidentiality of the information, and the Receiving Party shall further reasonably assist the Disclosing Party to obtain confidential treatment of such Confidential Information.

The Parties acknowledge that the terms of this Agreement shall be treated as Confidential Information of both Parties. For the avoidance of doubt, this Section 5.2 shall in no way prevent a Party from disclosing the existence of this Agreement or any terms of this Agreement in order to seek legal advice whenever deemed appropriate by such Party or to enforce such Party's rights under this Agreement, whether through arbitration proceedings, court proceedings or otherwise, or to defend itself against allegations or claims relating to this Agreement, or to disclose such terms as it may be advised in written opinion of outside counsel are required to be disclosed to comply with Applicable Law (a copy of which opinion shall be provided to the other Party).

(d) *Employees and Consultants*. Each Party hereby represents that all of its employees and any consultants to such Party or its Affiliated Companies that will have access to the Confidential Information of the other Party shall be bound by written obligations (or, in the case of counsel or other licensed professionals, bound by rules of professional conduct) to maintain such information in confidence consistent with the terms of this Agreement and not to use such information except as expressly permitted herein. Each Party agrees to enforce confidentiality obligations to which its employees and consultants (and those of its Affiliated Companies) are obligated with respect to any such Confidential Information and agrees to be responsible for any breach or violation by such Persons of any provisions of this Agreement or the Pharmatop License Agreement relating to the confidentiality or non-use of any such Confidential Information by such Persons.

(e) *Securities Filings*. In the event either Party proposes to file with the Securities and Exchange Commission or the securities regulators of any state or other jurisdiction a registration statement or any other disclosure document which describes or refers to this Agreement under the Securities Act of 1933, as amended, the Exchange Act, or any other Applicable Law relating to securities matters, that Party shall notify the other Party of such intention and shall provide such other Party with a copy of relevant portions of the proposed filing not less than five (5) Business Days prior to such filing (and any revisions to such portions of the proposed filing a reasonable time prior to the filing thereof), including any exhibits thereto relating to this Agreement, and shall use reasonable efforts to obtain confidential treatment of any information concerning this Agreement that such other Party requests be kept confidential, and shall only disclose Confidential Information which it is advised by counsel or the Securities and Exchange Commission is legally required to be disclosed. No such notice shall be required under this Section 5.2(e) if the substance of the description of or reference to this Agreement contained in the proposed filing has been included in any previous filing made by either Party hereunder or otherwise approved by the other Party.

(f) *Academic Publications*. The Parties recognize that independent investigators have been engaged, and will be engaged in the future, to conduct clinical trials and studies of the Products. The Parties recognize that such investigators operate in an academic

environment and may release information regarding such studies in a manner consistent with academic standards and as further provided in this paragraph. In the event that any such independent investigator of a Party desires to publish any abstract, manuscript or article or make any presentation (including verbal presentations) or other publication that includes any Confidential Information of the other Party, such Party shall (i) require such independent investigator to provide the other Party and its patent counsel the opportunity to review any proposed abstract, manuscript, article, presentation (including verbal presentations) or other publication at least thirty (30) days prior to its intended submission for publication or such presentation and (ii) upon request of the other Party not to submit any such abstract, article or manuscript for publication or not to make such presentation for such additional reasonable period of time (but not to exceed an additional thirty (30) days) to enable the other Party to secure patent protection for any material in such publication which it believes to be patentable or to consider the implications of publication on eventual commercialization.

(g) *Additional Confidentiality Obligations under the Pharmatop License Agreement*. The provisions of this Section 5.2 are in addition to and not in limitation of any applicable obligation of confidentiality under the Pharmatop License Agreement.

5.3 Restrictions Binding on Affiliated Companies and Investors. Each Party shall require each of its Affiliated Companies and investors to which Confidential Information of the other Party is disclosed as permitted hereunder to comply with the covenants and restrictions set forth in Sections 5.1 and 5.2 as if each such Affiliated Company and each such investor were a Party to this Agreement and shall be fully responsible for any breach of such covenants and restrictions by any such Affiliated Company or investor.

5.4 Alliance Management. Each of the Parties shall appoint one senior representative who possesses a general understanding of development, regulatory and commercialization issues to act as its Alliance Manager. The role of the Alliance Manager is to act as a single point of contact between the Parties to assure a successful working relationship. Each Party may change its designated Alliance Manager from time to time upon written notice to the other Party. Any Alliance Manager may designate a substitute to temporarily perform the functions of that Alliance Manager.

5.5 Liens.

(a) Cadence shall not during the term of this Agreement (i) grant any Lien (excluding any permitted sublicenses) with respect to this Agreement or any of the rights licensed or sublicensed to it under this Agreement or (ii) permit such a lien, security interest or other encumbrance (excluding any permitted sublicenses) to attach to this Agreement or any of such rights. For sake of clarity, any breach of this Section 5.5(a) by Cadence that is not cured within ten (10) Business Days after written notice thereof shall be deemed a material breach of this Agreement.

(b) BMS shall not during the term of this Agreement (i) grant any Lien (excluding any permitted sublicenses) with respect to any of the BMS Rights, BMS Patents or BMS Know-How that would prevent BMS from granting the licenses hereunder or performing its obligations under this Agreement, or (ii) permit such a Lien to attach to the BMS Rights,

BMS Patents or BMS Know-How. For sake of clarity, any breach of this Section 5.5(b) by BMS that is not cured within ten (10) Business Days after written notice thereof shall be deemed a material breach of this Agreement.

5.6 BMS Confidential Disclosure Agreements. Promptly following the Effective Date, BMS shall assign to Cadence the Confidential Disclosure Agreements executed by BMS and the other potential sublicensees considered by BMS in connection with the sublicense of the BMS Rights contemplated hereby, to the extent assignable; *provided*, *however*, that if BMS is not permitted by the terms of such Confidential Disclosure Agreements to so assign them, BMS shall request the other parties to such Confidential Disclosure Agreement to (i) return or destroy all the confidential information of BMS relating to the Products and the BMS Rights provided to them by BMS in connection with such transaction and (ii) certify to BMS that such confidential information has been returned or destroyed; *provided*, *further*, that BMS shall not have any obligation to bring any suit or take any other action against any such other party to enforce the obligations thereunder. BMS shall provide to Cadence copies of any such certifications received by BMS.

ARTICLE VI – REPRESENTATIONS AND WARRANTIES

6.1 Mutual Representations and Warranties. Each of BMS and Cadence represents and warrants to the other Party as follows:

(a) *Organization*. Such Party is a corporation duly organized, validly existing and in good standing (or subsisting) under the laws of the jurisdiction of its organization, is qualified to do business and is in good standing (or subsisting) as a foreign corporation or company in each jurisdiction in which the performance of its obligations under this Agreement requires such qualification, and has full corporate or company power and authority and possesses all governmental franchises, licenses, permits, authorizations and approvals (other than the termination or expiration of any waiting periods under the HSR Act, if applicable) necessary to enable it to perform its obligations under this Agreement, other than such franchises, licenses, permits, authorizations and approvals the lack of which, individually or in the aggregate, could not reasonably be expected to have a Material Adverse Effect.

(b) *Authorization*. The execution, delivery and performance by such Party of this Agreement have been duly authorized by all necessary corporate action and do not and will not require any further consent or approval of its shareholders or members. Such Party has the power and authority to execute and deliver this Agreement and to perform its obligations hereunder and to grant the rights and licenses granted (or to be granted) by it in this Agreement.

(c) *Binding Agreement*. Such Party has duly executed and delivered this Agreement, and this Agreement (assuming the due authorization, execution and delivery by each other party thereto), constitutes its legal, valid and binding obligation, enforceable against it in accordance with its terms, subject to applicable bankruptcy, insolvency, fraudulent transfer, reorganization, moratorium and similar laws and judicial decisions of general applicability relating to or affecting creditors' rights generally and to general principles of equity (regardless of whether enforceability is sought in equity or at law).

(d) *No Conflicts; Consents*. The execution and delivery by such Party of this Agreement do not, and the consummation of the transactions contemplated by this Agreement do not and will not, conflict with, or result in any violation of or default (with or without notice or lapse of time, or both) under, or give rise to a right of termination, cancellation or acceleration of any obligation or to loss of a material benefit under, or to increased, additional or accelerated rights or entitlements of any Third Party under, or result in the creation of any Lien upon any of the assets of such Party under, any provision of (i) its Organizational Documents, (ii) any Contract to which such Party is a party or by which any of its properties or assets is bound, except for the rights of Pharmatop under the Pharmatop License Agreement or (iii) any judgment, order or decree (collectively, "**Judgments**") or any Applicable Law applicable to such Party or its properties or assets. No consent, approval, license, permit, order or authorization (collectively, "**Consent**") of, or registration, declaration or filing with, any Governmental Entity (other than any filing under the HSR Act) or any other Third Party is required to be obtained or made by or with respect to such Party in connection with the execution, delivery and performance of this Agreement or the consummation of the transactions contemplated by this Agreement.

(e) *Litigation*. There are no (a) outstanding Judgments against or affecting such Party, or (b) claims, actions, suits, proceedings, arbitrations, investigations, inquiries, or hearings or notices of hearings (collectively, "**Proceedings**") pending or, to the knowledge of such Party, threatened in writing against or affecting such Party, its Affiliated Companies, by or against any Governmental Entity or any other Person, that in any manner challenges or seeks to prevent, enjoin, materially alter or materially delay the transactions contemplated by this Agreement or that, individually or in the aggregate, could reasonably be expected to have a Material Adverse Effect on such Party or on the exploitation (including the import, use, manufacture, sale and offer for sale) of the Products hereunder.

6.2 Additional Representations of Cadence. Without limiting the generality of the representations and warranties set forth in Section 6.1 above, Cadence represents and warrants to BMS as follows:

(a) *Financial Statements*. True and complete copies of the audited balance sheet of Cadence as of December 31, 2004, and the related statements of income, shareholders' equity and cash flows for the fiscal year ended on such date, together with the notes thereto and the unaudited consolidated balance sheets of Cadence and its subsidiaries as of December 31, 2005, and the related statements of income, shareholders' equity and cash flows for the twelve (12) months ended on such date (collectively, the "**Financial Statements**") have been Previously Disclosed. The Financial Statements are In Accordance With GAAP (as defined below). As used herein with respect to any financial statements, "**In Accordance With GAAP**" means that such financial statements: (i) are in accordance with the books and records of Cadence and its subsidiaries, if any, (ii) are true and correct and fairly present in all material respects the financial position, results of operations, shareholders' equity and cash flows of Cadence and its subsidiaries, if any, on a consolidated basis, if applicable, as of the dates and for the periods indicated, in each case in conformity with United States generally accepted accounting principles consistently applied during the applicable periods and (iii) if such financial statements are audited, include all required footnotes and, if such financial statements are unaudited, include all required footnotes concerning contingent liabilities, if any. The statements of income included

in the Financial Statements do not contain any items of special or nonrecurring income, revenue or expense and have not been affected by the inclusion of transactions entered into otherwise than on normal commercial terms or by any other factors rendering such profits for all or any of such periods exceptionally high or low, except as expressly specified therein. Except as specified in the Financial Statements or the notes thereto, the balance sheets included in the Financial Statements do not reflect any write-up or revaluation increasing the book value of any assets. The books and accounts of Cadence and its subsidiaries are true and complete in all material respects and fully and fairly reflect all of the transactions of Cadence and its subsidiaries.

(b) *Absence of Undisclosed Liabilities*. To the knowledge of Cadence, Cadence and its subsidiaries have no liability of any nature whatsoever (whether known or unknown, due or to become due, accrued, absolute, contingent, existing, inchoate or otherwise) including any unfunded obligation under any benefit plan (as defined in ERISA) or liabilities for Taxes, except for (i) liabilities reflected or reserved against in the consolidated balance sheet of Cadence and its subsidiaries as of December 31, 2005 (the "**Balance Sheet Date**") included in the Financial Statements (collectively, the "**Balance Sheet**"), or in the notes thereto, (ii) liabilities under the Loan and Security Agreement among Cadence, Oxford Finance Corporation and Silicon Valley Bank dated February 17, 2006 (the "**Loan Agreement**"), (iii) current liabilities incurred in the ordinary course of business and consistent with past practice from the Balance Sheet Date to the Effective Date which, individually and in the aggregate, do not exceed [***] and (iv) liabilities which individually or in the aggregate would not have a Material Adverse Effect on Cadence. The collateral pledged by Cadence pursuant to the Loan Agreement does not include any of Cadence's rights in, to or under this Agreement.

(c) *Absence of Material Adverse Effect*. To the knowledge of Cadence, since the Balance Sheet Date and through the Effective Date, Cadence and its subsidiaries have not experienced a Material Adverse Effect and no event or circumstance has occurred or developed which is reasonably likely to result in such a Material Adverse Effect or which has resulted, or is reasonably likely to result, in any loss or liability to Cadence and its subsidiaries in excess of [***].

Without limiting the foregoing, since the Balance Sheet Date there has not been, occurred or arisen: (i) any declaration, setting aside or payment of any dividend or distribution (whether in cash, stock or property) in respect of capital stock of Cadence or any of its subsidiaries, or any direct or indirect redemption, purchase or other acquisition of shares of such capital stock or any split, combination or reclassification of such capital stock (other than redemption of shares issued pursuant to early-exercised options under Cadence's 2004 Equity Incentive Award Plan), (ii) any Lien on any of the assets or properties of Cadence and its subsidiaries (other than the pledge of assets pursuant to the Loan Agreement); or (iii) any authorization, approval, agreement or commitment to do any of the foregoing. The pledge of assets pursuant to the Loan Agreement does not grant any Lien with respect to this Agreement or any of the rights licensed or sublicensed to it under this Agreement.

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(d) *Legal Matters*. Since Cadence's date of incorporation (May 26, 2004), there has not been any, and there is no, claim, action, suit, litigation, investigation, inquiry, review or proceeding (collectively, "**Cadence Claims**") pending against Cadence or any of its subsidiaries relating to the business or assets of Cadence or its subsidiaries before or by any court, arbitrator or

Governmental Entity; and to the knowledge of Cadence no such Cadence Claim has been threatened. Neither Cadence nor any of its subsidiaries is subject to any judgment, decree, writ, injunction, ruling, award or order of any Governmental Entity or any arbitrator relating to the business or assets of Cadence and its subsidiaries.

(e) *Receipt of Financing; Restrictions*. Between the Execution Date and the Effective Date, Cadence will have received additional financing in an amount that is not less than $50 million from the sale of equity securities. The holders of the equity securities of Cadence and its subsidiaries do not have (by virtue of the terms of such equity securities, by contract or otherwise) any right (mandatory or optional) to require the redemption of any of such equity securities. On or before the Effective Date, Cadence will have entered into the Loan Agreement obligating the lender or lenders thereunder to lend to Cadence not less than $7 million, subject to the terms and conditions set forth therein. Cadence has provided to BMS true and complete copies of the documents relating to such equity financing and such Loan Agreement.

6.3 BMS Rights.

(a) Pharmatop Patents. As of the Execution Date, BMS represents and warrants to Cadence as follows with respect to the Pharmatop Patents and Pharmatop Know-How:

(i) Schedule 6.3(a) sets forth a list of all the Pharmatop Patents. To the knowledge of BMS's in-house patent counsel after reasonable due diligence, (A) the most recent Patent report provided to BMS pursuant to Section 5.1 of the Pharmatop License Agreement relating to the Pharmatop Patents has been provided to Cadence, except for information that may have been redacted relating to Patents outside the Territory, and (B) BMS has not received any written notices of allowances for the Pharmatop Patents or written notices of interferences proceedings with respect thereto, except as previously disclosed to Cadence.

(ii) To the knowledge of BMS's in-house patent counsel after reasonable due diligence, there are no unpaid maintenance, annuity or renewal fees currently overdue for any of the Pharmatop Patents.

(iii) To the knowledge of BMS's in-house patent counsel, BMS is the sole and exclusive licensee of the Pharmatop Patents in the Territory.

(iv) BMS has not sublicensed, granted any interest in or options to the Pharmatop Patents to any Third Party in the Territory and covenants not do so prior to the expiration or termination of this Agreement, except in the exercise of BMS's retained rights pursuant to Section 2.2.

(b) To the knowledge of BMS's in-house counsel, BMS is not, nor has it received any notice that it is, in default (or that with the giving of notice or lapse of time or both it would be in default) with respect to the BMS Rights under the Pharmatop License Agreement that would permit Pharmatop to terminate, or exercise a right of rescission, revision or amendment of, the Pharmatop License Agreement with respect to the Territory and covenants that it shall not take, and shall cause its Affiliated Companies not to take, any action or omit to take any action after the Execution Date that would permit Pharmatop to terminate, or exercise a right of rescission, revision or amendment of, the Pharmatop License Agreement with respect to the Territory, other than the omission of the performance of obligations assumed by Cadence hereunder.

(c) To the knowledge of BMS's in-house patent counsel, BMS has not received written notice of any claim, action, suit or litigation alleging that BMS's exploitation (including the import, use, manufacture, sale and offer for sale) of the BMS Rights for the Product interferes with, infringes, or misappropriates any intellectual property rights of any Third Party (including written notice of any claim, action, suit or litigation that BMS must license or refrain from using any intellectual property rights of any Third Party in order to exploit(including the import, use, manufacture, sale and offer for sale) any Products. To the knowledge of BMS's in-house patent counsel, BMS has not received written notice that any claim, action, suit or litigation is pending or threatened which challenges the legality, validity, enforceability, use or ownership of any BMS Rights.

(d) BMS represents and warrants to Cadence that a true and correct copy of the Pharmatop License Agreement as of the Effective Date, including any and all amendments, supplements or other modifications thereto, except for the redaction of certain financial information in Section 7.1 thereof, has been Previously Disclosed. A copy of the Licensor Confirmation provided by Pharmatop with respect to certain intellectual property and other matters as of February 6, 2006, has been Previously Disclosed.

(e) To the knowledge of BMS, no circumstances or grounds exist that would entitle Pharmatop to terminate or exercise a right of rescission, revision, or amendment of the Pharmatop License Agreement with respect to the Territory, and the execution, delivery and performance of this Agreement will not constitute such a circumstance or ground.

(f) BMS has protected the Pharmatop Know-How in a manner not materially different from the manner in which it customarily protects its other proprietary know-how of comparable commercial value.

6.4 BMS Patents and Know-How. As of the Execution Date, BMS represents and warrants to Cadence with respect to the BMS Patents and BMS Know-How that to the knowledge of its in-house patent counsel:

(a) there are no unpaid maintenance, annuity or renewal fees currently overdue for any of the BMS Patents; and

(b) there are no claims, judgments or settlements against or owed by BMS and no litigation pending or threatened in writing relating to the BMS Patents; and

(c) BMS has protected the BMS Know-How in a manner not materially different from the manner in which it customarily protects its other proprietary know-how of comparable commercial value.

6.5 DISCLAIMER.

(a) EXCEPT FOR THE EXPRESS REPRESENTATIONS AND WARRANTIES SET FORTH IN THIS ARTICLE VI OR IN SECTION 5.2(D), BMS MAKES NO REPRESENTATIONS OR WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, WITH RESPECT TO THE BMS RIGHTS, BMS PATENTS OR BMS KNOW-HOW, IMPROVEMENTS, REGISTRATIONAL INFORMATION, REGULATORY FILINGS, APPROVALS, PRODUCT DATA, OTHER PRODUCT DATA OR REPORTS, STUDIES, PATENTS, PROCESSES, FORMULATIONS, TECHNIQUES OR OTHER TRADE SECRETS OR CONFIDENTIAL INFORMATION PROVIDED BY BMS TO CADENCE HEREUNDER OR ANY LICENSE GRANTED BY BMS HEREUNDER, OR WITH RESPECT TO ANY COMPOUNDS OR PRODUCTS. WITHOUT LIMITING THE FOREGOING, BMS MAKES NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, WITH RESPECT TO THE BMS RIGHTS, BMS PATENTS OR BMS KNOW-HOW OR ANY LICENSE GRANTED BY BMS HEREUNDER, OR WITH RESPECT TO ANY COMPOUNDS OR PRODUCTS. FURTHERMORE, NOTHING IN THIS AGREEMENT SHALL BE CONSTRUED AS A REPRESENTATION OR WARRANTY BY BMS THAT ANY OF THE FOREGOING IS VALID OR ENFORCEABLE OR THAT CADENCE'S USE THEREOF CONTEMPLATED HEREUNDER DOES NOT INFRINGE ANY PATENT RIGHTS OR OTHER INTELLECTUAL PROPERTY RIGHTS OF ANY THIRD PARTY.

(b) EXCEPT FOR THE EXPRESS REPRESENTATIONS AND WARRANTIES SET FORTH IN THIS ARTICLE VI OR IN SECTION 5.2(D), CADENCE MAKES NO REPRESENTATIONS OR WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, WITH RESPECT TO THE IMPROVEMENTS, REGISTRATIONAL INFORMATION, REGULATORY FILINGS, APPROVALS, PRODUCT DATA, OTHER PRODUCT DATA OR REPORTS, STUDIES, PATENTS, PROCESSES, FORMULATIONS, TECHNIQUES OR OTHER TRADE SECRETS OR CONFIDENTIAL INFORMATION PROVIDED BY CADENCE TO BMS HEREUNDER OR ANY LICENSE GRANTED BY CADENCE HEREUNDER, OR WITH RESPECT TO ANY COMPOUNDS OR PRODUCTS. WITHOUT LIMITING THE FOREGOING, CADENCE MAKES NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, WITH RESPECT TO ANY LICENSE GRANTED BY CADENCE HEREUNDER, OR WITH RESPECT TO ANY COMPOUNDS OR PRODUCTS. FURTHERMORE, NOTHING IN THIS AGREEMENT SHALL BE CONSTRUED AS A REPRESENTATION OR WARRANTY BY CADENCE THAT ANY OF THE FOREGOING IS VALID OR ENFORCEABLE OR THAT BMS'S USE THEREOF CONTEMPLATED HEREUNDER DOES NOT INFRINGE ANY PATENT RIGHTS OR OTHER INTELLECTUAL PROPERTY RIGHTS OF ANY THIRD PARTY.

6.6 LIMITATION OF LIABILITY. NOTWITHSTANDING ANYTHING IN THIS AGREEMENT OR OTHERWISE, (I) NEITHER PARTY SHALL BE LIABLE TO THE

OTHER (OR TO ANY INDEMNIFIED PARTIES) WITH RESPECT TO ANY SUBJECT MATTER OF THIS AGREEMENT, WHETHER UNDER ANY CONTRACT, NEGLIGENCE, STRICT LIABILITY OR OTHER LEGAL OR EQUITABLE THEORY, FOR ANY INCIDENTAL, INDIRECT, SPECIAL, EXEMPLARY, PUNITIVE, MULTIPLE, OR CONSEQUENTIAL DAMAGES (INCLUDING LOST PROFITS, LOSS OF USE, DAMAGE TO GOODWILL, OR LOSS OF BUSINESS), EXCEPT THAT SUCH LIMITATION SHALL NOT APPLY TO (A) PUNITIVE OR CONSEQUENTIAL DAMAGES PAID OR PAYABLE TO A THIRD PARTY BY AN INDEMNIFIED PARTY FOR WHICH THE INDEMNIFIED PARTY IS ENTITLED TO INDEMNIFICATION HEREUNDER, (B) A BREACH OF THE [***] COVENANT, (C) ANY FAILURE BY CADENCE OR ITS AFFILIATED COMPANIES TO (1) OBSERVE OR COMPLY WITH THE TERMS OF THE PHARMATOP LICENSE AGREEMENT OR (2) PERFORM ANY OF THE OBLIGATIONS UNDER THE PHARMATOP LICENSE AGREEMENT ASSUMED BY CADENCE HEREUNDER THAT, IN THE CASE OF EACH OF PART (1) AND (2) OF THIS CLAUSE (C) RESULTS IN A TERMINATION OF THE PHARMATOP LICENSE AGREEMENT WITH RESPECT TO ANY COUNTRY IN THE TERRITORY OR A TERMINATION OF THE PHARMATOP LICENSE AGREEMENT IN ITS ENTIRETY, (D) ANY BREACH OF THE PHARMATOP LICENSE AGREEMENT BY BMS OR ITS AFFILIATED COMPANIES (OTHER THAN WITH RESPECT TO ANY OBLIGATION TO BE PERFORMED BY CADENCE) THAT RESULTS IN A TERMINATION OF THE PHARMATOP LICENSE AGREEMENT WITH RESPECT TO ANY COUNTRY IN THE TERRITORY OR A TERMINATION OF THE PHARMATOP LICENSE AGREEMENT IN ITS ENTIRETY OR (E) ANY BREACH OF [***] OF THIS AGREEMENT BY BMS OR ITS AFFILIATED COMPANIES OR OF [***] OF THIS AGREEMENT BY CADENCE OR ITS AFFILIATED COMPANIES AS TO WHICH CADENCE OR BMS, AS THE CASE MAY BE, TERMINATES THIS AGREEMENT PURSUANT TO SECTION 8.3(B) (IT BEING UNDERSTOOD THAT A BREACH OF ANY OF SUCH SECTIONS IS NOT NECESSARILY A MATERIAL BREACH THAT WOULD PERMIT TERMINATION UNDER SECTION 8.3(B)), AND (II) EXCEPT AS PROVIDED IN [***] ABOVE, BMS SHALL NOT BE LIABLE IN RESPECT OF ANY BREACH OF ANY REPRESENTATION OR WARRANTY OF BMS CONTAINED IN THIS AGREEMENT IN AN AMOUNT GREATER THAN THE AMOUNTS PAID BY CADENCE TO BMS UNDER SECTION 4.1 OF THIS AGREEMENT.

ARTICLE VII – INDEMNIFICATION; ARBITRATION

7.1 Mutual Indemnification. Each Party (the "**Indemnifying Party**") shall indemnify, defend and hold harmless the other Party, its Affiliated Companies and their respective directors, officers, employees, and agents and their respective successors, heirs and permitted assigns (the "**Indemnitees**"), against any liability, damage, loss or expense (including reasonable attorneys' fees and expenses of litigation) (collectively, but subject to Section 6.6 hereof, "**Losses**") incurred by or imposed upon the Indemnitees, or any one of them arising out of or resulting from (or alleged to arise out of or result from) any of the following:

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(i) any breach of any representation or warranty of the Indemnifying Party contained in this Agreement; and

(ii) any breach of any covenant or agreement of the Indemnifying Party contained in this Agreement.

7.2 Additional Indemnification Obligations of Cadence. Without limiting its obligations under Section 7.1, Cadence further agrees to indemnify, defend and hold harmless BMS, its Affiliated Companies and their respective directors, officers, employees, and agents and their respective successors, heirs and assigns (the "**BMS Indemnitees**"), against any Losses payable by the BMS Indemnitees, or any one of them, to any Third Party arising out of or resulting from (or alleged to arise out of or result from) (A) any breach of the Pharmatop License Agreement (other than a breach by Pharmatop) resulting from (i) any failure of Cadence or any of its Affiliated Companies, sublicensees, contractors or agents to perform, observe or comply with any provision of the Pharmatop License Agreement that relates to the Territory (except to the extent that a breach by BMS of its obligations under this Agreement or the Pharmatop License Agreement or any other act or omission by BMS prevents such performance, observance or compliance by Cadence or its Affiliated Companies, sublicensees, contractors or agents) or (ii) the exercise by Cadence or its Affiliated Companies, sublicensees, contractors or agents of the BMS Rights sublicensed to Cadence under this Agreement, (B) the development of Products by or on behalf of Cadence or any of its Affiliated Companies or sublicensees for the Territory or any other jurisdiction as to which Cadence or any of its Affiliated Companies has or may acquire rights with respect to Products, (C) the marketing, promotion, sale, use, consumption of, or exposure to, Products in the Territory or any such other jurisdiction, (D) the manufacturing (other than pursuant to the Clinical Supply Agreement) of Products for sale, use or consumption in the Territory or any such other jurisdiction, (E) the use by Cadence and its Affiliated Companies or any of its or their sublicensees, contractors or agents of BMS's Product Data, Other Product Data or Regulatory Filings or other data, information, records, filings or Confidential Information that BMS provides to Cadence pursuant to this Agreement or (F) any failure by Cadence and its Affiliated Companies and its and their sublicensees to comply with Applicable Law in connection with the development and commercialization (including the manufacture, marketing, promotion and sale) of the Products hereunder.

7.3 Additional Indemnification Obligations of BMS. Without limiting its obligations under Section 7.1, BMS further agrees to indemnify, defend and hold harmless Cadence, its Affiliated Companies and their respective directors, officers, employees, and agents and their respective successors, heirs and assigns (the "**Cadence Indemnitees**"), against any Losses payable by the Cadence Indemnitees, or any one of them, to any Third Party arising out of or resulting from (or alleged to arise out of or result from) (A) any breach of the Pharmatop License Agreement (other than a breach by Pharmatop or a failure by Cadence or any of Cadence's Affiliated Companies or any of their sublicensees, contractors or agents to perform, observe or comply with any of the provisions of the Pharmatop License Agreement, except to the extent that a breach by BMS of its obligations under this Agreement or the Pharmatop License Agreement or any other act or omission by BMS prevents such performance, observance or compliance by Cadence or its Affiliated Companies, sublicensees, contractors or agents) resulting from (i) any failure of BMS or any of its Affiliated Companies or its or their sublicensees (other than Cadence), contractors or agents to perform, observe or comply with any provision of the Pharmatop License Agreement

that relates to the Territory (except to the extent such failure results from any act or omission of Cadence and its Affiliated Companies, sublicensees contractors and agents to perform, observe or comply with any provision of the Pharmatop License Agreement that relates to the Territory or with this Agreement), (B) any breach of the Pharmatop License Agreement by BMS or any of its Affiliated Companies or its or their sublicensees (other than Cadence), contractors or agents that arises out of activities of BMS or any of its Affiliated Companies or its or their sublicensees (other than Cadence) outside the Territory, (C) the exploitation (including the import, use, manufacture, sale and offer for sale) of the Products by BMS or any of its Affiliated Companies or its or their sublicensees (other than Cadence), contractors or agents outside the Territory or inside the Territory pursuant to the rights retained by BMS under this Agreement, (D) the exploitation (including the import, use, manufacture, sale and offer for sale) of the Products by BMS or any of its Affiliated Companies or its or their sublicensees (other than Cadence), contractors or agents inside the Territory prior to the Effective Date or (E) the use by BMS and its Affiliated Companies or any of its or their sublicensees (other than Cadence), contractors or agents of Cadence's Product Data, Other Product Data or Regulatory Filings or other data, information, records, filings or Confidential Information that Cadence provides to BMS pursuant to this Agreement.

7.4 Conditions to Indemnification; Third Party Claims. Subject to Article 12 of the Pharmatop License Agreement, to the extent applicable, a Party seeking indemnification under this Article VII (the "**Indemnified Party**") with respect to any claim brought by any Third Party shall give prompt notice of the claim to the Indemnifying Party and, provided that the Indemnifying Party is not contesting the indemnity obligation, shall permit the Indemnifying Party to control and assume the defense of any litigation relating to such claim and disposition of any such claim unless the Indemnifying Party is also a party (or likely to be named a party) to the proceeding in which such claim is made and the Indemnified Party gives notice to the Indemnifying Party that it may have defenses to such claim or proceeding that are in conflict with the interests of the Indemnifying Party, in which case the Indemnifying Party shall not be so entitled to assume the defense of the case. If the Indemnifying Party does assume the defense of any claim or proceeding, it (i) shall act diligently and in good faith with respect to all matters relating to the settlement or disposition of any claim as the settlement or disposition relates to Parties being indemnified under this Article VII, (ii) shall cause such defense to be conducted by counsel reasonably acceptable to the Indemnified Party and (iii) shall not settle or otherwise resolve any claim without prior notice to the Indemnified Party and the consent of the Indemnified Party if such settlement involves anything other than the payment of money by the Indemnifying Party. The Indemnified Party shall cooperate with the Indemnifying Party in its defense of any claim for which the Indemnifying Party has assumed the defense in accordance with this Section 7.4, and shall have the right (at its own expense) to be present in person or through counsel at all legal proceedings giving rise to the right of indemnification.

7.5 Insurance. Cadence shall, beginning with the initiation of its first clinical trial for a Product, maintain at all times thereafter during the term of this Agreement, and until the later of (i) [***] ([***])[***] after termination or expiration of this Agreement or (ii) the date that all statutes of limitation covering claims or suits that may be brought for personal injury based on

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the sale or use of a Product have expired in all countries in the Territory, comprehensive general liability insurance from a recognized, creditworthy insurance company having an Excellent rating (A rating or above by A.M. Best), a financial performance rating of at least Strong (A rating or above by A.M. Best) and an A.M. Best Class Size of at least VIII, on a claims-made basis, with endorsements for contractual liability and product liability, and with coverage limits of not less than [***] ([***]) per occurrence and, [***], [***]([***])in the aggregate or, [***], [***]([***]) in the aggregate and which shall name BMS as an "additional insured" thereunder. The minimum level of insurance set forth herein shall not be construed to create a limit on Cadence's liability hereunder. Within [***]([***])[***] following written request from BMS, Cadence shall furnish to BMS a certificate of insurance evidencing such coverage as of the date. Cadence shall provide BMS with not less than [***]([***]) days' prior written notice of any modification or cancellation of coverage by Cadence and shall provide written notice to BMS not less than [***]([***])[***] after receiving notice from its insurer (or insurance broker) of any modification or cancellation of coverage by the insurer. In the case of a modification or cancellation of such coverage, Cadence shall promptly provide BMS with a new certificate of insurance evidencing that Cadence's coverage meets the requirements in the first sentence of this Section. The collection by BMS of any proceeds under any such insurance policy shall not affect BMS's right to obtain indemnification or other remedies under this Agreement, except to the extent that the collection of such proceeds reduces BMS's Losses, and the assertion by BMS of a claim under any such insurance policy shall not impair BMS's right to assert a claim against Cadence or any other Person for indemnification or otherwise pursuant to this Agreement.

7.6 Arbitration. Except as set forth in Section 7.7, any controversy or claim arising out of or relating to this Agreement or the validity, inducement or breach thereof (a "**Dispute**") shall be settled by binding arbitration as follows:

(a) A Party may submit such Dispute to arbitration by notifying the other Party, in writing, of such Dispute and demanding arbitration of such Dispute in accordance with this Section 7.6. Any such Dispute shall, except as provided herein, be finally resolved under the Rules of Arbitration of the International Chamber of Commerce (the "**ICC**") before an arbitration tribunal of three (3) arbitrators appointed and ruling in accordance with such Rules of Arbitration (the "**Rules**"), except where the Rules conflict with this Section 7.6, in which case this Section shall control. Each of the arbitrators shall be an attorney who has at least fifteen (15) years of experience with a law firm or corporate law department of over twenty-five (25) lawyers or a judge of a court of general jurisdiction. The governing law set forth in Section 9.8 shall govern any such proceedings, unless otherwise required by Section 7.7. The language of the arbitration shall be English.

(b) Within thirty (30) days after the designation of the arbitrator, the arbitrator and the Parties shall meet, and each Party shall provide to the arbitrator a written summary of all disputed issues, such Party's position on such disputed issues and such Party's proposed ruling on the merits of each such issue.

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(c) The arbitrator shall set a date for a hearing, which shall be no later than thirty (30) days after the submission of written proposals pursuant to Section 7.6(b), for the presentation of evidence and legal argument concerning each of the issues identified by the Parties. The Parties shall have the right to be represented by counsel.

(d) The arbitrator shall use his or her best efforts to rule on each disputed issue within thirty (30) days after completion of the hearing described in Section 7.6(c). The determination of the arbitrator as to the resolution of any dispute shall be binding and conclusive upon all Parties. All rulings of the arbitrator shall be in writing and shall be delivered to the Parties except to the extent that the Rules provide otherwise. Nothing contained herein shall be construed to permit the arbitrator to award punitive, exemplary or any similar damages.

(e) [***].

(f) Any arbitration pursuant to this Section 7.6 shall be conducted in Chicago, Illinois or, if such arbitration includes Pharmatop as contemplated by Section 7.7, Paris, France. Any arbitration award may be entered in and enforced by any court with jurisdiction.

(g) The Parties acknowledge and agree that the breach by any Party of the provision of this Agreement related to the protection of trade secrets or confidentiality would not be fully compensable by money damages and would result in irreparable harm to the other Party. Notwithstanding anything in this Article 7, each Party shall have the right to seek injunctive or other equitable relief from a court of competent jurisdiction that may be necessary to avoid irreparable harm, maintain the status quo or preserve the subject matter of the arbitration, including any breach or threatened breach of Section 5.1 or 5.2.

7.7 Pharmatop Arbitration. In the event of any controversy or claim between Pharmatop and BMS relating to or affecting the rights thereunder with respect to the Territory arising out of or relating to the Pharmatop License Agreement or the performance by Cadence of its obligations under this Agreement or the Pharmatop License Agreement that is the subject of an arbitration proceeding pursuant to Section 13.1 of the Pharmatop License Agreement, Cadence agrees that, if requested by BMS (or if requested by Cadence to the extent such proceeding relates to the Territory) and to the extent permitted by the Pharmatop License Agreement or by Pharmatop or the arbitrators, (i) Cadence will (if requested by BMS) join in and participate in such proceeding; (ii) if requested by Cadence with respect to any such proceeding that relates to the Territory, BMS shall use reasonable efforts to seek to include Cadence in such proceeding, and (iii) if Cadence participates or is included in such proceeding, any controversy or claim between BMS and Cadence relating thereto shall be settled by arbitration in such proceeding to the extent possible rather than in a proceeding under Section 7.6. In the event of any controversy or claim between Pharmatop and Cadence arising out of or relating to the Pharmatop License Agreement or the performance by Cadence of its obligations under this Agreement or the Pharmatop License Agreement that is the subject of an arbitration proceeding

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pursuant to Section 13.1 of the Pharmatop License Agreement or otherwise, BMS shall be entitled to participate in such proceeding, and to the extent permitted by the Pharmatop License Agreement or by Pharmatop or the arbitrators, any controversy or claim between BMS and Cadence relating thereto shall be settled by arbitration in such proceeding. In the event BMS reasonably believes that the participation of Pharmatop in any arbitration proceeding between BMS and Cadence pursuant to Section 7.6 would facilitate the orderly resolution of such Dispute, BMS shall be entitled to have Pharmatop participate in such arbitration proceeding.

ARTICLE VIII – TERM AND TERMINATION

8.1 Term. This Agreement shall commence as of the Effective Date and, unless sooner terminated in accordance with the terms hereof or by mutual written consent, shall expire in each country in the Territory, on a country-by-country basis, upon the expiration of both the Royalty Term and BMS Patent Royalty Term in such country.

8.2 Automatic Termination. This Agreement shall terminate automatically in the event of the termination of the Pharmatop License Agreement. In the event of a partial termination of the Pharmatop License Agreement, this Agreement shall terminate in respect of the rights so terminated under the Pharmatop License Agreement.

8.3 Termination by Either Party. Either Party shall have the right to terminate this Agreement on a country-by-country basis (except that any termination with respect to the United States shall also apply to Canada), at its sole discretion, upon delivery of written notice to the other Party, upon the occurrence of any of the following:

(a) the Bankruptcy of the other Party; and

(b) a material breach of this Agreement by the other Party with respect to any country in the Territory (or, in the case of any covenant that is qualified by materiality, any breach) that is not cured within the Specified Number of Days (as defined below) after written notice of such breach is given; *provided* that such additional cure period shall not apply to any breach of Section 5.5; and *provided, further* that the Parties acknowledge that a series of breaches which are immaterial individually may, when considered in the aggregate, result in a material breach and that such opportunity to cure shall run in respect of each such immaterial breach from the date that the Party seeking to terminate has given notice of such material breach.

As used herein "**Specified Number of Days**" means ninety (90) days (or 180 days in the case of a termination based on the second proviso of the first paragraph of this Section 8.3(b)), except that:

(i) if [***][1] have not occurred:

(A) [***],

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(B) [***][2] and

(C) [***];

(ii) if the [***] has occurred, the Specified Number of Days shall be [***]([***])[***]; and

(iii) if the [***] has occurred, the Specified Number of Days shall be [***]([***])[***].

8.4 Termination by BMS. BMS shall have the right to terminate this Agreement, at BMS's sole discretion, upon delivery of written notice to Cadence, upon the occurrence of any of the following:

(a) the failure of Cadence or any of its Affiliated Companies, sublicensees, contractors or agents to perform, observe or comply with any provision of the Pharmatop License Agreement that relates to the Territory, the BMS Rights or the exercise of the rights sublicensed or licensed to Cadence under this Agreement or any other act or omission of Cadence or any of its Affiliated Companies or any of their sublicensees, contractors or agents that results in a material breach of the Pharmatop License Agreement or would permit Pharmatop to terminate, or exercise a right of rescission with respect to, the Pharmatop License Agreement (except to the extent that a breach by BMS of its obligations under this Agreement or any other act or omission by BMS prevents such performance, observance or compliance by Cadence or its Affiliated Companies, sublicensees, contractors or agents);

(b) the failure of Cadence to deliver to BMS any of the reports, statements or other information required to be delivered to BMS pursuant to Section 3.2(e) which failure is not cured within the ten (10) Business Day period provided for in such Section.

8.5 Termination by Cadence.

(a) Upon the occurrence of any of the following, Cadence shall have the right to terminate this Agreement on a country-by-country basis (except that, unless otherwise specifically provided herein, any termination with respect to the United States shall also apply to Canada), at Cadence's sole discretion, upon delivery prior written notice to BMS of not less than (A) thirty (30) days' more notice than is required under the Pharmatop License Agreement or (B) ninety (90) days if no notice period is specified under the Pharmatop License Agreement:

(i) the occurrence after the Effective Date of an event that relates to the Territory and would entitle BMS to terminate the Pharmatop License Agreement pursuant to Section 5.3, 6.2(a), 6.2(b), 6.3(a) or 6.3(b) thereof, whether or not BMS exercises such right of termination; *provided*, *however*, that if such right of termination relates only to a specific country in the Territory then the right of Cadence to terminate this Agreement shall apply only to such country; and *provided*, further, that if any such

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event would permit a reduction in the royalty payable to Pharmatop under the Pharmatop License Agreement and Cadence elects to pay such reduced royalty, then Cadence shall not have any right to terminate this Agreement as a result of such event; or

(ii) a failure by Pharmatop to perform any of its material obligations under the Pharmatop License Agreement with respect to the Territory that would permit BMS to terminate the Pharmatop License Agreement with respect to the Territory and is not cured within any cure period applicable under the Pharmatop License Agreement; *provided* that if such right of termination relates only to a specific country in the Territory then the right of Cadence to terminate this Agreement shall apply only to such country.

(b) If the [***][3] Date occurs, Cadence may terminate this Agreement upon not less than ninety (90) days' prior written notice to BMS.

8.6 Scope of Termination. Except as otherwise provided in this Agreement, any termination of this Agreement pursuant to this Article 8 shall be as to all countries in the Territory and all Products, except that in the event of a termination at the election of a Party the terminating Party may elect by written notice to the other Party to have such termination apply in respect to one (but not both) of the countries in the Territory, as designated by such Party in such notice, in which case the rights and obligations of the Parties as to the remaining country of the Territory shall be unaffected by such termination as to the non-terminated country; *provided*, *however*, that, except for a termination pursuant to Section 8.5(ii), any termination with respect to the United States shall also apply to Canada.

8.7 Effect of Termination. Upon termination of this Agreement with respect to any country or all countries in the Territory:

(a) All rights and licenses granted to Cadence in Article 2 and Sections 3.5, 3.6 and 3.7 shall terminate with respect to each terminated country and all rights of Cadence under the BMS Rights and the Pharmatop License Agreement, the BMS Patents and BMS Know-How shall revert to BMS, and Cadence shall cease all use of the BMS Rights, BMS Patents and BMS Know-How with respect to each terminated country, *provided* that, to the extent permitted by the Pharmatop License Agreement and unless this Agreement is terminated as a result of a breach or failure to comply by Cadence or any of its Affiliated Companies or their sublicensees, contractors or agents to comply with the terms and conditions of this Agreement or the Pharmatop License Agreement, Cadence shall have the right for one hundred eighty (180) days after such termination to sell off any Products already manufactured or ordered pursuant to non-cancelable purchase orders. All Net Sales of such sold off Products shall be subject to the Royalty payments provided for in Article IV.

(b) Cadence shall assign to BMS or BMS's designee free of charge all INDs, NDAs and other Regulatory Filings, Product Data, Other Product Data and Approvals owned or Controlled by Cadence relating to the Products (and all of Cadence's right, title and interest therein and thereto) in each terminated country, and Cadence shall provide to BMS or BMS's

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designee free of charge one (1) copy of all documents and filings contained in or referenced in any such filings, together with the raw and summarized data for any preclinical and clinical studies of the Products. Cadence shall take such actions with the applicable Drug Regulatory Authorities in each terminated country to transfer ownership and control of such Regulatory Filings to BMS not later than five (5) days after such termination.

(c) Cadence shall transfer to BMS or BMS's designee free of charge all Product Data, Other Product Data and other data generated in connection with any preclinical studies, clinical trials and other studies conducted by or on behalf of Cadence and its Affiliated Companies relating to the Products and within forty-five (45) days after such termination shall transfer to BMS or BMS's designee copies of all Regulatory Filings with Drug Regulatory Authorities in the terminated countries with respect to Products, rendered PDF copies of the applicable clinical study reports (and the appendices, tables, listings and graphs therein), the SAS data sets containing the raw data from the applicable clinical studies. If Cadence maintains such Product Data, Other Product Data and other data in electronic form, Cadence shall provide it to BMS or BMS's designee in electronic form, but Cadence shall have no obligation to reformat or otherwise alter or modify any materials or to create or recreate any such materials in electronic form in order to provide them to BMS.

(d) Cadence shall disclose to BMS in writing its manufacturing patents, processes, techniques and trade secrets for making the Products and BMS shall automatically have a fully paid up, exclusive, perpetual, worldwide, transferable, sublicensable right and license under know-how and patents Controlled by Cadence and its Affiliated Companies relating to any composition, formulation, method of use or manufacture of any Product solely for using, importing, making, having made, selling and offering for sale Products outside the Territory and in each terminated country.

(e) Cadence shall assign (or, if applicable, cause its Affiliated Company to assign) to BMS or BMS's designee free of charge all of Cadence's (and such Affiliated Companies') right, title and interest in and to any registered or unregistered trademark, trademark application, trade name or internet domain name that is specific to a Product in each terminated country (it being understood that the foregoing shall not include any trademarks or trade names that contain the name "Cadence").

(f) Cadence shall assign to BMS or BMS's designee free of charge all of Cadence's right, title and interest in any inventions owned by it pursuant to Section 2.7 (and any patent applications filed thereon and patents issued thereon) pertaining to the composition of matter or method of use or utility of any Product in each terminated country

(g) BMS shall be entitled to retain all amounts previously paid to BMS by Cadence under this Agreement.

(h) Neither Party shall be relieved of any obligation that accrued prior to the effective date of such termination or expiration, including any obligation of Cadence with respect to any amount due or payable to BMS that accrued or that arises out of acts or events occurring prior to the effective date of termination.

(i) Unless such termination was as a result of a breach of this Agreement by Cadence or any of its Affiliated Companies, sublicensees, agents or contractors or a failure of Cadence or any of its Affiliated Companies, sublicensees, agents or contractors to comply with or observe the terms of the Pharmatop License Agreement or a termination by Cadence pursuant to Section 8.5, Cadence shall have, unless the License has been terminated pursuant to Section 2.17(b), a fully paid up, perpetual, noncancelable and non-exclusive license (A) under the BMS Know-How, with the right to sublicense as provided in Section 2.4, to make and have made the Products anywhere in the world solely for use and sale within the Territory, (B) under the BMS Patents, with the right to sublicense as provided in Section 2.4, to import, use, sell and offer for sale Products in the Territory and (C) under the BMS Patents, with the right to sublicense as provided in Section 2.4, to make and have made the Products in the Territory solely for use and sale within the Territory; *provided*, *however*, that the licenses granted in clauses (B) and (C) of this paragraph shall not grant any right to the composition of matter of any Other Chemical Entity, or the right to make or have made any Other Chemical Entity or to any use not claimed by the BMS Patents.

(j) Notwithstanding the foregoing, in the event this Agreement terminates as the result of the termination of the Pharmatop License Agreement as the result of a material breach of that agreement by BMS (that is not the result of a breach of this Agreement by Cadence or any of its Affiliated Companies, sublicensees, agents or contractors or a failure of Cadence or any of its Affiliated Companies, sublicensees, agents or contractors to comply with or observe the terms of the Pharmatop License Agreement), the assets to be transferred and information to be disclosed to BMS or its designee pursuant to Sections 8.7(b), (c), (d), (e) and (f) shall not be transferred or disclosed to BMS or its designee but shall, at on the written request of BMS, be transferred to Pharmatop; provided, however, that (1) BMS shall have the right upon its request to have such assets transferred, and such information disclosed, to it or its designee on terms to be agreed by BMS and Cadence and (2) if Cadence obtains any damages or other remedy in respect of its cost of producing or obtaining such assets and information, such assets shall be transferred, and such information shall be disclosed, to BMS or its designee.

(k) The Parties hereto recognize that the assets to be assigned and transferred to BMS or its designee (or to Pharmatop or its designee) pursuant to this Section 8.7 are unique and are not available on the open market and that any breach of the terms of this Section 8.7 would give rise to irreparable harm for which money damages would not be an adequate remedy. Accordingly, the Parties agree that, in addition to all other remedies available to it, BMS shall be entitled to enforce the terms of this Section 8.7 by a decree of specific performance, without the necessity of proving the inadequacy as a remedy of money damages. In the event of failure to obtain such assignment, Cadence hereby consents and grants to BMS and its designee the right to access and reference (without any further action required on the part of Cadence, whose authorization to file this consent with any Regulatory Authority is hereby granted) any and all such Regulatory Filings, Product Data, Other Product Data, information and Approvals for any regulatory or other use or purpose in each terminated country.

8.8 Transition. Upon termination of this Agreement with respect to any country or all countries in the Territory, all actions then being controlled or undertaken by Cadence with respect to the applicable terminated countries in the Territory shall revert to the control of BMS or its designee, and Cadence and BMS (or BMS's designee) shall cooperate and use

commercially reasonable efforts to effect an orderly transfer and transition of such activities to BMS or its designee, and Cadence shall take any reasonable action requested by BMS to facilitate such transition. BMS and Cadence shall endeavor to effect such transition as promptly as reasonably practicable.

8.9 Survival. The following provisions shall survive termination or expiration of this Agreement, as well as any other provisions which by their nature are intended to survive termination or expiration: Section 2.8(c), BMS's rights of use and reference set forth in Section 2.9, Section 2.15, Section 4.8, Section 5.1, Section 5.2, Section 5.3, Section 6.6, Article 7 (other than Section 7.5), Article 8 and Article 9.

8.10 Bankruptcy. The Parties agree that in the event a Party becomes a debtor under Title 11 of the U.S. Code ("**Title 11**"), this Agreement shall be deemed to be, for purposes of Section 365(n) of Title 11, a license to rights to "intellectual property" as defined therein. Each Party as a licensee hereunder shall have the rights and elections as specified in Title 11. Any agreements supplemental hereto shall be deemed to be "agreements supplementary to" this Agreement for purposes of Section 365(n) of Title 11.

ARTICLE IX – MISCELLANEOUS

9.1 Amendments. This Agreement may be amended only by a writing signed by each of the Parties, and any such amendment will be effective only to the extent specifically set forth in such writing.

9.2 Counterparts; Facsimile Execution. This Agreement may be executed in any number of counterparts, and by each of the Parties on separate counterparts, each of which, when so executed, will be deemed an original, but all of which will constitute but one and the same instrument. Delivery of an executed counterpart of this Agreement by facsimile will be equally as effective as delivery of a manually executed counterpart of this Agreement.

9.3 Cumulative Remedies. The rights and remedies of the Parties under this Agreement are cumulative and not exclusive of any rights or remedies which the Parties would otherwise have. No single or partial exercise of any such right or remedy by a Party, and no discontinuance of steps to enforce any such right or remedy, will preclude any further exercise thereof or of any other right or remedy of such Party.

9.4 Entire Agreement. This Agreement and the Clinical Supply Agreement contain the entire agreement of the Parties with respect to the transactions contemplated hereby and supersedes all prior written and oral agreements, and all contemporaneous oral agreements, relating to such transactions.

9.5 Schedules. The Schedules attached to in this Agreement are an integral part hereof and all references to this Agreement include such Schedules.

9.6 Force Majeure.

(a) *General*. No Party shall be liable for any failure to perform its obligations under this Agreement (other than obligations to make payments of money) to the extent such performance has been delayed, interfered with or prevented by an event of Force Majeure, except that Pharmatop shall not be excused from performance of any obligation under the Pharmatop License Agreement assumed by it unless such performance is excused under such agreement

(b) *Definition*. As used in this Section, "**Force Majeure**" means any circumstances whatsoever which are not within the reasonable control of the Party affected thereby, including an act of God, an act of any Governmental Entity (including any Drug Regulatory Authority), war, insurrection, riot, strike or labor dispute, shortage of materials, fire, explosion, flood, government requisition or allocation, breakdown of or damage to plant, equipment or facilities, interruption or delay in transportation, fuel supplies or electrical power, embargo, boycott, order or act of civil or military authority. The Party who declares an event of Force Majeure shall give prompt notice to the other Party of such declaration.

(c) *Duty to Mitigate*. If the performance of any obligation has been delayed, interfered with or prevented by an event of Force Majeure, then the Party affected by such event will take such actions as are reasonably available to remove the event of Force Majeure or to mitigate the effect of such occurrence, except that labor disputes will be settled at the sole discretion of the Party affected thereby.

(d) *Suspension of Certain Obligations*. If an event of Force Majeure occurs, the obligations of the Parties under this Agreement (other than obligations to make payments of money) will be suspended during, but not longer than, the continuance of the event of Force Majeure.

9.7 Assignment.

(a) BMS may, without Cadence's consent, assign or transfer all of its rights and obligations hereunder, in connection with any transfer of all of BMS's rights under the Pharmatop License Agreement with respect to the Territory to any Affiliated Company of BMS or to any Third Party (including a successor in interest); *provided*, that such assignee or transferee agrees in a writing provided to Cadence to be bound by the terms of this Agreement.

(b) Upon [***] ([***])[***] advance written notice to BMS and subject to BMS's (and, if required by the Pharmatop License Agreement, Pharmatop's) prior written approval, which approval may be withheld or granted by BMS in its sole discretion (and by Pharmatop in accordance with the Pharmatop License Agreement), Cadence may assign or transfer all of its rights and obligations hereunder to a Third Party [***]; *provided*, that such Third Party shall have agreed prior to such assignment or transfer to be bound by the terms of this Agreement in a writing provided to BMS and Pharmatop. Cadence may assign or transfer all of its rights and obligations hereunder without such consent to an Affiliated Company of Cadence (so long as such assignment or transfer includes all Approvals in the Territory, all

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manufacturing assets relating to this Agreement, and all rights and obligations under this Agreement); *provided*, that such Affiliated Company shall have agreed prior to such assignment or transfer to be bound by the terms of this Agreement in a writing provided to BMS; and *provided, further,* that all such rights and obligations automatically revert to Cadence free of any Liens in the event such company ceases to be an Affiliated Company of Cadence. For the purposes of clarification, transfers to a successor in interest by reason of merger, consolidation or sale of substantially all of the assets of Cadence shall be governed by Section 9.7(c).

(c) Cadence may assign or transfer all of its rights and obligations hereunder without such consent to a successor in interest by reason of merger, consolidation or sale of substantially all of the assets of Cadence (and so long as such assignment or transfer includes, without limitation, all Approvals in the Territory, all manufacturing assets relating to this Agreement, and all rights and obligations under this Agreement); *provided*, that such successor in interest shall have agreed prior to such assignment or transfer to be bound by the terms of this Agreement in a writing provided to BMS.

(d) Subject to the foregoing, this Agreement shall inure to the benefit of and be binding on the Parties' successors and permitted assigns.

(e) Any assignment or transfer in violation of the foregoing shall be null and void and wholly invalid, the assignee or transferee in any such assignment or transfer shall acquire no rights whatsoever, and the non-assigning non-transferring Party shall not be required to recognize, such assignment or transfer.

(f) No assignment by any Party of any of its rights or obligations under this Agreement shall relieve such Party from any of its obligations hereunder and the assignor shall remain jointly and severally liable with the assignee for the performance of the assigned obligations.

9.8 Governing Law. This Agreement is a contract under the laws of the State of New York and for all purposes will be governed by, and construed and enforced in accordance with, the laws of said State, without giving effect to any internal conflict of law rules.

9.9 Headings. All titles and headings in this Agreement are intended solely for convenience of reference and will in no way limit or otherwise affect the interpretation of any of the provisions hereof.

9.10 Notices. All notices, consents, requests, demands and other communications required or permitted under this Agreement: (a) will be in writing; (b) will be sent by messenger, certified or registered U.S. mail, a reliable express delivery service or facsimile (with a copy sent by one of the foregoing means), charges prepaid as applicable, to the appropriate address(es) or fax number(s) set forth below; and (c) will be deemed to have been given on the date of receipt by the addressee (or, if the date of receipt is not a Business Day, on the first Business Day after the date of receipt), as evidenced by (i) a receipt executed by the addressee (or a responsible person in his or her office), the records of the Person delivering such communication or a notice to the effect that such addressee refused to claim or accept such communication, if sent by messenger, U.S. mail or express delivery service, or (ii) a receipt generated by the sender's fax

machine showing that such communication was sent to the appropriate number on a specified date, if sent by facsimile. All such communications will be sent to the following addresses or numbers, or to such other addresses or numbers as any Party may inform the others by giving five (5) Business Days' prior notice:

If to Cadence:

Cadence Pharmaceuticals, Inc.
12730 High Bluff Drive, Suite 410
San Diego, CA 92130
Attn: President & CEO
Fax No.: (858) 436-1401

With copies to:

Cadence Pharmaceuticals, Inc.
12730 High Bluff Drive, Suite 410
San Diego, CA 92130
Attn: Vice President, Business Development
Fax No.: (858) 436-1401

If to BMS:

Bristol-Myers Squibb Company
Route 206 & Province Line Road
Princeton, NJ 08540
Attn: Senior Vice President –Corporate Business Development
Fax No.: (609) 252-7128

With a copy to:

Bristol-Myers Squibb Company
Route 206 & Province Line Road
Princeton, NJ 08540
Attn: Vice President and SeniorCounsel, Licensing and Business Development
Fax No.: (609) 252-4232

9.11 Severability. Any provision of this Agreement which is prohibited or unenforceable in any jurisdiction will, as to such jurisdiction, be ineffective to the extent of such prohibition or unenforceability without invalidating the remaining portions hereof or affecting the validity or enforceability of such provision in any other jurisdiction.

9.12 No Third Party Beneficiaries. This Agreement is made solely for the benefit of the Parties hereto and their successors and permitted assigns, and, except as specifically set forth in this Agreement, no other Person has, or is entitled to enforce, any rights, benefits or obligations under this Agreement. Nothing set forth in this Agreement shall diminish, affect or impair the rights of Pharmatop under the Pharmatop License Agreement.

9.13 Waivers. The due performance or observance by the Parties of their respective obligations under this Agreement will not be waived, and the rights and remedies of the Parties hereunder will not be affected, by any course of dealing or performance or by any delay or failure of any Party in exercising any such right or remedy. The due performance or observance by a Party of any of its obligations under this Agreement may be waived only by a writing signed by the Party against whom enforcement of such waiver is sought, and any such waiver will be effective only to the extent specifically set forth in such writing.

9.14 Documentary Conventions. As used in this Agreement, (a) whenever the context may require, any pronoun shall include the corresponding masculine, feminine and neuter forms; (b) the words "include," "includes" and "including" shall be deemed to be followed by the phrase "without limitation;" (c) the terms "hereof," "herein," "hereby," "hereunder" and

derivative or similar words refer to this entire Agreement and (d) unless otherwise specified, the terms “Section” or “Exhibit” or “Schedule” refer to the specified Section, Exhibit or Schedule of or to this Agreement. All references to generally accepted accounting principles shall refer to United States generally accepted accounting principles, and all accounting terms not defined in any agreement or instrument shall have the meanings determined by United States generally accepted accounting principles as in effect from time to time. References to a Person are also to its permitted successors and permitted assigns. Unless otherwise expressly provided herein, any reference to a statute, instrument or other agreement in this Agreement means such statute, instrument or agreement as it may from time to time be amended, modified or supplemented, including (in the case of agreements or instruments) by waiver or consent and (in the case of statutes) by succession of comparable successor statutes.

9.15. Consents and Approvals. All consents or approvals of the Parties contemplated hereunder shall not be unreasonably withheld, delayed or conditioned unless expressly stated as otherwise.

9.16. Absence of Presumption. Each of the Parties acknowledges and agrees that this Agreement has been diligently reviewed by and negotiated by and between them, that in such negotiations each of them has been represented by competent counsel and that the final agreement contained herein, including the language whereby it has been expressed, represents the joint efforts of the Parties hereto and their counsel. Accordingly, in interpreting this Agreement or any provision hereof, no presumption shall apply against any Party hereto as being responsible for the wording or drafting of this Agreement or any such provision, and ambiguities, if any, in this Agreement shall not be construed against any Party, irrespective of which Party may be deemed to have authored the ambiguous provision.

9.17. Relationship of Parties. Nothing in this Agreement shall be construed to (i) create or imply a general partnership or joint venture between the Parties, (ii) make either Party the agent of the other for any purpose, (iii) give either Party the right to bind the other, (iv) create any duties or obligations between the Parties except as expressly set forth herein (other than the implied obligation of good faith), or (v) grant any direct or implied licenses or any other right other than as expressly set forth herein.

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SIGNATURE PAGE TO IV APAP AGREEMENT

IN WITNESS WHEREOF, the Parties have duly executed this Agreement as of the Execution Date.

BRISTOL-MYERS SQUIBB COMPANY

By: /s/ Tamar Howson
Name: Tamar Howson
Title: SVP, Corporate & Business Development

CADENCE PHARMACEUTICALS, INC.

By: /s/ Theodore R. Schroeder
Name: Theodore R. Schroeder
Title: President and CEO

SCHEDULE 1.1

BMS PATENTS

US Patent Nos. 6,593,331 and 6,511,982

Any US Patent that issues pursuant to [***]

and any continuations, continuations-in-part, divisions, reissues, re-examinations, extensions and renewals of any of the foregoing.

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

SCHEDULE 6.3(a)

PHARMATOP PATENTS

U.S. Patent 6,992,218

Canadian Patent (application) 2 415 403

U.S. Patent 6,028,222

Canadian Patent (application) 2 233 924

Exhibit 10.12

CERTAIN MATERIAL (INDICATED BY AN ASTERISK) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

PHARMATOP LICENSE AGREEMENT

License Agreement

This agreement (the "Agreement") is entered into as of the 23rd day of December, 2002 by and among SCR Pharmatop, a civil law partnership organized under the laws of France, having its head office's address at 10, Square St. Florentin, 78150 Le Chesnay, France, recorded with the Register of Commerce and Companies of Versailles under No. 407552702 ("PHARMATOP"), and Bristol-Myers Squibb Company, a corporation organized under the laws of the State of Delaware, USA, having its head office's address at 345 Park Avenue, New York, New York 10154 USA (referred to hereafter as "BMS").

W I T N E S S E T H

WHEREAS, PHARMATOP is the owner of certain patents, patent applications, and know-how relating to parenteral paracetamol formulations;

WHEREAS, PHARMATOP has entered into a license agreement dated April 12, 1999 on these patents, patent applications and know-how covering a certain number of countries in Europe, Africa, the Middle East and Asia with UPSA S.A., a subsidiary of BMS; and

WHEREAS, BMS wishes to acquire an exclusive license under such patents, patent applications, and know-how of PHARMATOP in the Territory (as defined below), and PHARMATOP is willing to grant BMS such an exclusive license under the terms and conditions of this Agreement.

NOW, THEREFORE, in consideration of the above premises and the covenants contained herein, the parties agree as follows:

Article 1—Definitions

The following definitions apply for the purposes of this Agreement:

1.1 The term "Affiliated Companies" shall mean any entity that directly or indirectly controls, is controlled by or is under common control with a Party to this Agreement, and

for such purpose “control” shall mean the power to direct or cause the direction of the management or the policies of the entity, whether through the ownership of voting securities, by contract or otherwise.

1.2 The term “Advertising and Promotion” means customary activities that are reasonably incident to the advertising and promotion of the Product in a country in the Territory (it being understood that Phase IV clinical studies are not part of Advertising and Promotion). The term “Advertising and Promotional Costs” means the out-of-pocket costs and expenses paid by BMS or its Affiliates to a Third Party (and a reasonable charge for internal copying expenses for promotional materials).

1.3 The term “Calendar Quarter” shall mean each of the periods of time from (a) January 1 through March 31; (b) April 1 through June 30; (c) July 1 through September 30; and (d) October 1 through December 31.

1.4 The term “Competing Product” means any one or more non-opiate analgesic parenterally-administered liquid solution products, in a stable and readily injectible form for the treatment of post-operative pain (but which can not be another Injectible APAP Product). For purposes of this Agreement, [***] shall be deemed an opiate product, the marketing of which shall not be restricted by this Agreement in any way.

1.5 The term “Derivative” of paracetamol means any compound whose chemical structure is derived from the chemical structure for paracetamol through structural modifications and/or chemical changes that retain those portions of paracetamol’s chemical structure that are known to contribute materially to the activity, specificity and selectivity of paracetamol.

1.6 The term “Diligent Efforts” means the carrying out of obligations or tasks in a sustained manner consistent with the efforts that BMS devotes to a product or a research, development or marketing project of similar market potential, profit potential or strategic value resulting from its own research efforts, based on conditions then prevailing.

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

1.7 The term “FDA” shall mean the U.S. FDA or corresponding administrative body in Canada, Mexico, or in any other country elsewhere in the Territory.

1.8 The term “Injectible APAP Product” means any parenterally administered dosage form of paracetamol or propacetamol, or any Derivative thereof, whether alone or in combination with one or more other drugs (as defined, as of the Effective Date, in Section 201 of the United States Federal Food, Drug and Cosmetic Act).

1.9 The term “Licensed Know-how” refers to precautions and procedures required to enable the manufacture of the liquid paracetamol solution, stable and ready for use by injection, that are owned by, controlled by, or licensed (with right to sublicense) to PHARMATOP at any time during the term of this Agreement, whether or not described in the Patent and in the Patent Applications, and that represent Confidential Information of PHARMATOP. The current said precautions and procedures are described in ***Appendix 5*** attached hereto, and made a part hereof.

1.10 The term “Licensed Patents” shall mean (a) the Patent, (b) the Patent Applications, (c) any other patents granted and patent applications applied for in the Territory relating to the manufacture, formulation, use or sale of the Products that are owned by, controlled by, or licensed to PHARMATOP during the term of this Agreement, and (d) any continuations, continuations-in-part, divisions, reissues, re-examinations, extensions, and renewals of any of the patent applications and patents listed in (a)-(c), and all patents which may be granted on any patent applications in (b)-(d) in the Territory.

1.11 The term “Licensed Rights” shall mean the Licensed Patents and the Licensed Know-How.

1.12 The term “Marketing Period” shall mean, for a given country in the Territory, the period running from the first day on which Products are sold in such country until the end of the Agreement with respect to such country.

1.13 The term “NDA” shall mean a new drug application submitted to the FDA seeking approval to manufacture, promote, market, distribute, or sell a Product in a country in the Territory.

1.14 The term “Net Sales” shall mean the total revenue invoiced by BMS, Affiliated Companies, or sub-licensees from the sale of a Product to independent Third Parties less the following amounts: (a) credits, allowances and rebates to, and chargebacks from the account of, such customers for spoiled, damaged, out-dated and returned Product; (b) trade discounts, cash discounts, quantity discounts, rebates and other price reduction programs, and other charge back payments; (c) sales, value-added and other similar taxes (including duties or other governmental charges levied on, absorbed or otherwise imposed on the sales of Products including, without limitation, governmental charges otherwise measured by the billing amount); (d) customs duties, surcharges and other governmental charges incurred in connection with the exportation or importation of the Product; and (e) bad debts on Product sales written off in accordance with generally accepted accounting principles, consistently applied. For the purposes of this definition, samples distributed by BMS, its Affiliates, or sub-licensees to their customers free of charge, and any Product used or provided for clinical or research purposes, shall not be included in Net Sales.

1.15 The term “Patent” shall mean US patent No. 6,028,222 issued on 22nd February 2000, a copy of which is attached hereto in ***Appendix 1*** as ***Exhibit A*** and made a part hereof, and any patent or supplementary protection certificate that PHARMATOP may obtain that depends on such patent or that is granted based on the Patent Applications.

1.16 The term “Patent Applications” shall mean (a) international patent application PCT/FR 97/01452, filed on 5th August 1997, a copy of which is attached hereto in ***Appendix 1*** as ***Exhibit B***, (b) international patent application PCT/FR01/01749, filed on 6th June 2001, a copy of which is attached hereto in ***Appendix 1*** as ***Exhibit C***, and (c) any other patent application that PHARMATOP may file that depends on a Patent or is based on claims contained in the patent applications specified above.

1.17 The term “Presentation” shall mean dosage and pharmaceutical form.

1.18 The term “Primary Detail Equivalent (PDE)” shall mean either [***] where

(a) a [***] means [***]; and

(b) a [***] means [***]; and

(c) a [***] means [***].

All PDEs shall be [***] and shall be reported by BMS in accordance with [***].

1.19 The term “Product” shall mean any parenterally administered dosage form containing paracetamol (or any Derivative thereof) alone or in combination with one or more drugs (as defined, as of the execution of this Agreement, in Section 201 of the United States Federal Food, Drug and Cosmetic Act), and for which the manufacture, use or sale in a country in the Territory (x) would otherwise infringe the Licensed Patents but for the license rights granted to BMS in Article 2 hereof and/or (y) incorporates or uses to any material extent any Know-How licensed to BMS under Article 2 hereof.

1.20 The term “Royalty Term” means, with respect to a given country in the Territory, the date commencing with the date of first commercial sale of a Product in such country, and terminating upon the later of (a) the date that is ten (10) years after such first commercial sale of a Product in such country, or (b) the date that the manufacture, use or sale of a Product in such country is no longer covered by any Valid Claim of a Licensed Patent licensed to BMS hereunder in such country.

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

1.21 The term “Target Product Profile” means the target Product profile attached as *Appendix 2* hereto.

1.22 The term “Tax” shall mean any tax, levy, impost, duty, charge, assessment or fee of any nature (including interest, penalties and additions thereto) that is imposed by any government or other taxing authority.

1.23 The term “Territory” shall mean the United States (including Puerto Rico and all U.S. possessions and territories), Canada and Mexico.

1.24 The term “Third Party” means any person or entity other than PHARMATOP, BMS, and their respective Affiliated Companies.

1.25 The term “U.S. FDA” shall mean the United States Food and Drug Administration and any successors thereto.

1.26 The term “Valid Claim” shall mean a claim in any unexpired issued patent that has not been held invalid or unenforceable by a non-appealed or unappealable decision by a court or other appropriate body of competent jurisdiction, and which is not admitted to be invalid through disclaimer, dedication to the public, and which has not been cancelled or abandoned in accordance with or as permitted by the terms of this Agreement or by mutual written agreement.

1.27 The term “Year” means, as to a given country in the Territory, the period beginning on the date of first commercial sale of Product in such country and ending on the first March 31, June 30, September 30 or December 31 that is closest (before or after) to the date that is twelve months following such first commercial sale, and each twelve (12) month period thereafter during the Royalty Term.

Additional defined terms are as follows:

Defined Term	Section in Which Defined
Affected Country	6.2(a)
Combination Product	7.2(b)
Confidential Information	10.1
Grace Period	4.6(c)
Guaranteed Payments	7.3
ICC	13.1
Improvement	8.1
Inspection	7.5(b)
Inventors	6.1(a)
NewPharm	6.1(a)
Registrational Information	3.1
Retained Sum	6.5(a)
Transaction	4.6(c)
Transaction Date	4.6(c)

Article 2—License

2.1 PHARMATOP hereby grants to BMS an exclusive, royalty-bearing license, with right to sublicense, under the Licensed Rights, to import, use, sell and offer for sale, make and have made, Products in the Territory. Furthermore, PHARMATOP also hereby grants to BMS the right to make and have made the Products outside the Territory for use within the Territory, subject to the consent of UPSA S.A. for the countries for which an exclusive manufacturing right has been granted by PHARMATOP to UPSA S.A. Except as may be otherwise agreed in writing by PHARMATOP in its sole discretion, the license granted to BMS shall only permit it to sell Products that are packaged, finished products ready for use, and the license shall not extend to any sales in bulk or of semi-finished products except to BMS sublicensee(s).

2.2 PHARMATOP does not promise or undertake to continue its research and development work in the field of the Licensed Rights. If, however, at its sole discretion, PHARMATOP does continue such work, it agrees to keep BMS fully informed on the results of its work, and if it makes any inventions or develops any Know-How relating to the Product, such inventions and know-how will be licensed to BMS pursuant to Section 2.1.

2.3 PHARMATOP shall not itself use the Licensed Rights in any way, directly or indirectly, including through licenses, for the manufacture, use, importation, and/or sale of Injectible APAP Products in the Territory. PHARMATOP covenants and warrants that it shall not develop, manufacture, or sell, or provide any assistance to any Third Party for the purpose of developing, manufacturing or selling, any Injectible APAP Products for use in a country in the Territory during the Marketing Period for such country. Notwithstanding the foregoing, PHARMATOP shall have the right to use, manufacture, sell and license the Licensed Rights in connection with other products other than Injectible APAP Products in the Territory or any other country where PHARMATOP has granted to BMS or one of its Affiliated Companies exclusive rights under any of its patents and know- how to sell such products in such country, and any such use shall not violate the exclusivity provisions of this Agreement in respect of the Licensed Rights granted to BMS hereunder; provided, however, that PHARMATOP shall give to BMS a right of first refusal to license the right to use, manufacture and sell such other products in the Territory under terms and conditions proposed by PHARMATOP.

2.4 PHARMATOP shall not assign or sell its rights under the Licensed Rights in the Territory to a Third Party without (a) requiring the assignee or purchaser to assume all of PHARMATOP's obligations under this Agreement in its own name and (b) obtaining BMS' prior consent in writing, which may not be unreasonably withheld so long as PHARMATOP agrees to be jointly and severally liable with the proposed assignee/purchaser for all obligations owed BMS under the terms of this Agreement.

2.5 BMS may assign its rights under this Agreement to a Third Party, in whole or in part, provided that (i) the assignee entity expressly assumes all of BMS' obligations under this Agreement, unconditionally and in writing, so that it becomes directly obligated towards PHARMATOP, (ii) BMS remains jointly obligated with the assignee entity for all of its obligations under this Agreement; and (iii) PHARMATOP has given its prior written consent to such assignment, which consent shall not be unreasonably withheld or delayed. BMS may also assign or otherwise transfer this Agreement and the license granted hereby to an Affiliated Company or successor in connection with a merger, consolidation, reorganization, or sale or other transfer of its entire business, provided, in

such case, that any such assignee or transferee has agreed in writing to be bound by the terms and provisions of this Agreement or is so bound by operation of law.

2.6 BMS may grant sub-licenses to Affiliated Companies and Third Parties provided that (a) BMS provides PHARMATOP with advance notice in writing of each sub-license, (b) no sub-license attempts to reduce or limit any of PHARMATOP's rights under this Agreement, (c) BMS agrees to be liable for the actions of any sub-licensee, and (d) PHARMATOP is given the same right to supervise the activities of the sub-licensee as it has under the terms of this Agreement to supervise BMS' activities. BMS' right to grant sub-licenses in accordance with this Section shall include the right to delegate responsibility for marketing the Products in one or more countries in the Territory.

2.7 If the Products are manufactured by a company other than BMS, whether an Affiliated Company or not, BMS must provide PHARMATOP with the identity(ies) of the manufacturer(s), and provide proof to PHARMATOP that (a) the manufacturer(s) has been informed in writing that the products to be made are subject to the Licensed Patents held by PHARMATOP and (b) the manufacturer(s) has agreed to manufacture the products only pursuant to agreement with BMS and solely for the benefit of BMS and its sublicensees. The above restrictions do not apply to raw materials, packaging items or other incidental articles from outside suppliers, or to the performance of packing operations in accordance with customary practices in the pharmaceutical industry.

2.8 Any sub-licensee hereunder shall be required to assume all of the obligations of BMS under this Agreement with respect to the rights sublicensed. BMS will indemnify and hold PHARMATOP harmless from the failure of any sub-licensee to perform its obligations relating to Products in the same manner as BMS is obligated to indemnify and hold PHARMATOP harmless under this Agreement if BMS (rather than the sublicensee) had so failed to perform. PHARMATOP shall have the same rights to audit any sub-licensee's activities relevant to its sublicensing agreement, and to inspect any sub-licensee's facilities involved in the manufacture of Products, in the same manner as PHARMATOP has with respect to BMS' activities and facilities hereunder.

2.9 In the event that BMS makes sales of Products to an Affiliated Company or sub-licensee, then, notwithstanding anything to the contrary in Section 1.14 hereof, the calculation of Net Sales for purposes of determining royalties owed to PHARMATOP under Section 7.2 hereof shall be based on the greater of (x) [***] and (y) [***] [***]

2.10 Nothing in this Agreement shall be construed to grant a Party any rights in any intellectual property rights, information or data owned or controlled by any other Party or its Affiliates, except as expressly set forth in this Agreement.

2.11 Within [***] after the execution of this Agreement, BMS will inform PHARMATOP whether, and in what other countries of the world where BMS does not already possess such rights, BMS is interested in obtaining rights to develop and market the Product. If BMS notifies PHARMATOP that BMS is interested, then the Parties will use all reasonable efforts to conclude an agreement within [***] thereafter in which PHARMATOP grants BMS the exclusive right in such countries in which BMS indicated an interest; provided that the Parties can agree on mutually acceptable terms and conditions during such [***] Should any such negotiations terminate without the grant of an exclusive license to BMS in a given country, PHARMATOP shall be free thereafter to conduct negotiations with any Third Party and grant licenses to the Product to any Third Party in such country; provided, however, that BMS shall be entitled to exercise a right of first refusal with respect to any such country as follows: Before PHARMATOP may accept an offer from, or make an offer to, a Third Party on financial terms more favorable to the Third Party, when taken as a whole, than those last offered by PHARMATOP to BMS to acquire such rights in such country, PHARMATOP will inform BMS of such offer and shall allow BMS a period of [***] in which to elect whether to acquire such rights under such terms as are offered to or by PHARMATOP with the Third Party.

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Article 3—PHARMATOP's Rights to Information

3.1 Subject to Section 3.3, PHARMATOP shall be entitled, for the protection and advancement of its rights in the Licensed Rights outside the Territory, to either obtain from BMS, or have the right to reference, all information and conclusions relating to or resulting from any analytical, galenical, stability, toxicology or pharmacokinetic work and/or clinical studies and clinical trials conducted by BMS relating to the Products and all materials in the NDA submitted to the U.S. FDA for the Products (collectively, the "Registrational Information") for the purpose of developing, manufacturing, registering, seeking marketing approval for and selling an Injectible APAP Product in any country outside the Territory where BMS or any of its Affiliates have not been licensed rights under any PHARMATOP patent or know-how under a separate agreement with PHARMATOP; provided, however, that BMS has the reciprocal right (subject to payment by BMS in the same manner as PHARMATOP is obligated under Section 3.3) to obtain and use any such similar registrational information obtained by PHARMATOP's licensees with respect to the development and marketing of any such Injectible APAP Product in any such country. Subject to Section 3.3, BMS hereby expressly permits PHARMATOP to use the Registrational Information to attempt to secure a licensee for the sale and use of the Products outside the Territory in which BMS or any of its Affiliates does not have exclusive license rights under any separate agreement with PHARMATOP, provided, that the Registrational Information is treated as Confidential Information of BMS and is disclosed to a potential licensee only pursuant to an appropriate confidentiality agreement as set forth in Section 3.3 and that PHARMATOP remains responsible to BMS for any breach by such potential licensee of its confidentiality and non-use obligations.

3.2 Subject to Section 3.3, PHARMATOP or the licensee shall be entitled to use the Registrational Information as part of new drug applications out of the Territory and shall not owe any compensation to BMS for same. BMS shall have no liability or responsibility for any use made by PHARMATOP and its licensees of the Registrational Information, and, subject to sections 12.3 and 12.4, PHARMATOP shall indemnify,

defend and hold BMS and its Affiliates harmless from any use made by PHARMATOP, its Affiliated Companies, or its or their licensees of the Registrational Information.

3.3 Before PHARMATOP shall have the right to access or use any of the Registrational Information as provided in this Article 3 for purposes of any regulatory filing, [***] shall reimburse [***] [***] of the [***] [***] to develop or obtain the Registrational Information. [***] shall not be required to reimburse [***] for the purpose of sharing such Registrational Information, under agreement of confidentiality, with a Third Party to the extent reasonably required for such Third Party to determine its interest in licensing the Product in any countries where BMS and its Affiliates do not have license rights; provided, that the Registrational Information to be made available to the Third Party shall not include the actual Investigational New Drug (IND) or NDA filing, any clinical trial or adverse event database, or any study results which have not been made publicly available or filed to the NDA. Such sharing may include such Third Party having reasonable access to such Registrational Information at BMS, at PHARMATOP's expense, in order to conduct reasonably necessary due diligence. Such Third Party shall not have access to the Registrational Information until it shall have executed a confidentiality agreement, in form and substance acceptable to PHARMATOP and BMS, in which BMS either is a party to the confidentiality agreement or is entitled to enforce such confidentiality as an express third party beneficiary thereof under the terms of the confidentiality agreement and applicable law.

Article 4—Development and use obligations

4.1 BMS shall use its Diligent Efforts to obtain NDA approvals (and other regulatory authorizations) required to develop and market the Products in each country in the Territory.

4.2 Neither Party warrants, represents or guarantees that the Products will obtain NDA approvals in the Territory.

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4.3 During the preparation and pendency of the various NDAs, BMS shall advise PHARMATOP in writing on a confidential basis at least [***] as to actions taken, or to be taken, the likely date of presentation of NDAs, any problems encountered, and the likely date of NDA approvals. Within [***] after the Effective Date and thereafter [***] until NDA Approval is received in a given country, BMS will provide an estimate of the Product development timelines in such country and for all studies that it is then undertaking or that it plans to undertake within the following [***] in such country and will update such timelines on a [***] basis thereafter; provided, that it is understood that, all forecasts are estimates for review by PHARMATOP only, are not guaranteed or warranted and may not be relied upon in any way, and, except as permitted by Article 10, may not be disclosed to Third Parties. PHARMATOP shall submit to BMS in writing any comments on studies or applications conducted or submitted by BMS. BMS must reply to any such comments in reasonable detail, so that PHARMATOP can make an assessment of BMS' performance of its obligations with respect to this Article 4; provided that BMS shall remain solely responsible for the development and regulatory strategy for the Product.

4.4 If any matter or issue (including, but not limited to, an unexpected safety issue, manufacturing problems or significant additional studies are required by U.S. FDA) arises which is likely to materially obstruct or significantly delay the issue of an NDA approval in a given country by more than [***], particularly the U.S. NDA approval, BMS must inform PHARMATOP immediately and the parties must then consult with each other to examine and determine whether any corrective measures should be undertaken to supplement or amend the NDA in such country. If the proposed corrective measures are not economically or technically viable to implement, then BMS may elect to terminate this Agreement as to such country (and if the affected country is the United States, then it may elect to do so either as to all countries or just the U.S.), in which case [***] all licenses and rights granted to BMS hereunder shall immediately terminate with respect to such country(ies), and PHARMATOP shall recover its entire freedom with respect to the Licensed Rights in such country(ies) [***]

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[***] (and without BMS being liable to PHARMATOP in any manner on account of such termination) and the terms of Section 9.3(b) shall apply.

4.5 Once an NDA approval has been obtained, along with any other necessary approvals, BMS shall use Diligent Efforts to market the Products in the country in which approval has been obtained. BMS shall, at least [***], provide to PHARMATOP a written report on the means and operations used by it to promote the Products. Within [***] [***] [***] and thereafter [***] until the end of the Royalty Term for a given country, BMS will provide its sales forecast for the following [***] and will update such forecast (and provide actual sales performance results by Presentation) on a [***] basis thereafter; provided, that it is understood that all sales forecasts are estimates for review by PHARMATOP only, are not guaranteed or warranted and may not be relied upon in any way, and may not be disclosed to Third Parties. On receiving these reports, PHARMATOP may ask BMS in writing for reasonable further information and/or clarifications that directly concerns the Product and that BMS may lawfully provide so as to enable PHARMATOP to assess BMS' performance of its obligations under this Section.

4.6

(a) Except as provided in section 4.6(c), BMS agrees that, during the Marketing Period for a given country in the Territory, it will not sell and/or market any Injectible APAP Product other than the Product. BMS represents that it currently has no intention of developing and/or marketing other Injectible APAP Product for use in the Territory. For any country in the Territory where BMS is already marketing a propacetamol product on the Effective Date of this Agreement, BMS agrees that, subject to any legal commitments it may have to Third Parties as of the Effective Date and consistent with any requirements of applicable law, BMS will (1) upon launch of the Product in such country, cease active promotion and marketing of the propacetamol product in such country and transition customers of the propacetamol product over to the Product in a manner that does not unduly

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jeopardize BMS' customer relationships and allows for BMS' inventory of propacetamol products to be appropriately worked down; and (2) not sell or license its rights to the propacetamol product to any Third Party for sale or use in such country.

(b) Subject to Section 7.4, nothing in this Agreement shall restrict or affect BMS' ability to develop and market at any time during the term of this Agreement, in any country in the Territory, one or more parenterally-administered products containing an analgesic or an opiod (as long as such product is not another Injectible APAP Product). BMS shall inform PHARMATOP promptly of any decision to market any parenteral opiate or non-opiate product for the treatment of post-operative pain.

(c) Nothing in any provision of this Agreement shall, expressly or impliedly, preclude or restrict BMS (or any of its Affiliated Companies) in any way from (1) acquiring the voting stock or other securities, or the assets, of any Third Party, (2) selling voting stock or other securities, or any of their assets, to any Third Party, or (3) merging, amalgamating, taking over or consolidating (or engaging in any similar transaction) with any Third Party (any of the foregoing a "Transaction"), where such Third Party is developing or marketing its own Injectible APAP Product, subject to the following: If such Third Party becomes an Affiliated Company of BMS by reason of such Transaction and is then marketing its own Injectible APAP Product in a country in the Territory, then BMS shall inform PHARMATOP in writing, within [***] after the consummation of such Transaction has been publicly announced ("Transaction Date"), whether BMS will divest or cause the divestiture of the competing Injectible APAP Product in such country(ies). If BMS informs PHARMATOP that it plans to so divest, then BMS shall use commercially reasonable efforts to divest itself of such competing Injectible APAP Product in a manner consistent with its reasonable business judgement and to complete such divestiture of the competing Injectible APAP Product as promptly as practicable following notification by BMS to PHARMATOP of the decision to divest. BMS shall have

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until the date that is [***] after the applicable Transaction Date to complete such divestiture (the "Grace Period"); provided, that, so long as BMS demonstrates to PHARMATOP's reasonable satisfaction that BMS used commercially reasonable efforts to effect such divestiture within such [***] Grace Period, but was unable reasonably to effect such divestiture, then such [***] Grace Period shall be extended for such additional [***] periods thereafter as is necessary to enable such competing Injectible APAP Product to be in fact divested, so long as BMS continues to demonstrate to PHARMATOP's reasonable satisfaction that BMS is using commercially reasonable efforts to effect such divestiture within such period, and provided further that in no event shall the aggregate Grace Period exceed [***] BMS shall keep PHARMATOP reasonably informed of its efforts and progress in effecting such divestiture until it is completed. The sale, promotion or marketing of any such competing Injectible APAP Product by BMS or any of its Affiliated Companies within the Territory during such Grace Period pursuant to this Section 4.6(c) shall not be grounds for termination of this Agreement under Section 4.6(a). Nothing in this Paragraph is intended to affect BMS' obligation to use Diligent Efforts to market the Product during the Grace Period.

If BMS notifies PHARMATOP that BMS does not plan to divest the competing Injectible APAP Product, then, BMS shall have [***] after the Transaction Date in which to sublicense or sell the rights to the Product to a Third Party, and if BMS is unable to do so within such [***], then PHARMATOP may terminate this Agreement with respect to the affected country(ies) at any time thereafter upon not less than [***] written notice to BMS and the terms of Section 9.3(b) shall apply.

4.7 All INDs and NDAs for any Product shall be owned solely by BMS, and BMS shall be responsible for all regulatory filings to be made thereto.

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Article 5—Patent Application Examination

5.1 PHARMATOP shall use its best efforts to diligently prosecute the Patent Applications and to have the Patent Applications granted by the patent offices concerned, within the customary timeframes. PHARMATOP agrees to keep BMS informed on the progress of the examination of the applications; to reply diligently in consultation with BMS to comments made by the examiners (and Third Parties where appropriate); and, to take other reasonable and customary actions to avoid delays with the issuance of the patents or a reduction to the scope thereof.

(a) PHARMATOP will promptly notify BMS in writing after each Notice of Allowance and patent issuance in the Territory. The parties will cooperate to ensure a timely filing in the Orange Book with respect to an issued patent.

(b) PHARMATOP and BMS will cooperate to ensure timely filings for any available Patent Term Restoration on the Product (currently, filings must be made within 60 days after NDA Approval).

(c) With respect to any Patent Right filed, prosecuted or maintained by PHARMATOP, each patent application, office action, response to office action, request for terminal disclaimer, voluntary amendment, interference proceeding filing or action, and request for reissue or re-examination of any patent issuing from such application shall be provided by PHARMATOP to BMS sufficiently prior to any such application, filing or request to allow reasonable time for adequate review and comment by BMS. PHARMATOP will also provide BMS copies of all correspondence and other material documents received or prepared by PHARMATOP in the prosecution, maintenance, and enforcement of the Licensed Patent Rights.

(d) PHARMATOP shall provide to BMS, on a quarterly basis, a written patent report that includes the serial number, docket number and status of each Licensed Patent.

(e) Within 90 days after execution of this Agreement, PHARMATOP will also ensure that a signed and duly notarized Assignment Document, assigning the entire right, title and interest in US Patent No. 6,028,222 from Francois Dietlin and Daniele Fredj to SCR Pharmatop, is filed in the United States Patent and Trademark Office.

(f) PHARMATOP will ensure that Patent Applications filed in the Territory will include at least the same claims as filed in the PCT Applications as of the Effective Date.

5.2 PHARMATOP will, to the greatest extent practicable, prosecute the Patent Applications as currently filed (or that will be filed in the Territory pursuant to section 5.1(f)), and agrees not to alter the terms so as to materially narrow the scope thereof or abandon any material pending claims unless consented to by BMS, or as otherwise is reasonable in light of the prosecution of the Patent Applications. PHARMATOP does not guarantee to BMS that the patents will be issued in terms similar to those of the Patent Applications. PHARMATOP will not abandon any issued claims or admit that any such issued claims of the Patents are unenforceable by disclaimer or otherwise, without BMS' prior written consent.

5.3 During the entire period of examination of the Patent Applications, BMS will comply with all its obligations towards PHARMATOP, including, but not limited to its financial obligations, and shall not be entitled to suspend them on the ground that the examiners or Third Parties have commented on or challenged the filed Patent Applications. BMS will be entitled to terminate this Agreement with respect to a particular country, or obtain a reduction in the royalty rate for sales therein, in accordance with Sections 6.2 and 6.3 below, as a result of a final patent office decision that definitively rejects a Patent Application in such country(ies).

5.4

(a) PHARMATOP shall pay the annual fees due to the patent offices in a timely manner to maintain the Patents in force until their expiry. [***] will reimburse

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[***], commencing from and after the [***] of the Effective Date of this Agreement, for its payment of the annual maintenance fees in any country in the Territory where no Products have been sold as of the time of such payment, provided that [***] provides proof of such payment and requests such reimbursement. For budgeting purposes, [***] shall provide to [***], on February 1 and August 1 of each Year, a reasonably detailed estimate of the out-of-pocket expenses it expects to incur, in the next six (6) months, with respect to Licensed Patents.

(b) If PHARMATOP files for and obtains new Patents in a country in the Territory based on Inventions made after the Effective Date of this Agreement that is likely to have the effect of extending BMS' period of marketing exclusivity, [***] will reimburse [***] for [***] of its costs of filing and prosecuting the corresponding patent applications in such country, including [***] reasonable out-of-pocket legal fees and expenses, on presentation of appropriate supporting documents; provided, however, that (a) [***] shall not be obligated to make any such reimbursement to [***] prior to the [***] of the Marketing Period in such country or in any year in which an Injectible APAP Product is marketed by a Third Party in such country, and (b) any such reimbursement paid by [***] for a given country will be returned to [***] if, prior to the [***] of the Marketing Period in such country, an Injectible APAP Product which does not infringe the Patents is marketed in such country.

Article 6—Additional Provisions Affecting the Patents

6.1

(a) PHARMATOP represents and warrants that Francois Dietlin and Daniele Fredj (the "Inventors") solely discovered or derived the inventions covered by the Patents, as well as the Know-How embodied in the formulation of the Product, through their own research and efforts and without misappropriating the trade secrets or confidential information of any Third Party, and that the Inventors have

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never been employed by or provided services to Fresenius. It further represents that the portion of the inventions covered by U.S. patent No. 6,028,222 was duly assigned by the Inventors to Newpharm, a company organized under the laws of France having its head office's address at 10, square St. Florentin, 78150 Le Chesnay, France ("Newpharm") which obtained French patent No. 2.751.875 and that Newpharm subsequently assigned the associated ongoing research and priority rights to PHARMATOP as set forth in the agreement attached as ***Exhibit D*** and confirmed by Newpharm in the letter attached hereto as ***Exhibit E***. PHARMATOP also represents that it is the sole owner of the Licensed Rights, and otherwise has the sole right to exclusively license and grant rights to them, and that, to the best of its knowledge, each invention is patentable.

(b) BMS represents that, to its knowledge as of the Effective Date, and having examined the Patent and the Patent Applications, it has not identified, and otherwise has no knowledge of, any reasons why the Patent might be invalid or why the Patent Applications could not be granted under conditions enabling the license herein to be effectively implemented.

(c) PHARMATOP represents and warrants to BMS that: (i) there is no action, suit or proceeding pending or threatened in writing as of the Effective Date by any Third Party against PHARMATOP, its Affiliated Companies, or any of the Inventors named in the Patents which, if adversely determined, would have a material adverse effect upon the issued claims of the Patents in the Territory as of the Effective Date or upon the issuance of any claims of the Patent Applications in the Territory as of the Effective Date; (ii) the issued claims of the Patent in the Territory which cover the manufacture, use, importation or sale of Product are not dominated by any issued patents of any Third Party in the Territory; and (iii) except as disclosed in ***Appendix 3*** (*re Fresenius*), it is not aware of any infringement by any Third Party as of the Effective Date of any of the Patents in the Territory.

6.2

(a) If PHARMATOP is:

(i) unable to obtain, without material alteration or restriction as to scope and content, issuance in the Territory of the claims being prosecuted as of the Effective Date on the PCT Patent Applications filed as of the Effective Date; or

(ii) unable to maintain, or a material alteration of the scope or content occurs with respect to, any of the claims under any of the Patents issued as of the Effective Date or on any patents issued on Patent Applications filed as of the Effective Date;

then BMS may at its option terminate this Agreement for any of the countries so affected (an "Affected Country"), or, if the affected country is the United States, then either as to the United States or as to all countries in the Territory. Any such termination shall require (A) not less than [***] prior written notice, if after [***] in the [***] or (B) not less than [***] [***] prior written notice, if [***] in the [***].

(b) If a Third Party should market in any country in the Territory a parenterally-administered liquid solution product, in a stable and readily injectible form, that (x) contains paracetamol and one or more other analgesic ingredients, (y) uses any of the technology contained within any issued claim of any Licensed Patent in such country or any Licensed Know-How, and (z) is not considered to infringe any Patent within the Licensed Rights in such country (whether by judicial determination or settlement, by joint agreement of PHARMATOP and BMS, or by both Parties failure to prosecute such Third Party for infringement under Section 6.5), then BMS may elect to terminate this Agreement pursuant to Section 9.3(a) for any such Affected Country, or, if the Affected Country is the United States, then as to all countries in the Territory.

(c) If BMS opts to terminate this Agreement pursuant to section 6.2(a) or section 6.2(b) with respect to one or more Affected Countries, it shall be under the terms and conditions of section 9.3(b). BMS shall not be entitled to obtain from PHARMATOP the return of any sums paid to PHARMATOP before the date of said termination unless BMS can establish that the refusal to issue the patent (or

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the withdrawal thereof) is due to a knowingly inaccurate representation made by PHARMATOP in Section 6.1 of this Agreement. BMS shall be permitted thereafter to sell Products already manufactured by such termination date, provided that it pays PHARMATOP the contractual royalties on such sales provided for in Article 7. BMS shall not be restricted in any way thereafter from manufacturing and selling another Injectible APAP Product in such terminated country(ies) for which the manufacture or sale in such country (x) does not infringe the Licensed Patents and (y) does not use to any material extent any Licensed Know-How.

(d) In the event that BMS opts to maintain the Agreement in effect in an Affected Country under section 6.2(a) or 6.2(b), then:

(i) if such Affected Country is [***], the Guaranteed Payment provision (section 7.3) shall be [***] thereafter effective as of the [***] in which BMS elected to maintain the Agreement and each [***]thereafter; and

(ii) the royalty rate on all Net Sales in such country for any quarter in a given Year will be reduced by [***] for each such quarter in which:

[***]

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[***]

6.3

(a) Should the Patents (or their inventorship) be the subject of an administrative or judicial challenge by a Third Party, PHARMATOP will undertake at its expense, in consultation and liaison with BMS, to take all appropriate measures to oppose the challenge by the Third Party. Subject to Sections 12.3 and 12.4, PHARMATOP shall defend, indemnify and hold harmless BMS from any liabilities, losses, costs or damages, which shall include costs or judgements whether for money or equitable relief, and reasonable legal expenses and reasonable attorney's fees, arising out of any such claims, suits or challenges. PHARMATOP shall not enter into a settlement agreement with such Third Party without the written consent of BMS, which shall not be unreasonably withheld. PHARMATOP shall not enter into a settlement agreement with such Third Party without the written consent of BMS, which shall not be unreasonably withheld. BMS shall have the right to participate and be represented in any such suit by its own counsel at its own expense. The pendency of any administrative or judicial claim or action by a Third Party challenging the Patents will not permit BMS to cease or suspend its performance of its obligations under this Agreement, including its financial obligations. If the Third Party's claim or action succeeds so as to deprive PHARMATOP of any of its rights on Licensed Patents in a country in the Territory, then BMS may terminate this Agreement as to such country in the same manner as it would have been entitled to terminate pursuant to Section 6.2(a)(ii) and 6.2(c) (with BMS providing the same written notice of termination required thereby unless the outcome of such Third Party's claim or action would require BMS to cease marketing of the Product prior to the end of the notice period) or to continue to market the Product subject to Section 6.2(d).

(b) In the event that PHARMATOP fails or elects not to defend any such action, suit, or challenge, then BMS may defend such action, suit or proceeding at its own expense, in its own name and the name of PHARMATOP, and entirely under

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BMS' own direction and control. PHARMATOP will reasonably assist BMS (at BMS' expense) in any action or proceeding being prosecuted or defended by BMS, if so requested by BMS or required by law. PHARMATOP shall have the right to participate and be represented in any such suit by its own counsel at its own expense. No settlement of any such action or defense which restricts the scope or affects the enforceability of a Licensed Patent may be entered into by BMS without the prior consent of PHARMATOP, which consent shall not be unreasonably withheld. If the Third Party's claim or action succeeds so as to deprive PHARMATOP of any of its rights on Licensed Patents in a country in the Territory, then BMS may terminate this Agreement as to such country in the same manner as it would have been entitled to terminate pursuant to Section 6.2(a)(ii) and 6.2(c) (with BMS providing the same written notice of termination required thereby unless the outcome of such Third Party's claim or action would require BMS to cease marketing of the Product prior to the end of the notice period) or to continue to market the Product subject to Section 6.2(d).

6.4 PHARMATOP represents that, to its knowledge, the manufacture and sale of the Products in Territory will not infringe any intellectual property right of any Third Parties and, subject to sections 12.3 and 12.4, PHARMATOP will hold BMS harmless against any Third Party action or claim asserting an infringement of such rights. In the event such an action or claim is brought by a Third Party, then, subject to section 6.3, BMS will be obligated to continue to perform its obligations under this Agreement, including its financial obligations.

6.5

(a) In the event that a Third Party is manufacturing and/or marketing anywhere in the Territory an Injectible APAP Product for which the manufacture, use or sale thereof infringes a Valid Claim under the Licensed Patents, the Parties shall consult with each other in order to attempt to end such infringement, and shall take all appropriate action to do so. BMS shall have the right in the first instance, but not the obligation, to initiate legal action against an infringing party under its

own direction and control. PHARMATOP will reasonably assist BMS ([***]) in any action or proceeding being prosecuted if so requested, and will lend its name to such actions or proceedings if requested by BMS or required by law. No settlement of any such action which restricts the scope, or adversely affects the enforceability, of a Licensed Patent may be entered into by BMS without the prior written consent of PHARMATOP, which consent shall not be unreasonably withheld.

(b) If BMS elects not to bring any action for infringement described in Section 6.5(a) and so notifies PHARMATOP in writing, then PHARMATOP may bring such action at its own expense, in its own name and entirely under its own direction and control. BMS will reasonably assist PHARMATOP ([***]) in any action or proceeding being prosecuted if so requested, and will lend its name to such actions or proceedings if requested by PHARMATOP or required by law. No settlement of any such action which restricts the scope, or adversely affects the enforceability, of any Licensed Patent may be entered into by PHARMATOP without the prior written consent of BMS, which consent shall not be unreasonably withheld.

(c) If either Party brings such an action or defends such a proceeding under this Section 6.5 and subsequently ceases to pursue or withdraws from such action or proceeding, it shall promptly notify the other Party and the other Party may substitute itself for the withdrawing Party under the terms of this Section 6.5.

(d) In the event either Party exercises the rights conferred in this Section 6.5 and recovers any damages or other sums in such action, suit or proceeding or in settlement thereof, such damages or other sums recovered shall first be applied to all out-of-pocket costs and expenses incurred by the Parties in connection therewith, including attorneys fees. If such recovery is insufficient to cover all such costs and expenses of both Parties, it shall be shared in proportion to the total of such costs and expenses incurred by each Party. If after such reimbursement any funds shall remain from such damages or other sums recovered, such funds

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shall be retained by [***]; provided, [***].

(e) BMS will be obliged to continue performing its obligations towards PHARMATOP during the pendency of any legal action against a Third Party; provided, however, that, during such period of time [***] shall pay [***] [***] of the royalties contractually due on Net Sales in the country where the infringing injectible APAP Product is being marketed, with the balance (the "Retained Sums") temporarily retained by [***] If the outcome of the litigation is the invalidation of a Patent, the provisions of Section 6.2 will be applicable, and, if [***] elects to continue as provided in Section 6.2(c), [***](f) Any infringement of the Patents by an Affiliated Company of BMS whom BMS has not sublicensed shall be deemed to be a breach of Agreement by BMS.

6.6 PHARMATOP does not make any representations of warranties with respect to the Patents other than those expressly stated in this Article 6.

6.7 BMS will have sole liability to Third Parties for any injuries or death caused to any person by reasons of the manufacture, use or sale of the Products manufactured or sold pursuant to this Agreement, and will indemnify PHARMATOP against claims by Third Parties based on product liability as provided for in Section 12.2.

6.8 In the event that BMS reasonably believes after consultation with PHARMATOP that it is required to obtain a license from a Third Party in order to practice the Licensed Patents and Know-how, then any license fees or other royalties payable by BMS to such Third Party with respect to same shall be [***].

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Article 7—License Fees and Royalties

7.1 BMS shall make the following lump sum, non-refundable (except as provided in section 12.3 or as may be otherwise expressly provided in this Agreement) payments to PHARMATOP:

(a) Within fifteen (15) business days following execution of this Agreement, the sum of [***].

(b) Within ten (10) business days [***], the sum of [***] This amount will be paid only [***], [***]

7.2

(a) Subject to the Guaranteed Payments provided for in Section 7.3 and to sections 6.2, 6.5(e), 6.8, 7.2(b), 7.2(c) and 12.3 hereof, BMS shall make the following royalty payments to PHARMATOP:

i. [***] percent ([***]%) of the Net Sales of Products during the [***] and [***] [***] in a given country;

ii. [***] percent ([***]%) of the Net Sales of Products during the [***] in a given country;

iii. [***] percent ([***]%) of the Net Sales of Products during the [***] in a given country; and

iv. [***] percent ([***]%) of Net Sales of Products during the [***], and all subsequent [***] of the Royalty Term thereafter in a given country, unless this Agreement is sooner terminated in such country.

Upon payment of all royalties due PHARMATOP in a given country through the end of the Royalty Term for such country, BMS shall have a fully paid-up license under Section 2.1 to use the Licensed Rights in such country to develop, make, use and sell the Products.

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(b) [***] then the effective royalty rate for sales of such Combination Products shall be [***] [***] of the royalty rate paid by BMS to such Third Party for the Combination Product, subject to a [***] of the royalty payable to PHARMATOP of [***] BMS will provide evidence, reasonably satisfactory to PHARMATOP, of any [***](c) [***] [***] [***]. [***]

7.3 Subject to Section 12.3 hereof, during each of the first [***] of the Marketing Period in the United States, BMS shall pay royalties to PHARMATOP equal to the greater of (i) [***] or (ii) the [***]do not conform in all respects [***]Further, in any quarter in any Year in [***]

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[***] be multiplied by a fraction the numerator of which is [***]and the denominator of which is the sum of the numerator plus [***]using a mutually agreed upon methodology for calculating [***]during such quarter[***]The Parties will review the procedures[***]from time to time to ensure that they are fair and equitable to both Parties.

7.4

(a) In the event that BMS markets a Competing Product in a country in the Territory during the Royalty Term for such country, BMS agrees that:

(i) During the [***] period following the launch of such Competing Product (commencing with the [***] of the [***] following such launch), BMS will continue to provide for the Product at least [***] of the Primary Detail Equivalents (PDEs) and will continue to spend on the Product at least [***] of the Advertising and Promotional Costs that it spent, as determined on an [***] for the Product during the [***] period preceding such Competing Product launch; and

(ii) During the [***] period following the launch of such Competing Product, BMS will continue to provide for the Product at least [***] of the Primary Detail Equivalents (PDEs) and will continue to spend on the Product at least [***] of the Advertising and Promotional Costs that it spent, as determined on an [***] for the Product during the [***] period preceding such Competing Product launch and the [***] period following such Competing Product launch; and

(iii) During the [***] period following the launch of such Competing Product, BMS will continue to provide for the Product at least [***] of the Primary Detail Equivalents (PDEs) and will continue to spend on the Product at least [***] of the

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Advertising and Promotional Costs that it spent, as determined on an [***] for the Product during the [***] period following such Competing Product launch.

Notwithstanding the foregoing, in the event that such Competing Product is launched during the period that Guaranteed Payments under Section 7.3 are payable, then subsections 7.4(a)(i)-(iii) shall not apply except with respect to those full [***] periods following such Competing Product launch that occur after the expiration of the payment of such Guaranteed Payments during such [***].

Further, this Section 7.4(a) shall only apply to the [***] Competing Product that BMS may launch within each country in the Territory

(b) BMS will provide PHARMATOP, within [***] [***] after the end of each [***] period following such Competing Product launch with sufficient information regarding BMS' PDE detailing and Advertising and Promotional spending to enable PHARMATOP to make a reasonable, competent assessment as to whether BMS has fulfilled its obligations under Section 7.4(a) above.

(c) In the event that BMS fails to fulfill any of (i), (ii) or (iii) under section 7.4(a) above, then PHARMATOP may, upon ninety days written notice to BMS, terminate this Agreement at any time within thirty days after PHARMATOP receives the information from BMS required for PHARMATOP to determine that BMS has failed to fulfill such obligations, in which event [***], all licenses and rights granted to BMS hereunder shall immediately terminate, and PHARMATOP shall recover its entire freedom with respect to the Licensed Rights in such country [***] and the terms of Section 9.3(b) shall apply. If PHARMATOP elects to terminate BMS' rights, such termination shall be PHARMATOP's sole remedy and BMS shall not be liable for any additional damages to PHARMATOP with respect to such failure.

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7.5

(a) The contractual royalties will be calculated and will be payable quarterly for sales made in each Calendar Quarter in the Royalty Term. A detailed statement, country by country and by Presentation, will be prepared and sent by BMS to PHARMATOP within [***] of the end of each Calendar Quarter ([***] [***] after the last quarter in an Agreement Year to allow for additional time to determine any adjustments required to be made on an annual basis), accompanied by payment of the royalties due PHARMATOP. If the annual reconciliation shows an amount due by either Party to the other, the amount due shall be paid as follows: BMS shall pay any amount due by it at the same time as it provides the reconciliation to PHARMATOP. PHARMATOP shall repay any amount due by it to BMS within [***] after the receipt by it of such reconciliation report.

(b) PHARMATOP may, on reasonable (but not less than [***]) written notice to BMS, have a calculation statement audited at its own expense by an accounting firm selected by PHARMATOP that is reasonably acceptable to BMS and that is bound by a written agreement of confidentiality to BMS. The, auditor's assignment will be limited to reviewing the accuracy of a calculation statement sent by BMS (the "Inspection"), and to disclosing only if there are any errors in payment and, if an error exists, the amount of such error(s) and the calculation thereof, and no additional or any other information. If an audit discloses that the amount of royalties owed to PHARMATOP was understated by more than [***] [***], then [***] must reimburse [***] for the cost of the audit, in addition to paying the additional royalties together with interest on the additional amounts, calculated from the date on which the additional amount should have been paid, as provided in section 7.7. Such audit rights may be exercised [***], and any such audit shall apply [***].

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7.6 BMS shall make all payments to PHARMATOP in United States Dollars by electronic funds deposit, to a French bank and account number designated in writing by the *Gerant* of PHARMATOP. Each Party shall bear its own expenses with respect to any such electronic funds transfer. When products are sold for monies other than United States dollars, the monies due will first be determined in the foreign currency of the country in which such products were sold and then converted into equivalent United States currency, on a monthly basis, using the applicable U.S. Federal Reserve rate in effect on the last business day of each calendar month. Each quarterly Royalty Payment shall cover three (3) such monthly conversions. PHARMATOP agrees that it will be solely responsible for all payments owed to Newpharm or the Inventors.

7.7 Any amounts not paid on its due date by BMS to PHARMATOP will bear simple interest on the outstanding balance at the [***] the applicable period, calculated from the contractual due date until the date of payment, without the need for a formal notice to pay or any other notice.

7.8 Neither the payment of interest by BMS nor the acceptance of the same by PHARMATOP shall effect a waiver of any of PHARMATOP's rights or remedies under this Agreement.

7.9 BMS shall pay any and all excise, sales, use, value added, and other similar Taxes solely arising as a result of Product sales under this Agreement. Where required to withhold any tax in connection with any payment hereunder to PHARMATOP due to applicable law, treaty, rule or order of a governmental body, BMS shall deposit such taxes with the appropriate tax or revenue authorities as a deduction from such royalty or other payment, and shall notify PHARMATOP and, upon request of PHARMATOP, BMS shall furnish satisfactory evidence of such withholding and payment. [***] shall not be required to gross up or reimburse [***] for any such withholdings. BMS shall reasonably cooperate with PHARMATOP in obtaining exemption from withholding taxes where available under applicable law. PHARMATOP shall be solely responsible for all taxes levied on PHARMATOP's revenues, profits or income arising out of this Agreement.

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7.10. BMS agrees that it will not engage in any fraudulent transactions relating to sales of the Products that are specifically designed to reduce or avoid royalty payments to PHARMATOP.

Article 8—Improvements made by BMS

BMS shall promptly inform PHARMATOP of any adaptation, improvement, enhancement or upgrade (collectively, an "Improvement") BMS makes with respect to the formulation and/or manufacture of the Products, whether such Improvement can be protected by patent or not. BMS will remain the owner of any such Improvement that it makes to the Products; provided, however, that BMS must grant to PHARMATOP, upon request, a non-exclusive, [***] license to practice and use the Improvement, including the right to grant sublicenses, outside of the Territory solely in connection with the manufacture, use or sale of the Products; provided, that any sub-licensee of such rights shall have granted reciprocal rights to PHARMATOP which can be sublicensed to BMS.

Article 9—Term / Termination

9.1 Unless terminated earlier pursuant to the terms of this Agreement, the term of this Agreement shall run on a country-by-country basis until the end of the Marketing Period. Upon the expiration of this Agreement in a country, BMS will have no further financial obligations towards PHARMATOP for sales made in such country after such expiration.

9.2 Should either Party fail to perform any of material obligations of this Agreement, and fail to cure such breach or default within ninety (90) days alter receiving a written notice from the non-breaching Party specifying the breach and demanding that it be cured, then the non-breaching Party shall have the right to terminate this Agreement; provided, that if the material breach is restricted to a given country, termination shall be as to such country only.

9.3

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(a) BMS may, in its sole discretion, terminate this Agreement at any time during the Marketing Period with respect to a given country at any time, provided that (i) it gives written notice at least twelve (12) months in advance, and (ii) BMS has paid all amounts due under this Agreement as of the date of such notice. If BMS terminates this Agreement pursuant this section 9.3(a), then BMS agrees not to market any other Injectible APAP Product in such country for a period of [***] following termination; provided, that this section 9.3(a) shall not apply to any Injectible APAP product marketed by BMS (x) that is thereafter acquired by BMS or any of its Affiliates as a result of a Transaction (as such term is defined in section 4.6(c)) that occurs following the giving of such notice of termination and which was a marketed product of the Third Party at the Transaction Date or (y) that is marketed by BMS in accordance with the last sentence of section 6.2(c) as a result of a termination by BMS pursuant to section 6.2(c) or 6.3(a).

(b) Upon the effective date of a termination by BMS pursuant to this Section 9.3, BMS will transfer to PHARMATOP, at PHARMATOP's expense, the NDA approvals, so that PHARMATOP may take over, in the affected country(ies) in the Territory, the marketing of the Products (directly or through any Third Parties of its choice). The Parties shall in good faith consult on the procedures for this transfer of the marketing information and contracts (covering stocks, current orders, official records, etc), endeavoring to ensure that the marketing is disturbed, as little as possible, by the transfer and that each Party continues to comply with its obligations under applicable law. BMS shall also license or assign to PHARMATOP without charge any trademark/tradename used by BMS that is specific to the Products; however, no rights will be assigned or licensed to PHARMATOP under any names, marks, or logos used by BMS and its Affiliates on the Product that are also used on their other products (e.g., the Bristol-Myers Squibb name). At its option, PHARMATOP may commence marketing the Products (directly or indirectly) at any time after its receipt of the termination notice. The Parties agree to negotiate in good faith a smooth transition of marketing for the Product as well as an orderly disposition of BMS' Product inventory during the [***] notice period referred to in section 9.3(a).

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9.4 PHARMATOP shall have the right to terminate this Agreement on ninety (90) days' written notice if BMS either opposes any of the Patent Applications or challenges or contests the validity or enforceability of any of the Licensed Patents.

9.5 In the event that this Agreement is terminated or rejected by a Party or its receiver or trustee under applicable bankruptcy laws due to such Party's bankruptcy, then all rights and licenses granted under or pursuant to this Agreement by such Party to the other Party are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11 of the United States Bankruptcy Code and any similar law or regulation in any other country, licenses of rights to "intellectual property" as defined under Section 101(35A) of Title 11 of the Bankruptcy Code. The Parties agree that all intellectual property rights licensed hereunder, including without limitation any patents or patent applications in any country of a Party covered by the license grants under this Agreement, are part of the "intellectual property" as defined under Section 101(35A) of the Bankruptcy Code subject to the protections afforded the non-terminating Party under Section 365(n) of the U.S. Bankruptcy Code, and any similar law or regulation in any other country.

Article 10—Confidentiality and Publicity

10.1 All information of a proprietary or confidential nature disclosed by one Party to the other or developed by the other Party under this Agreement ("Confidential Information") shall be maintained in confidence, not disclosed to any Third Party, and used only for the purposes of this Agreement. Each Party may disclose the other Party's Confidential Information to Affiliated Companies, agents, legal and financial representatives, or consultants under obligations of confidentiality, non-disclosure and non-use at least equivalent to the obligations set forth in this Article. The obligations of confidentiality, non-disclosure and non-use set forth in this Agreement shall expire five (5) years after the date of termination or expiration of this Agreement.

10.2 The obligations of confidentiality, non-disclosure and non-use set forth shall not apply to information: (a) that was previously known to the receiving Party or any of its Affiliated Companies free of restriction as evidenced by the records of such Party; (b) that is or

becomes generally available to the public through no fault of the receiving Party; (c) that is acquired in good faith by the receiving Party or any of its Affiliated Companies from a Third Party not under an obligation of secrecy to the disclosing Party with respect to such information; or (d) that is independently developed by employees or agents of the receiving Party or any of the Affiliated Companies without reliance on Confidential Information disclosed under this Agreement.

10.3 Notwithstanding the obligations of confidentiality, non-disclosure, and non-use set forth herein, a Party may:

(a) disclose Confidential Information to a regulatory agency that is necessary to obtain regulatory approval in a particular jurisdiction or as otherwise required by law or judicial process;

(b) disclose Confidential Information to a government official or agency if the disclosure is necessary to protect the health and safety of a Party's workers or the public or as required by law or for defending, enforcing, or prosecuting patent applications and patents; and

(c) disclose Confidential Information reasonably required in connection with the development, manufacture, use, sale, external testing, or marketing of Products in the Territory in accordance with the terms of this Agreement.

10.4 Except as set forth in this section, neither Party shall disclose the nature or existence of this Agreement to any Third Party, or the relationship between the parties hereunder, without the prior written consent of the other Party, except that each Party shall be permitted, without the prior permission of the other Party, to disclose the existence of this Agreement and the nature of the licenses granted hereunder as required by law or judicial process and to its accountants and attorneys. PHARMATOP shall be permitted, without the prior permission of BMS, to disclose the existence of this Agreement and the nature of the licenses granted hereunder on a confidential basis to a) potential licensees pursuant the provisions of section 3.1, but not other terms and conditions; and b) as to the terms of this Agreement, its existing or potential investors and commercial bankers. BMS shall be

permitted, without the prior permission of PHARMATOP, to disclose the existence and terms of this Agreement on a confidential basis to potential sublicensees, copromotion partners, merger and acquisition candidates and collaborators.

10.5 The provisions of this Article shall govern the exchange of Confidential Information between the parties on or after the execution of this Agreement. The rights and obligations of this Article shall survive termination of this Agreement.

Article 11—Warranties, Representations and Acknowledgements

11.1 PHARMATOP warrants and represents that it is a partnership duly organized and validly existing under the laws of France, and has all power and authority to carry on its business as now being conducted and to own its properties and is duly licensed or qualified in each jurisdiction in which its failure to qualify would have a material adverse effect on its business, financial condition or operations. PHARMATOP represents that, as of the Effective Date, the assets of PHARMATOP, excluding the Patents and Patent Applications, are valued at less than [***] and that its revenues for calendar year 2002 will be less than [***].

11.2 PHARMATOP warrants and represents that it has full legal power and authority to enter into this Agreement and to consummate the transactions contemplated hereby; that the execution, delivery and performance of this Agreement by it has been duly authorized by all requisite legal action; and that this Agreement has been duly executed and delivered by it and constitutes a valid and binding obligation enforceable in accordance with its terms, subject, as to enforcement, to applicable bankruptcy, reorganization, insolvency, moratorium, and other laws affecting creditors' rights generally from time to time in effect.

11.3 PHARMATOP represents and warrants that neither PHARMATOP nor any of its respective Affiliated Companies is a party to, subject to or bound by any agreement or any judgment, award, order, writ, injunction or decree of any court, governmental body or arbitrator that would conflict with or be breached by the execution, delivery or

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performance of this Agreement by it or that could prevent the carrying out of this Agreement.

11.4 PHARMATOP represents and warrants that to the best of its knowledge there is no (i) action, suit, dispute, or governmental, administrative, arbitration, or regulatory proceeding pending or threatened in writing or (ii) any investigation pending or threatened in writing against or relating to PHARMATOP, its Affiliated Companies, or their officers, general partners, and stockholders that, in either case could prevent the carrying out of this Agreement.

11.5 PHARMATOP warrants and represents that it exclusively owns or controls by agreement or license all right, title and interest in and to the Licensed Rights as defined herein and that it has the full right and authority to enter into this Agreement and to carry out the transactions contemplated herein.

11.6 PHARMATOP warrants and represents that it has no outstanding encumbrances or agreements, either written or oral, relating to the use of the Licensed Rights in the Territory, and that it has not granted nor will grant during the term of this Agreement or any renewal hereof, any similar rights, license, consent, or privilege in the Territory to any Third Party with respect to the rights granted herein.

11.7 BMS represents and warrants that BMS is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware.

11.8 BMS represents and warrants that it has full corporate power and authority to enter into this Agreement and to consummate the transactions contemplated hereby; that the execution, delivery and performance of this Agreement have been duly authorized by all requisite corporate action; and that this Agreement has been duly executed and delivered by BMS and constitutes a valid and binding obligation of BMS, enforceable in accordance with its terms, subject, as to enforcement, to applicable bankruptcy, reorganization, insolvency, moratorium, and other laws affecting creditors' rights generally from time to time in effect.

11.9 BMS represents and warrants that neither it nor any of its Affiliated Companies, is a party to, subject to or bound by any agreement or any judgment, award, order, writ, injunction or decree of any court, governmental body or arbitrator, which would conflict with or be breached by the execution, delivery or performance of this Agreement by BMS or which could prevent the carrying out of this Agreement.

11.10 BMS represents and warrants that to the best of its knowledge there is no (i) action, suit, dispute, or governmental, administrative, arbitration, or regulatory proceeding pending or threatened in writing or (ii) any investigation pending or threatened in writing against or relating to BMS, its Affiliated Companies, or their officers and stockholders that, in either case could prevent the carrying out of this Agreement.

11.11 BMS represents and warrants that all consents of Third Parties, including, without limitation, governmental authorities and non-governmental self-regulatory agencies which regulate the business of BMS, necessary to the execution and delivery of this Agreement by BMS or to its performance as of the Effective Date of the transactions contemplated hereby have been obtained and all filings with and notifications to such governmental authorities (including non-governmental self-regulatory agencies), regulatory agencies or other entities have been effected.

11.12 BMS covenants that it will use its commercially reasonable efforts such that all Products manufactured, labeled, advertised, and sold by or on behalf of BMS under this Agreement shall comply in all material respects with all applicable requirements of the U.S. Food, Drug and Cosmetic Act and all other laws and regulations applicable thereto.

11.13 Except as disclosed in ***Appendix 3*** (*re Fresenius*), PHARMATOP represents that, as of the date of full execution of this Agreement, there are, to the best of its knowledge, no Third Party patents that would materially affect BMS' ability to sell Products or PHARMATOP's ability to obtain patent protection for Licensed Rights.

11.14 The representations and warranties of the parties set forth in this Article and in Section 6.1 shall survive the termination, cancellation or expiration of this Agreement without limitation.

Article 12—Indemnification; Limitation on Liability

12.1 Subject to Sections 12.3 and 12.4, each Party hereby agrees to indemnify, defend and hold the other Party, its Affiliates, its licensees, and its and their officers, directors, employees, consultants, contractors, sublicensees and agents (collectively, the "Indemnitees") harmless from and against any and all damages or other amounts payable to a Third Party claimant (by enforceable judgement, settlement or otherwise), as well as any reasonable attorneys' fees and costs of litigation incurred by such Indemnitee as to any such Claim (as defined in this Section 12.1) until the indemnifying Party has acknowledged that it will provide indemnification hereunder with respect to such Claim as provided below, (collectively, "Damages") resulting from claims, suits, proceedings or causes of action ("Claims") brought by such Third Party against such Indemnitee based on: (a) a breach of a representation or warranty by the indemnifying Party contained in this Agreement; (b) breach of this Agreement or applicable law by such indemnifying Party; (c) negligence or willful misconduct of a Party, its Affiliates or (sub)licensees, or their respective employees, contractors or agents in the performance of this Agreement; and/or (d) breach of a contractual or fiduciary obligation owed by it to a Third Party (including without limitation misappropriation of trade secrets).

12.2 Subject to Section 12.4, BMS hereby agrees to indemnify, defend and hold harmless PHARMATOP and its directors, agents and employees from and against any and all damages and other amounts payable to a Third Party claimant (by enforceable judgement, settlement or otherwise), as well as any reasonable attorneys' fees and costs of litigation incurred by such PHARMATOP indemnitee as to any Claim (as defined below) until BMS has acknowledged that it will provide indemnification hereunder with respect to such Claim, as a result of any suits, claims, actions, and demands ("Claims") made by such Third Party against such PHARMATOP Indemnitee that are based, directly or indirectly, on the manufacture, use, or sale of any Products by BMS or its Affiliates, agents or sublicensees, except to the extent such Claims result from (a) a breach of a representation or warranty by PHARMATOP contained in this Agreement; (b) breach of this Agreement or applicable law by PHARMATOP; (c) negligence, fraud, or willful misconduct by PHARMATOP or its employees, contractors or agents; and/or (d) breach

of a contractual or fiduciary obligation owed by PHARMATOP or an of its employees or shareholders to a Third Party (including without limitation misappropriation of trade secrets), or as provided in section 6.3(a).

12.3 In the event that PHARMATOP is obligated to indemnify BMS as to a given amount for a given Claim under this Agreement or is obligated to BMS for any damages of any character for any breach of this Agreement (such damages and Claims, together, a "PHARMATOP Payment Obligation"), BMS shall only be entitled to recover from PHARMATOP with respect to such PHARMATOP Payment Obligation as follows:

(a) If such PHARMATOP Payment Obligation relates to a breach by PHARMATOP of any of its representations or warranties under this Agreement, BMS may recover directly from PHARMATOP (or, if PHARMATOP fails to meet its obligations, from its general partners) damages with respect to such PHARMATOP Payment Obligation up to an amount that does not exceed [***] of all amounts then paid to PHARMATOP by BMS pursuant to sections [***] and [***], less all amounts previously paid directly by PHARMATOP to BMS (i.e., other than by royalty offset) with respect to any other PHARMATOP Payment Obligations pursuant to this subsection (a) and pursuant to section 12.3(b). To the extent that such amount is not sufficient to cover the entire amount due BMS, BMS may recover any remaining amount due it only by offsetting and withholding the amount due against any future royalties due BMS under section 7.2 or 7.3 until such amount is paid.

(b) If such PHARMATOP Payment Obligation relates to a breach by PHARMATOP of any provisions of this Agreement other than its representations and warranties under this Agreement, BMS may recover directly from PHARMATOP (or, if PHARMATOP fails to meet its obligations, from its general partners) damages with respect to such PHARMATOP Payment Obligation up to an amount that does not exceed [***] of all amounts then paid to PHARMATOP by BMS pursuant to section [***] and [***], less all amounts previously paid directly by PHARMATOP to BMS (i.e., other than by royalty offset) with respect to any

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other PHARMATOP Payment Obligations pursuant to this subsection (b) and, to the extent relating to amounts previously paid by BMS pursuant to sections [***] and [***], with respect to any other PHARMATOP Payment Obligations previously paid directly by PHARMATOP to BMS pursuant to section [***] To the extent that such amount is not sufficient to cover the entire amount due BMS, BMS may recover any remaining amount due it only by offsetting and withholding the amount due against any future royalties due BMS under section [***] or [***] until such amount is paid.

For the avoidance of doubt, it is expressly agreed between the Parties that these limitations are intended to be cumulative to cover all PHARMATOP Payment Obligations. In other words, if monies are paid or deducted under 12.3(a) (from amounts other than payments under section 7.1), such payments or deductions reduce monies available for payment or deduction under 12.3(b), and vice-a-versa.

12.4 As used in this section 12.4, "Indemnitee" shall mean a party entitled to indemnification under the terms of Section 12.1 or 12.2. It shall be a condition precedent to an Indemnitee's right to seek indemnification under such Section 12.1 or 12.2:

(a) shall inform the indemnifying Party under such applicable Section of a Claim as soon as reasonably practicable after it receives notice of the Claim;

(b) shall, if the indemnifying Party acknowledges that such Claim falls within the scope of its indemnification obligations hereunder, permit the indemnifying Party to assume direction and control of the defense, litigation, settlement, appeal or other disposition of the Claim (including the right to settle the claim solely for monetary consideration); provided, that the indemnifying Party shall seek the prior written consent (not to be unreasonably withheld or delayed) of any such Indemnitee as to any settlement which would materially diminish or materially adversely affect the scope, exclusivity or duration of any Patents licensed under this Agreement, would require any payment by such Indemnitee, would require an admission of legal wrongdoing in any way on the part of an Indemnitee, or would amend this Agreement; and

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(c) shall fully cooperate (including providing access to and copies of pertinent records and making available for testimony relevant individuals subject to its control) as reasonably requested by, and at the expense of, the indemnifying Party in the defense of the Claim.

Provided that an Indemnitee has complied with the foregoing, the indemnifying Party shall provide attorneys reasonably acceptable to the Indemnitee to defend against any such Claim. Subject to the foregoing, an Indemnitee may participate in any proceedings involving such Claim using attorneys of its/his/her choice and at its/his/her expense. In no event may an Indemnitee settle or compromise any Claim for which it/he/she intends to seek indemnification from the indemnifying Party hereunder without the prior written consent of the indemnifying Party, or the indemnification provided under such Section 12.1 or 12.2 as to such Claim shall be null and void.

12.5 PHARMATOP represents and warrants that it is a general partnership under French law, that its general partners are Daniele Fredj and Francois Dietlin, and that under French law, each of the general partners are responsible for the liabilities of PHARMATOP.

12.6 The liability, limitation of liability, and indemnification provisions set forth in this Section 12 shall survive the termination, cancellation or expiration of this Agreement [***]

Article 13—Arbitration

13.1 Any controversy or claim arising out of or relating to this Agreement or the validity, inducement, or breach thereof, shall be settled by arbitration before a arbitration tribunal of three (3) arbitrators appointed and ruling in accordance with the Arbitration Rules of the International Chamber of Commerce Arbitration Association ("ICC") then pertaining, except where those rules conflict with this provision, in which case this provision controls. Any court with jurisdiction shall enforce this clause and enter judgment on any award. The arbitrators shall be attorneys who have at least fifteen (15) years of experience with a law firm or corporate law department of over twenty five (25) lawyers or who were a judge of a court of general jurisdiction. They shall not be a citizen of the

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United States, Mexico, Canada, or France and shall not have its usual professional office in one of these countries. They shall be selected within ten (10) days of commencement of the arbitration by common consent of Parties or if Parties fall to agree in the stated time, through selection procedures administered by the ICC. The arbitration shall be held in the city of Paris, France. Within forty-five (45) days of initiation of arbitration, the parties shall reach agreement upon and thereafter follow procedures assuring that the arbitration will be concluded and the award rendered within no more than six months from selection of the arbitrator. Failing such agreement, the ICC will design and the parties will follow procedures that meet such a time schedule.

13.2 All proceedings shall be conducted, and all documents submitted, in the English language. [***].

13.3 Each Party has the right prior to the commencement of an arbitration and, if the arbitrators cannot hear the matter within an acceptable period or can not award effective relief, during the arbitration, to seek and obtain from an appropriate court provisional remedies such as attachment, preliminary injunction, or replevin, to avoid irreparable harm, maintain the status quo or preserve the subject matter of the arbitration.

Article 14—General provisions

14.1 Any delays in or failures of performance by a Party under this Agreement shall not be considered a breach of this Agreement if and to the extent caused by occurrences beyond the reasonable control of the Party affected, including but not limited to acts of God; acts, regulations or laws of any government; strikes or other concerted acts of workers; fires; floods; explosions; riots; wars; rebellions; and sabotage.

14.2 BMS shall obtain any and all governmental approvals required to authorize, implement or enforce this Agreement or any of the terms and conditions hereof.

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14.3 No change in, addition to or waiver of any of the provisions of this Agreement shall be valid or binding unless in writing and duly executed by the Party against whom enforcement of the change, addition or waiver is sought. Any such waiver shall constitute a waiver only with respect to the specific matter described in such writing and shall in no way impair the rights of the Party granting such waiver in any other respect or at any other time.

14.4 Neither the waiver by any of the parties hereto of a breach of or a default under any of the provisions of this Agreement, nor the failure by any of the parties, on one or more occasions, to enforce any of the provisions of this Agreement or to exercise any right or privilege hereunder, shall be construed as a waiver of any other breach or default of a similar nature, or as a waiver of any of such provisions, rights or privileges hereunder.

14.5 Headings herein are for the parties' convenience only, and shall not be used to interpret this Agreement.

14.6 Except to the extent otherwise provided herein, each Party, shall bear its own expenses and costs in connection with the transactions contemplated hereby, including the preparation, execution and delivery of this Agreement and compliance herewith.

14.7 All matters affecting the interpretation, validity, performance and enforcement of this Agreement shall be governed by the laws of the state of New York (USA), without regard or giving effect to its choice or conflict of law principles other than Section 5-1401 of the New York General Obligations Law.

14.8 If any provision of this Agreement is invalid or unenforceable in any jurisdiction, the remaining provisions hereof shall remain in effect and such invalidity or unenforceability shall not affect the validity or enforceability of such provision in any other jurisdiction. The parties shall replace such ineffective provision for such jurisdiction with a valid and enforceable provision which most closely approaches the purpose of this Agreement, and in particular, the provision to be replaced.

14.9 PHARMATOP and BMS are independent contractors and shall not be deemed to be partners, joint venturers or each other's agents, and neither shall have the right to act on

behalf of the other except as expressly provided hereunder or otherwise expressly agreed to in writing.

14.10 The parties have incorporated in this Agreement all representations, warranties, covenants, commitments and understandings on which they have relied in entering into this Agreement and, except as provided for herein, neither Party has made any covenant or other commitment to the other concerning its future action. Accordingly, this Agreement, together with the appendixes and exhibits attached hereto, (i) constitute the entire agreement and understanding between the parties with respect to the matters contained herein, and there are no promises, representations, conditions, provisions or terms related thereto other than those set forth in this Agreement, and (ii) supersede all previous understandings, agreements and representations between the parties, written or oral relating to the subject matter hereof.

14.11 All communications, reports, payments and notices required by this Agreement shall be made in writing and addressed to the parties at their respective addresses set forth below or to such other address as requested by a Party by notice in writing to the other parties:

If to PHARMATOP:

SCR Pharmatop
10, square St. Florentin
78150 Le Chesnay
FRANCE
Attention: Gerant
Phone: 33-1-39-545577

If to BMS:

Bristol-Myers Squibb Company
Route 206 and Province Line Road
Princeton, New Jersey 08540-4000
Attn: President for Consumer Medicines

with a copy to the Vice President and Senior Counsel, BMS Consumer Medicines, at the same address.

All such notices, reports, payments and communications shall be deemed given or made and effective (i) when delivered personally; or (ii) when received, if sent by recognized overnight courier or by registered or certified mail, return receipt requested and postage prepaid.

14.12 In order to insure that this license can be used validly against Third Parties, extracts of this Agreement will be registered on the patent offices' registers by BMS as deemed necessary by BMS, at its expense.

[The next page is the signature page]

IN WITNESS WHEREOF, and intending to be legally bound, the parties hereto have caused this Agreement to be executed in triplicates by their duly authorized representatives as of the 23rd day of December 2002.

SCR PHARMATOP

By: /s/ Daniele Fredj
Name: Daniele Fredj
Title: Gerant

By: /s/ Francois Dietlin
Name: Francois Dietlin
Title: Gerant

BRISTOL-MYERS SQUIBB COMPANY

By: /s/ [illegible]
Name:
Title:

APPENDICES AND EXHIBITS

Appendix 1 :	Patent Related Disclosures and Documents
Exhibit A:	US Patent No. 6,028,222 issued on 22nd February 2000
Exhibit B:	International Patent Application PCT/FR 97101452, filed on 5th August 1997
Exhibit C:	International Patent Application PCT/FR01/01749, filed on 6th June 2001
Exhibit D:	D-1: Assignment Document covering the portion of the inventions covered by U.S. patent No. 6,028,222 assigned by the Inventors to Newpharm for all other countries of the world (which obtained French patent No. 2.75 1.875) and as to which Newpharm subsequently assigned the associated ongoing research and priority rights to PHARMATOP. D-2: Assignment of inventions covering U.S. patent No. 6,028,222 assigned by the Inventors to PHARMATOP for the United States
Exhibit E:	Letter from NewPharm confirming the assignment in Exhibit D
Appendix 2:	Target Product Profile
Appendix 3:	Exceptions to PHARMATOP Representations and Warranties
Appendix 4:	Guaranteed Payment Schedule
Appendix 5:	Description of Licensed Know-How

US006028222A

United States Patent [19]
Dietlin et al.

[11] **Patent Number:** **6,028,222**
[45] **Date of Patent:** **Feb. 22, 2000**

[54] **STABLE LIQUID PARACETAMOL COMPOSITIONS, AND METHOD FOR PREPARING SAME**

[75] Inventors: **Francois Dietlin,** Le Pecq.; **Daniele Fredj**, Gif-sur-Yvette, both of France

[73] Assignee: **SCR Pharmatop**, France

[21] Appl. No.: **09/051,246**

[22] PCT Filed: **Aug. 5, 1997**

[86] PCT No.: **PCT/FR97/01452**

§ 371 Date: **Jun. 5, 1998**

§ 102(e) Date: **Jun. 5, 1998**

[87] PCT Pub. No.: **WO98/05314**

PTC Pub. Date: **Feb. 12, 1998**

[30] **Foreign Application Priority Date**

Aug 05, 1996 [FR] France 96 09858

[51] **Int. Cl.**[7] **CO7C 209/90**

[52] **U.S. Cl.** **564/4**; 514/617, 564/2; 564/5; 564/6; 564/7; 564/223

[58] **Field of Search** 564/4,5,6,7, 564/2,223 514/617

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,727,064	2/1988	Pitha	514/58
4,855,326	8/1989	Fuisz	514/777
5,658,919	8/1997	Ratnaraj et al	514/269

FOREIGN PATENT DOCUMENTS

952395	9/1995	WIPO

OTHER PUBLICATIONS

XP 002045737, 1995
XP 002045739, 1985
XP 002045740, 1983
XP 002030816, 1986

Primary Examiner—Shailendra Kumar
Attorney, Agent, or Firm—Bierman, Muserlian and Lucas

[57] **ABSTRACT**

Novel stable paracetamol compositions for use in therapeutic chemistry and specifically galenic pharmacy are disclosed. The compositions contain a solution of paracetamol in an aqueous solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A water-insoluble inert gas is carefully bubbled through the aqueous solvent to remove oxygen from the medium. Said compositions may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable compositions for relieving pain.

28 Claims, No Drawings

STABLE LIQUID PARACETAMOL COMPOSITIONS, AND METHOD FOR PREPARING SAME

This application is a 371 of PCT/FR97/01452, filed Aug. 5, 1997.

FIELD OF THE INVENTION

The present invention relates to novel stable, liquid, analgesic formulations, containing paracetamol as main active ingredient, either in combination or not, with an analgesic derivative.

DISCUSSION OF THE PRIOR ART

It has been known for many years and notably from a paper of FAIRBROTHER J. E. entitled: Acetaminophen, published in Analytical Profiles of Drug Substances (1974), volume 3, pp. 1-109, that paracetamol in the presence of moisture, and all the more in aqueous solution, may be hydrolysed to yield p-aminophenol, which compound may itself be broken down into quinone-imine. The rate of decomposition of paracetamol is enhanced as the temperature is increased and upon exposure to light.

In addition, the instability of paracetamol in aqueous solution as a function of the solution's pH has been extensively described. Thus, according to a paper entitled "Stability of aqueous solution of N-acetyl-p-aminophenol" (KOSHY K. T. and LACH J.I.J. *Pharm. Sci*., 50 (1961), pp. 113-118), paracetamol in aqueous solution is unstable, a fact which primarily correlates with hydrolysis both in acidic and basic environment. This breakdown process is minimal at a pH close to 6, the half-life of the product thus degraded namely being as high as 21.8 years at 25° C.

According to Arrhenium law and knowing the specific reaction constant as determined by these authors, the time needed to observe a 5% decrease in paracetamol concentration of an aqueous solution stored at 25° C. at the optimal pH as been predicted to be 19 months. Besides hydrolysis, the paracetamol molecule separately undergoes another kind of decomposition that involves formation of a quinone-imine that may readily polymerize with generation of nitrogen-containing polymers.

These polymers and in particular those stemming from N-acetyl-p-benzoquinone-imine have been further described as being the toxic metabolite of paracetamol, which is endowed notably with cytotoxic and hemolytic effect. The decomposition of this metabolite in aqueous medium is still more complex and gives rise to p-benzoquinone and hydroquinone (D. DAHLIN, J. Med. Chem., 25 (1982), 885-886).

In the current state of the art and in view of the quality control requirements specific to pharmaceutical practice regulations, the stability of paracetamol in aqueous solutions is thus insufficient and does not allow the formulation of liquid pharmaceutical compositions for injection. As a result, the successful preparation of liquid pharmaceutical formulations for parenteral administration, based on paracetamol, has not been achieved.

A number of trials has been undertaken to slow down the decomposition of paracetamol in aqueous solution. Thus, in a paper entitled: Stabilization by ethylenediamine tetraacetic acid of amide and other groups in drug compound, (FOGG Q. G. and SUMMAN, A. M., *J. Clin. Pharm. Ther.*, 17: (1992), 107-109), it is stated that a 0.1% aqueous solution of paracetamol has a p-aminophen content resulting from hydrolysis of paracetamol, approximating 19,8% of the initial concentration of paracetamol, as observed after storage in the dark during 120 days. Addition of EDTA at a rate de 0.0075% brings down the decomposition rate to 7%. On the other hand, distilling an alkaline solution of paracetamol results in an ammonia concentration of 14%, in presence or not of 1000 ppm of ascorbic acid. Owing to its properties, ascorbic acid is indeed quite adapted to such stabilization. However, upon exposure to bright light, a paracetamol solution containing 1000 ppm of ascorbic acid does after all generate ammonia with a yield of 98%. In contrast, addition of EDTA (0.0075%) to such a solution cuts down decomposition rate, with an ammonia yield not higher than 14%.

Despite of such efforts, it has not been possible to prepare aqueous liquid solutions of paracetamol. In particular solutions for injection, having a guaranteed stability.

SUMMARY OF THE INVENTION

The present invention is aimed at solving the above stated problem in an appropriate manner. It is directed to stable pharmaceutical compositions of paracetamol in an aqueous solvent having added thereto a free radical antagonist. The aqueous solvent may be water or else aqueous mixtures containing water and a polyhydric compound such as polyethylene-glycol (PEG) 300, 400, 1000, 1540, 4000 or 8000, propylene glycol or tetraglycol. A water-soluble alcanol such as for example ethanol may also be used.

DETAILED DESCRIPTION OF THE INVENTION

Stability of the aqueous solutions mentioned above does not solely depend on the choice of a given carrier. It also depends on other variables, such as careful adjustment of pH, removal of oxygen dissolved in the carrier and addition of a free radical antagonist or a free radical scavenger.

Removal of dissolved oxygen is readily accomplished by bubbling an inert gas and preferably by bubbling nitrogen.

The appropriate free radical antagonist is chosen among the derivatives of ascorbic acid, those derivatives bearing at least a thiol functional group and straight chain or cyclic polyhydric compounds.

Preferred ascorbic acid derivatives are D- or L-ascorbic acid, an alkali metal ascorbate, an alkaline earth metal ascorbate or even still an aqueous medium-soluble ascorbic acid ester.

Free radical scavengers, bearing a thiol functional group may be an organic compound substituted by one or more thiol functional groups, of the aliphatic series such as cystein, acetylcystein, thioglycollic acid and salts thereof, thiolactic acid and salts thereof, dithlothreltol, reduced glutathion, thiourea, thioglycerol, methionine and mercaptoethane sulfonic acid.

The polyol used as a free radical scavenger is preferably a straight chain or a cyclic, polyhydroxy alcohol such as mannitol, sorbitol, inositol, isosorbide, glycerol, glucose and propylene-glycols.

Among free radical scavengers required pour stabilizing paracetamol, the ascorbic acid derivative currently preferred is sodium ascorbate. Preferred thiol functional group substituted derivatives are cystein, reduced-slate glutathion, N-acetylcystein and mercaptoethane sulfonic acid.

It may appear as convenient to combine several free radical scavengers as far as they are water-soluble and mutually compatible. Especially convenient free radical scavengers are mannitol, glucose, sorbitol or even glycerol.

These may be readily combined.

It may appear as convenient to add to the preparation one or a number of complexing agents to improve stability of the molecule since the active ingredient is sensitive to the presence of trace metals that eventually speed up its decay.

Complexing agents are exemplified by nitrilotriacetic acid, ethylene diamino tetraacetic acid, ethylene diamino, N, N'-diacetic-N, N'-dipropionic acid, ethylene diamino tetraphosphonic acid, 2,2'-(ethylene diamino)dibutyric acid, or ethylene-glycol bis(diaminoethyl ether) N,N,N',N'-tetraacetic acid and sodium or calcium salts thereof.

The complexing agent also acts to complex bivalent ions (copper, zinc, calcium) that may be present and that have a negative influence of the aging of the formulation throughout storage.

The gas that is bubbled into the solution to drive out oxygen, may be nitrogen or carbon dioxide or still an inert gas. Nitrogen is favoured.

Isotonicity of the preparation may be achieved by adding an appropriate quantity of sodium chloride, glucose, levulose or postassium chloride, or calcium chloride, or calcium gluconoglucoheptonate, or mixtures thereof. The preferred isotonizing agent is sodium chloride.

The buffer used is a buffer compatible with parenteral administration in humans, the pH of which may be adjusted between 4 and 8. Preferred buffers are based on alkali metal ou alkaline earth metal acetates or phosphates. A more preferred buffer is sodium acetate/hydrogene phosphate adjusted to the required pH with hydrochloric acid or sodium hydroxide. The concentration of such a buffer may be comprised between 0.1 and 10 mg/ml. The preferred concentration is confined in the range of 0.25 to 5 mg/ml.

On the other hand, preparations for injection have to be sterile and should lend themselves to heat treatment sterilization. It is known that in certain conditions, antioxidants such as glutathion are broken down]FIALAIRC A. et al., *J. Pharm. Biomed. Anal.*, vol. 10, No 6, pp. 457-460 (1992)]. The breakdown of reduced glutathion during heat treatment sterilization ranges from 40 to 77% depending on the selected temperature conditions. During such sterilization procedures, it is convenient to employ means capable of preserving the integrity of these antioxidants. Addition of complexing agents to aqueous solutions inhibits thermal decomposition of thiol derivatives, such as glutathion.

Liquid pharmaceutical compositions according to the invention are preferably compositions intended for injection. The paracetamol content of the solution may range from 2 mg/ml to 50 mg/ml in case of so called dilute solutions, i.e. that can be directly infused by intravenous route and from 60 mg/ml to 350 mg/ml where so-called concentrated solution are considered, i.e. either intended for direct injection by intravenous or intramuscular route, or intended to be diluted prior to slow infusion administration. The preferred concentrations are comprised between 5 and 20 mg/ml for dilute solutions and between 100 and 250 mg/ml for concentrated solutions.

Pharmaceutical compositions according to the invention may further contain another active ingredient that enhances the specific effect of paracetamol.

In particular, the pharmaceutical compositions according to the invention may contain a CNS-acting analgesic such as for example a morphinic analgesic.

The morphinic analgesic is selected among the morphinic derivatives of natural, semi-synthetic or synthetic origin and piperidine derivatives selected from the following list, which is no way intended to be exhaustive: buprenorphine, dramadol, codeine, dextromoramide, dextropropoxyphene, hydrocodone, hydromorphone, ketobemidone, levomethadone, levorphanol, meptazinol, methadone, morphine, nalbuphine, nicomorphine, dizocine, diamorphine, dihydrocodeine, dipipanone, methorphane, dextromethorphane.

Preferred morphinic derivatives are codeine sulfate or morphine hydrochloride.

The codeine or codeine derivative concentration, expressed in terms of codeine base, is comprised between 0.2% and 25% in relation to the paracetamol content. The preferred codeine derivative is codeine sulfate. The concentration thereof is set between 0.5 and 15% in relation to the paracetamol content.

The morphine or morphine derivative concentration, expressed in terms of morphine base, is comprised between 0.05 and 5% in relation to the paracetamol content. The preferred morphine derivative is morphine hydrochloride the concentration of which is preferably set between 0.5 and 15% in relation to paracetamol content.

The compositions according to the invention may further have added thereto an anti-inflammatory agent such as of the of AINS type and in particular a phenylacetic acid compound. Such agents are exemplified by ketoprofen, flurbiprofen, tiaprofenic acid, niflumic acid, diclofenac or naproxen.

Compositions according to the invention may in addition incorporate an antiemetic either a CNS-acting neuroleptic such as haloperidol or chlorpromazine or metopimazine or of the gastrokinetic-mediated type such as metochlopramide or domperidone or even a serotoninergic agent.

Compositions in accordance with the invention may further incorporate an anti-epileptic drug such as sodium valproate, clonazepam, carbamazepine or phenytoin.

It may also be possible to combine paracetamol with a corticosteroid such as for example prednisone, prednisolone, methyl prednisone, dexamethasone, betametasone or an ester thereof.

Paracetamol can further be combined with a tricyclic antidepressant such as amitriptiline, imipramine, clomipramine.

Anti-inflammatory agents may be included in concentrations ranging from 0.100 g to 0.500 g per 1000 ml of formulated product.

In Case of Concentrated Solutions

The water content expressed in percentage is preferably in excess of 5% of the total volume and more preferably comprised between 10 and 65%.

The quantity of propylene glycol formulated in percentage is preferably in excess of 5% and more preferably comprised between 20 and 50%.

The PEG used is preferably PEG 300, PEG 400, PEG 1000, PEG 1540 or PEG 4000. Concentrations used are comprised between 10 and 60% in weight. PEG 300 and PEG 400 are further preferred. Preferred concentrations range from 20 to 60%.

Ethanol concentrations range from 0 to 30% of total volume and preferably range from 0 to 20%.

Tetraglycol concentrations used do not exceed 15% to allow for maximal quantities that can daily be received by parenteral administration viz 0.7 ml/kg of body weight.

Glycerol concentration varies from 0.5 to 5% as a function of the viscosity of the medium suitable for use depending on the administrative route.

In Case of Dilute Solutions

The quantity of water used given in percentage is preferably in excess of 20% of the total volume and preferably is comprised between 25 and 100%.

The quantity of propylene-glycol employed given in percentage is preferably comprised between 0 and 10%.

The PEG used is preferably PEG 300, PEG 400, or PEG 4000 with PEG 4000 being most preferred. Preferred concentrations range from 0 to 10%. Tetraglycol concentrations used do not exceed 5%. In preference, they are comprised between 0 and 4%.

The ascorbic acid or ascorbic acid derivative concentration which is used is preferably more than 0.05 mg/ml and more desirably, comprised between 0.15 mg/ml and 5 mg/ml. Higher quantities may indeed be used, without exceeding the solubility limits. Higher ascorbic acid or ascorbic acid derivative concentration are administered to human beings for prophylactic or therapeutic purposes.

Thiol derivative concentration is comprised between 0.001% and 30% and more desirably, comprised between 0.005% and 0.5% for dilute solutions, and between 0.1% and 20% for concentrated solutions.

The pH of the solution is desirably adjusted taking into consideration the optimal stability of paracetamol in aqueous solution, i.e. at a pH around 6.0.

The thus prepared composition may be packaged in glass sealed vials, or in stoppered glass vials or in bottles made of a polymer material such as polyethylene, or in soft material bags made from polyethylene, polyvinyl chloride or polypropylene.

The composition may be sterilized by heat treatment, for example at 121° C. during 20 minutes or else by sterile filtration.

Currently preferred compositions in accordance with the invention have the following ingredients:

Concentrated solutions

Ingredient	Injection solution of paracetamol alone (per ml)	Injection solution of paracetamol associated to a morphinic compound (per ml)	
		Codeine	Morphine
paracetamol	0.160 g	0.160 g	0.160 g
Codein sulfate.3H_2O	—	0.0036 g	—
Morphine hydrochloride.3H.$_2$O	—	—	0.00037
Propylene glycol	0.270 ml	0.270 ml	0.270 ml
PEG 400	0.360 ml	0.360 ml	0.360 ml
Sodium acetate	0.002 g	0.002 g	0.002 g
Reduced glutathion	0.002 g	0.002 g	0.002 g
Hydrochloric acid 1 N	q.s. pH 6.0*	q.s. pH 6.0*	q.s. pH 6.0*
Water for injection	q.s. 1000 ml	q.s. 1000 ml	q.s. 1000 ml
Nitrogen	q.s.f. bubbling	q.s.f. bubbling	q.s.f. bubbling

The pH specified above is the actual pH that has been measured by a pH-meter after obtaining a 5 fold dilution of the solution with distilled water. It will be noted that the apparent pH of the pure solution is different.

Using this solution composed of a solvent mixture constituted by 30% of propylene-glycol, by 40% of polyethylene-glycol 400 and by 30% of water (solution no 20), it is possible to dissolve about 200 mg/ml of paracetamol at 20° C. Choosing a concentration of 160 mg/ml allows one to be sure that no recristallization will occur, notably at low temperatures. In such situations, a volume of 6,25 ml of said solution contains 1000 mg of paracetamol.

Dilute solutions

Ingredient	Injection solution of paracetamol alone (per ml)	solution of paracetamol associated to codein (per ml)	
		Such morphinic compound is codein	Such morphinic compound is morphine
paracetamol	0.0125 g	0.125 g	0.125 g
Codein sulfate. 3H.$_2$O	—	0.00018 g	—
Morphine hydrochloride. 3H_2O	—	—	0.000019 g
Mannitol	0.025 g	0.025 g	0.025 g
Sodium hydrogen phosphate dihydrate	0.0025 g	0.00025 g	000025 g
Sodium chloride	0.002 g	0.002 g	0002 g
Disodium ethylene diamino tetraacetate	0.0001 g	0.0001 g	0.0001 g
Hydrochloric acid or sodium hydroxide	q.s. pH 5.5	q.s. pH 5.5	q.s. pH 5.5
Water for injection	q.s.f. 1000 ml	q.s.f. 1000 ml	q.s.f. 1000 ml
Nitrogen	q.s.f. bubbling	q.s.f. bubbling	q.s.f. bubbling

The compositions according to the invention find therapeutic applications as pain relief drugs. For moderate pain, the solutions merely contain paracetamol. For acute pain, the solutions further contain a morphinic analgesic. Furthermore, the paracetamol solutions exert antipyretic activity.

The following examples are given by way of illustration and not by limitation.

EXAMPLE I

Determination of the Optimal Solvent Mixture

1.1 Concentrated solutions

Increasing quantities of paracetamol were introduced in the solvent mixtures. The dissolution rate of paracetamol increases with rise in temperature, so that the solubility tests in the individual media were run by heating the solvent mixture to 60° C. After dissolution was judged complete, the solutions were stored for 72 hours either at 25° C. or 4° C.

The solubility values are listed in the following table:

Test a*	Water (ml)	Propylene glycol (ml)	PEG 400 (ml)	Ethanol	Tetraglycol (ml)	Solubility at +4° C. (mg/ml)	Solubility at +25° C. (mg/ml)
1	0.3	0.4	0.3	—	—	110	130
2	0.4	0.3	0.3	—	—	110	130
3	0.16	0.3	0.4	—	0.15	190	230
4	0.5	—	0.5	—	—	110	150
5	0.4	0.3	0.2	0.1	—	<110	120
6	0.5	0.3	0.1	0.1	—	<100	130
7	0.4	0.4	0.1	0.1	—	<100	150
8	0.5	0.3	0.2	—	—	<100	120
9	0.6	0.3	0.2	—	—	<100	<100
10	0.5	0.4	0.1	—	—	<100	<100
11	0.55	0.3	0.05	0.1	—	<100	<100
12	0.45	0.4	0.05	0.1	—	<100	120
13	0.65	0.3	0.05	—	—	<100	<100
14	0.55	0.3	0.05	—	—	<100	<100
15	0.4	0.4	0.2	—	—	<100	<150
16	0.45	0.45	0.1	—	—	<100	<100
17	0.4	0.2	0.4	—	—	160	200
18	0.5	0.2	0.3	—	—	160	160
19	0.5	0.1	0.3	—	—	100	190
20	0.3	0.3	0.4	—	—	190	200
21	0.3	0.3	0.35	—	0.15	160	210
22	0.25	0.25	0.35	—	0.15	170	220

The solubility values of the solvent mixtures do not increase in a consistent manner with increasing temperature. Solubility is not enhanced if ethanol is added.

In addition, due to oversaturation phenomena which are observed in such solutions, notably in media containing PEG, a delayed recristallization was noted subsequent to cooling. In these conditions, the solutions under study were kept for 14 days at 20° C., then there was added, to the solutions displaying no cristals following this time interval, a paracetamol germ cristal in order to elicit cristallization of potentially oversaturated solutions. Finally, it was found that solutions no 20 and no 3 have the highest solubility with respect to paracetamol, which threshold was comprised between 160 mg/ml and 170 mg/ml depending on temperature.

1.2 Dilute solutions

Paracetamol is quantities well exceeding the solubility threshold was introduced in the solvent mixtures previously warmed to 30° C. After stirring and cooling at 20° C., the solutions were filtered. The paracetamol content of these solutions was determined by reading the absorbance at 240 nm of a 1:200 dilution of the filtrate.

The results are recorded in the following tables.

	concentration of paracetamol (mg/50 ml)
Water	720
5% Glucose	710
4.82% levulose	730
7% mannitol	680
5% sorbital	685
0.9% sodium chloride	615
10% Calcium gluconoglucoheptonate	670
Lestradet's solution (5% glucose, 0.2% sodium chloride, 0.15% potassium chloride, 1.1% calcium gluconoglucoheptonate)	730
Ringer's solution (0.7% sodium chloride, 0.1% potassium chloride, 0.1% sodium chloride)	730
Ringer's solution-Phosphate (0.7% sodium chloride, 0.182% monopotassium phosphate, 0.182% calcium chloride)	710
Ringer's solution-acetate (0.7% sodium chloride, 0.131% potassium acetate 0.013% calcium chloride)	715
Urea 0.3 M	725
Type of solution (the following solutions were prepared in Ringer's solution)	
Pure Ringer's solution	735
4.0% PEG 4000 + 1.0% propylene-glycol + 0.5% ethanol	905
4.0% PEG 4000 + 1.0% propylene-glycol + 1.0% ethanol	905
4.0% PEG 4000 + 1.0% propylene-glycol + 2.0% ethanol	930
Type of solution (the following solutions were prepared in 0.9% sodium chloride solution)	
0.9% sodium chloride	615
+0.6% tetraglycol	640
+1.2% tetraglycol	680
+3.0% tetraglycol	720
1.0% PEG 4000	630
1.0% PEG 4000 + 0.6% tetraglycol	660
1.0% PEG 4000 + 1.2% tetraglycol	710
3.0% PEG 4000 + 2.0% tetraglycol	950

Paracetamol solubility is increased by the presence of PEG.

Solubilities of paracetamol in mixtures of PEG 4000 and 0.9% sodium chloride solutions were determined in distilled water, at concentrations ranging from 0 to 7%, as a function of temperature.

The results are given in the following table:

PEG 4000 concentration (%/vol.) in 0.9% sodium chloride solution	Solvent volume (ml) required to dissolve 1000 mg of paracetamol as a function of temperature				
	4° C.	17° C.	22° C.	30° C.	42° C.
0%	130	92	80	65	42
1%	99	78	67	63	47
2%	91	72	63	59	45
3%	80	64	56	54	41
4%	82	62	57	49	36
5%	79	59	51	46	34
7%	78	61	48	42	30

4.1 Concentrated solution

Ingredient	Quantity	
	Solution without nitrogen bubbling	Solution subjected to nitrogen bubbling
Paracetamol	0.160 g	0.160 g
Propylene-glycol	0.270 ml	0.270 ml
PEG 400	0.360 ml	0.360 ml
Sodium hydroxide or HCl 1N	q.s. pH 6.0	q.s. pH 6.0
Nitrogen	none	q.s.f. purging and filling

Water for injection	q.s.f 1000 ml	q.s.f. 1000 ml

Solution 20 containing paracetamol in a quantity of 160 mg/ml, adjusted to pH 6.0 by sodium hydroxide or hydrochloric acid 1N, was either subjected or not subjected to nitrogen gas bubbling. Tightly stoppered and capped vials packed by dispensing 10 ml of such solutions under nitrogen atmosphere or air, were sterilized by autoclaving at 121° C. during 20 minutes. The percentage of secondary peaks was then measured by liquid chromatography with respect to the main peak of paracetamol, as well as was the pink color strength by reading the solution absorbance by absorption spectrophotometry at peak absorbance wavelength, that is 500 nm.

Results

Solution tested	Secondary peaks in % of main peak of paracetamol	absorbance of the solution at 500 nm
Autoclaved solution packed without nitrogen	0.054	0.08
Autoclaved solution packed under nitrogen	0.036	0.03

It is therefore seen that the difference in color of the solution packed under nitrogen is very striking.

In order to check if 0% and 1% PEG-paracetamol solutions remain clear under cold storage, the following solutions ere prepared:

Ingredient	Solution without PEG	Solution with PEG added
Paracetamol	1 g	1 g
PEG 4000	—	1 g
0.9% Sodium chloride solution in water for injection	0.036	0.03
	q.s. 125 ml	q.s. 100 ml

After storage of these solutions at 4° C. during 10 days, none of the vials tested showed cristallization. Presence of PEG is therefore not mandatory if the solutions are to remain clear throughout the time interval studied.

EXAMPLE II

Tests Conducted for Characterizing Paracetamol Breakdown in Solution

2.1 Demonstrating paracetamol instability in solution

A paracetamol solution in water or in solution no 20 shows rapidly a pink color upon exposure to light or storage at high temperature. At 50° C., color development occurs in 2 weeks time. Appearance of such color tinge correlates with an increase in solution absorbance at a peak absorbance wavelength of 500 nm. According to the paper of Fairbrother mentioned above, exposure of paracetamol to moisture can result in hydrolysis with formation of para-aminophenol, followed by oxydation, with appearance of a pink color, typical of the production of quinoneimine.

2.2 Identifying the breakdown products of paracetamol

In aqueous or partially aqueous solutions, p-aminophenol is not detected during storage. Rapid production of colored products having a pink tinge is noted, the reaction rate being a function of temperature and light. In course of time, such derivatives are increasingly dark and evolutes to brown color.

All occurs as if, in contrast to what has been reported in the literature, the breakdown of paracetamol first involves an oxydative process followed by hydrolysis. According to this theory, paracetamol may react with an oxidant present in solution, for example oxygen dissolved in the aqueous layer. This mechanism may involve the production of free radicals resulting in molecular coupling, a fact that may account for the production of colored derivatives evoluting in color from pink to brown.

2.3 Tests for demonstrating inhibition of free radical production

A typical reaction involving the production of free radicals involves adding a 30% aqueous solution of hydrogen peroxide and a copper pentahydrate solution at a concentration of 62.5 mg/ml, to a 1.25% aqueous solution of paracetamol. In a matter of minutes, there develops a color reaction resulting in a color shift from yellow to dark brown. The color intensity observed decreases if free radical scavengers or glycerol are prior added to the paracetamol solution. Color intensity is a function of type of the type of free radical scavenger added, in the following decreasing order as judged by color intensity.

Paracetamolalone>paracetamol+N-acetylcystein>paracetamol+cystein>paracetamol+sorbitol>paracetamol+mannitol> paracetamol+glycerol.

EXAMPLE III

Stabilizing paracetamol solution by selecting the pH that allows maximal stability

3.1 Concentrated solution

Ingredient	Quantity
Paracetamol	0.160 g
Propylene-glycol	0.270 ml
PEG 400	0.360 ml
Sodium hydroxide 1N or Hydrochloric acid 1N q.s.f.	pH 7.0-8.0-9.0-9.5-10.0 corresponding to actual pH: pH 5.8-6.7-7.1-7.5-8.0-8.5
Nitrogen q.s.f.	purging and filling
Water for injection	q.s. 1000 ml

Solution 20 containing paracetamol in a concentration of 160 mg/ml was adjusted to different pH's: the apparent pH is given in comparison to actual pH (between parenthesis) after a 5 fold-dilution: 7,0 (5,8)-8,0 (8,7)-8,5 (7,1)-9,0 (97,5)-9,5 (8,0)-10.0 (8,5) using a sodium hydroxide or normal hydrochloric acid solution. Vials that had been filled under nitrogen atmosphere by dispensing 10 ml of such solutions, tightly stoppered and capped, were sterilized by autoclaving at 121° C. for 20 minutes, and then in every case exposed, either to a temperature of 105° C. in the dark for 72 hours, or to a radiation of an actinic light at 5000° K. and 25° C. during 264 hours.

Results

After autoclaving, only the solution adjusted to pH 10 shows a pink tinge. After storage at 105° C. for 72 hours, absorbance at 500 nm as well as the concentration of breakdown products of paracetamol were minimal in the pH range from 7,5 to 9,5. Upon storage in the presence of light, the color strength is enhanced as the pH is increased. Color development is extremely weak at pH 7,0 (actual pH 5,8). Neither the paracetamol content, nor the breakdown products are affected by pH.

3.2 Diluted solution

Ingredient	Quantity
Paracetamol	0.008 g
Sodium chloride	0.0067 g
Disodium phosphate dihydrate	0.0012 g
5% Citric acid q.s.f.	pH 5.0-6.0-7.0
Nitrogen q.s.f.	bubbling and filling

Water for injection	q.s.f. 1000 ml

The aqueous solution diluted and buffered having a paracetamol content of 8 mg/ml was adjusted to different pH values: pH 5,0-7,0 using a citric acid solution.

Vials that had been packed under nitrogen atmosphere by dispensing 10 ml of such solution, were tightly stoppered and capped, sterilized by autoclaving at 121° C.

for 20 minutes, and then in every case exposed to 70° C. in the dark during 231 hours.

Results

Following autoclaving, only the solution adjusted to pH 7 shows a pink color. After storage, this same solution displays the brightest pink color. At pH 6,0 and 5,0 the solutions are faintly colored.

EXAMPLE IV

Stabilization of Paracetamol in Solution by Oxygen Removal Through Nitrogen Bubbling

4.2 Diluted solution

Solution Tested

Ingredient	Quantity	
	Solution without nitrogen bubbling	Solution subjected to nitrogen bubbling
Paracetamol	0.008 g	0.008 g
Sodium chloride	0.008 g	0.008 g
Disodium phosphate dihydrate	000.1 g	0.001 q
5% Citric acid	q.s.f. pH 6.0	q.s.f. pH 6.0
Nitrogen	none	q.s.f. purging and filling
Water for injection	q.s.f. 1000 ml	q.s.f. 1000 ml

The diluted aqueous solution containing paracetamol is adjusted to pH 6,0 by means of a citric acid solution.

Vials that had been filled under a nitrogen atmosphere by dispensing 10 ml of such solutions, were tightly stoppered and capped and then stored inside an incubator at 98° C. for 15 hours.

The percentage of secondary peaks in relation to the main peak of paracetamol was measured by liquid chromatography, so was the pink color strength by reading the solution absorbance by absorbance spectrophotometry at a peak absorption wavelength, that is 500 nm.

Results

Solution tested	Secondary peaks in % of paracetamol main peak	Solution absorbance at 500nm
Solution packed without nitrogen atmosphere	1.57	0.036
solution packed under nitrogen atmosphere	0.44	0.016

The pink color of the solution packed under nitrogen atmosphere is considerably tainter than that observed for the solution obtained after sterilization under nitrogen of the solution packed without nitrogen.

EXAMPLE V

Stabilizing Solutions of Paracetamol by Adding Free Radical Antagonists

5.1 Concentrated solution

Ingredient	Quantity
Paracetamol	0.160 g
Propylene-glycol	0.270 ml
PEG 400	0.360 ml
Hydrochloric acid 1N Or NaOH 1N q.s.f.	pH 6.0
Free radical scavenger (see quantitative results)	q.s.f. (see quantitative results)
Nitrogen q.s.f.	purging and filling
Water for injection	q.s.f 1000 ml

The solutions thus prepared are divided in 10 ml capacity vials, stoppered with a Bromobutyl stopper and capped with an aluminium cap. After autoclaving at 121° C. for 20 minutes, the vials were stored for 48 hours, either in the presence of actinic light at 5500° K. at room temperature or at 70° C. in the dark. The preparation was examined for any change in color.

Results

Free radical scavenger	Concentration	Appearance of the solution upon exposure to light Color intensity	Appearance of solution at 70° C. Color intensity
No scavenger	—	pink (+)	pink (++)
Sodium disulfite	0.295 mg/ml	colorless	Colorless
Sodium ascorbate	1.0 mg/ml	yellow (+)	yellow (+)
Reduced glutathion	1 mg/ml	colorless	colorless
Reduced glutathion	8 mg/ml	colorless	colorless
Cystein hydrochloride	1 mg/ml	cloudy	cloudy
a-monothioglycerol	1 mg/ml	colorless	colorless
Dithiothreitol	1 mg/ml	colorless	colorless
Mannitol	50 mg/ml	colorless	colorless

5.2 Dilute solution

Solutions tested

	Quantity		
	Formulation A	Formulation B	Formulation C
Paracetamol	0.008 g	0.01 g	0.0125 g
Sodium chloride	0.008 g	0.008 g	0.00486 g
Disodium phosphate dihydrate or sodium acetate	0.001 g	0.001 g	0.00125 g
Hydrochloric acid	q.s. pH 6.0	q.s. pH 6.0	q.s pH 5.5
C.R.L.	q.s (see quantitative results)		
Nitrogen q.s.f.	purging and filling		
Water	q.s.f. 1000 ml		

The solutions thus prepared were divided in 10 ml, 100 ml or 80 ml capacity vials, stoppered with a Bromobutyl stopper and capped with an aluminium cap. The preparation was examined for any pink color development.

After autoclaving at 121° C. for 20 minutes, the vials were stored for 48 hours, either in the presence of actinic light at 5500° K. at room temperature or at 70° C. in the dark (formula A).

After autoclaving at 124° C. for 7 minutes, the vials were stored for 48 hours at room temperature in the dark (formulation B and C). The preparation was examined for any pink shift and the paracetamol as well as CRL were measured where a thiol derivative was used.

Results (CRL=free radical scavenger)

C.R.L used	Concentration	Solution appearance upon exposure to light: color	Solution appearance upon exposure to light: strength	Solution appearance at 70°: Color	Solution appearance at 70°: strength
No C.R.L	—	pink	(+)	pink	(++)
Thiourea	0.5 mg/ml	colorless		colorless	
Dithiothreitol	1 mg/ml	colorless		colorless	
a-monothio-glycerol	1 mg/ml	colorless		colorless	
gluthathion	1 mg/ml	colorless		colorless	
Sodium	0.2 mg/ml	pink	(+)	pink	(+)
ascorbate	0.4 mg/ml	colorless		yellow	(+)
	0.6 mg/ml	pink	(+)	yellow	(+)
	1.0 mg/ml	colorless		yellow	(+)
Cystein	0.05 mg/ml	colorless		colorless	
hydrochloride	0.1 mg/ml	colorless		colorless	
	0.25 mg/ml	colorless		colorless	
	0.5 mg/ml	colorless		colorless	
	0.75 mg/ml	colorless		colorless	
	1 mg/ml	colorless		colorless	
	2 mg/ml	colorless		colorless	
	5 mg/ml	colorless		colorless	

C.R.L. used	Concen-tration	Solution appearance: color	Solution appearance: strength	Dosage (in % of theoretical volume): C.R.L.	Dosage (in % of theoretical volume): para-cetamol
Cystein hydrochloride monohydrate	0.2 mg/ml	colorless		80%	99.2%
Cystein hydrochloride monohydrate	0.5 mg/ml	colorless		95%	99.6%
N-acetylcystein	0.2 mg/ml	colorless		88%	99.2%
Mannitol	20 mg/ml	colorless			
Mannitol	40 mg/ml	Colorless			
Mannitol	50 mg/ml	Colorless			
Glucose	50 mg/ml	Colorless			

EXAMPLE VI

Stabilization of Solutions of Paracetamol Containing a Morphinic Compound by Addition of a Free Radical Scavenger

6.1 Concentrated solution

Solutions tested

Ingredient	Quantity
Paracetamol	0.160 g
Codein phosphate	0.008 g
Propylene-glycol	0.270 ml
PEG 400	0.360 ml
Hydrochloric acid 1N q.s.	q.s. pH 6.0
Free radical scavenger	q.s. (see quantitative results)
Water for injection	q.s.f. 1000 ml

The solutions thus prepared were divided in 10 ml capacity vials, stoppered with a Bromobutyl stopper and capped with a removable aluminium cap. After autoclaving at 121° C. for 20 minutes, the vials were stored for 48 hours either under actinic light at 5500° K. at room temperature, or at 70° C. in the dark. The preparation was inspected for any change in color.

Results

Free radical scavenger	Concentration	Solution apperance upon exposure to light: color	Solution apperance upon exposure to light: strength	Solution apperance 70° C: color	Solution apperance 70° C: strength
No free radical scavenger	—	pink	(+)	pink	(++)
Sodium disulfite	0.295 mg/ml	yellow	(+)	yellow	(++)
Sodium ascorbate	1.0 mg/ml	yellow	(++)	yellow	(+++)
reduced glutathion	1 mg/ml	yellow		amber yellow	(+++)
	8 mg/ml	colorless		yellow	(++)
	16 mg/ml	colorless	(+)	yellow	(+)
Dithio-threitol sodium hypo-phosphite	1 mg/ml	violet pink	(+++)	violet pink	(++++)
	5mg/ml	pink	(+)	pink	(++)

6.2 Dilute solutions

Solutions tested

Ingredient	Quantity
Paracetamol	0.008 g
Codein phosphate	0.0004 g
Sodium chloride	0.008 g

Disodium phosphate dihydrate	0.0015 g
Hydrochloric acid	q.s.f. pH 6.0
Free radical scavenger	q.s. (see results)
Nitrogen q.s.f.	purging and filling
Water for injection	q.s.f. 1000 ml

The solutions thus prepared were divided in 10 ml capacity vials, stoppered with a Bromobutyl stopper and capped with an aluminium cap. After autoclaving at 121° C. for 20 minutes, the vials were stored for 48 hours, either under actinic light at 5500° C. at room temperature, or at 70° C. in the dark. The preparation was examined for any change in color.

For the solution not containing any free radical scavenger and for the solution containing 0.5 mg/ml of cystein hydrochloride as free radical antagonist, paracetamol as well as codein are measured by high performance liquid chromatography, immediately after autoclaving, in comparison with identical solutions not subjected to autoclaving.

Appearence scoring of the solutions

Free radical scavenger	Concentration	Solution apperance upon exposure to light		Solution apperance 70° C	
		color	strength	color	strength
No free radical scavenger	—	pink	(+)	pink	(+)
Sodium disulfite	0.295 mg/ml	colorless		colorless	
Dithio-threitol	0.5 mg/ml	colorless		colorless	
Monothio-glycerol	0.5 mg/ml	grey		grey	
Reduced glutathion	2.0 mg/ml	colorless		colorless	
N-acetylcystein	2.0 mg/ml	grey	(+)	grey	(+)
Cystein hydro-chloride	0.05 mg/ml	colorless		pink	
	0.1 mg/ml	colorless		colorless	
	0.25 mg/ml	colorless		colorless	
	0.5 mg/ml	colorless		colorless	
	0.75 mg/ml	colorless		colorless	
	1.0 mg/ml	colorless		colorless	
	2.0 mg/ml	colorless		colorless	
	5.0 mg/ml	colorless		colorless	(+)

Assay results of paracetamol and codein

Solution tested	Ingredient assayed	non sterilized solution	after sterilization
Solutions with no free radical scavenger added	paracetamol	0.0078 g/ml	0.0077 g/ml
	codein	0.00043 g/ml	0.00042 g/ml
Solution containing 0.5 mg/ml of cystein hydrochloride	paracetamol	0.0082 g/ml	0.0081 g/ml
	codein	0.00042 g/ml	0.00042 g/ml

There is noted the lack of color development one one hand and excellent preservation of the active ingredients after heat treatment sterilization on the other hand.

EXAMPLE VII

Biological Tolerance to the Preparation

7.1 Hematological tolerance

Tested solutions

Ingredient	Quantity
Paracetamol	0.160 g
Propylene-glycol	0.270 ml
PEC 400	0.360 ml
Nitrogen q.s.f.	purging and filling
Water for injection	q.s.f. 1000 ml

The solution pH was not adjusted. The apparent pH is 7.6, corresponding to an actual pH of 6.5.

Whole human blood is incubated with the solution under study, in equal proportions by volume. 2 ml were drawn at 10 minutes intervals and centrifuged for 5 minutes at 5000 rpm. 100 .mu.l of the supernatant were diluted in 1 ml of distilled water. The absorbance of this solution was determined against a water blank at 540 nm, peak absorption wavelength of hemoglobin.

The study was run in comparison with a negative control (physiological saline) and a positive control (pure water for injection).

Results

The absorbances of the individual solutions after different incubation periods are provided in the following table.

Solution	TO	10 min	20 min	30 min	40 min	50 min	60 min
Water p.p.i	2.23	2.52	2.30	2.37	2.38	2.33	2.36
Physio-logical saline	0.04	0.05	0.05	0.05	0.04	0.05	0.04
Sol. Tested	0.09	0.19	0.27	0.25	0.24	0.24	0.25

7.2 Muscular tolerance

Solution tested

Ingredient	Quantity
Paracetamol	0.160 g
Propylene-glycol	0.270 ml
PEG 400	0.360 ml
Nitrogen q.s.f.	purging and filling
Water for injection	q.s.f. 1000 ml

The pH of this solution was not adjusted. Apparent pH is equal to 7,6.

Sprague-Dawley rats, weighing between 260 g and 450 g were anesthesized with an i.p. injection of ethyl carbamate (2 ml/kg of a 50% aqueous solution). The extensor digitorum longus muscle was dissected from the right or left hind leg, and placed in buffer medium having the following composition:

Ingredient	Quantity
Sodium chloride	6.8 g
Potassium chloride	0.4 g
Dextrose	1.0 g
Sodium bicarbonate	2.2 g
Phenol red (sodium salt)	0.005 g
Distilled water q.s.f.	1 liter
Hydrochloric acid 1N q.s.f.	pH 7.4

The muscle is transiently fixed to a board and maintained in position by tendons. The test product was injected in an amount of 15 .mu.l by means of a 25 .mu.l-capacity Hamilton seringe no 702. The muscle is then placed over a grit and immersed in the buffer solution kept at 37° C. with carbogen bubbling throughout the incubation period. At 30 minutes intervals, the muscles were introduced in a tube containing fresh buffer at 37° C. The procedure was repeated 4 times. The buffer solution hence incubated is assayed for creatine kinase activity.

The study was run in parallel with:

muscle alone not subjected to injection (blank)

needle alone (introducing the needle without product injection)

physiological saline

Triton X-100 solution (negative controls)

solution 20

solution 20+paracetamol 160 mg/ml.

Creatine kinase was measured using a Hitachi 704 model analyzer in conjunction with a reagent kit sold under tradename high performance Enzyline CK NAC 10 (Biomerieux).

Results

The creatine kinase activity (IU/l) of the individual solutions after variable incubation periods are provided in the table given hereinafter:

Solution tested	30 min	60 min	90 min	120 min	Total
Muscle alone	23 .±. 6	24 .±. 12	15 .±. 7	13 .±. 5	75
Needle alone	35 .±. 6	33 .±. 10	20 .±. 4	18 .±. 7	106
Physiological saline	30 .±. 6	10 .±. 12	17 .±. 6	23 .±. 4	100
Triton-X	1802 .±. 2114	1716 .±. 978	155 .±. 89	289 .±. 251	14962
Solution 20 (excipients)	71 .±. 24	89 .±. 40	39 .±. 27	62 .±. 39	261
Solution 20 + paracetamol	141 .±. 40	150 .±. 60	68 .±. 63	34 .±. 24	393

No necrosis signs were recorded using the composition according to the invention as no significant difference between the results of test and excipient solutions was noted.

What is claimed is:

1. A stable, liquid formulation consisting essentially of acetaminophen dispersed in an aqueous medium containing a buffering agent and at least one member of the group consisting of a free radical scavenger and a radical antagonist.

2. The formulation of claim 1 wherein the aqueous medium has been deoxygenated by bubbling a water-insoluble inert gas.

3. The formulation of claim 1 wherein the aqueous medium is buffered at a pH of 4 to 8.

4. The formulation of claim 3 wherein the aqueous medium is buffered at a pH of 5.5 to 6.

5. The formulation of claim 1 containing a free radical antagonist selected from the group consisting of ascorbic acid ascorbic acid derivatives, organic compounds having at least one thiol and a alkyl polyhydroxylated and cycloalkyl polyhydroxylated compounds.

6. The formulation of claim 5 wherein the ascorbic acid derivatives are selected from the group consisting of D-ascorbic acid, L-ascorbic acid, alkali metal ascorbates, alkaline earth metal ascorbates and water-soluble ascorbic acid esters.

7. The formulation of claim 5 wherein the organic compound having at least one thiol is aliphatic or cycloaliphatic.

8. The formulation of claim 1 containing a free radical scavenger containing at least one thiol is selected from the group consisting of thiolglycolic acid, thiolacetic acid, dithiothreitol, reduced glutathion, thiourea, a-thioglycerol, cystein, acetlcystein and mercaptoethane sulfonic acid.

9. The formulation of claim 1 wherein the free radical scavenger is an aliphatic polyhydroxy alkanol of 2 to 10 carbon atoms.

10. The formulation of claim 9 wherein the polyhydroxy alkanol is a cyclic glucitol or a straight chain glucitol of 6 to 10 carbon atoms.

11. The formulation of claim 9 wherein the polyhydroxy alkanol is glycerol or propylene glycol.

12. The formulation of claim 10 wherein the cyclic glucitol is selected from the group consisting of mannitol, sorbitol, inositol, glucose and levulose.

13. The formulation of claim 1 also containing at least one complexing agent.

14. The formulation of claim 1 wherein the acetaminophen has a concentration of 2 to 350 mg/ml.

15. The formulation of claim 14 wherein the concentration is 60 is 350 mg/ml.

16. The formulation of claim 14 diluted to a concentration of 2 to 50 mg/ml.

17. The formulation of claim 1 also containing an isotonizing agent in an amount to obtain isotonicity.

18. The formulation of claim 1 sterilized by heat treatment.

19. The formulation of claim 1 further containing an effective amount of an analgetic agent.

20. The formulation of claim 19 the analgetic agent is a morphine analgetic selected from the group consisting of natural morphines, semi-synthetic morphines, synthetic morphines, phenylpiperidines, nipecotic acid compounds, phenylcyclohexanol compounds and phenylazepine compounds.

21. The formulation of claim 20 having a concentration of acetaminophen is 0.05 to 5% by weight when morphine is present.

22. The formulation of claim 20 having an acetaminophen concentration of 0.2 to 2.5% by weight when codeine is present.

23. The formulation of claim 1 further containing an anti-inflammatory agent of the phenylacetic acid type.

24. The formulation of claim 23 wherein the anti-inflammatory agent is ketoprofen.

25. The formulation of claim 1 further containing an antiemetic agent.

26. The formulation of claim 1 further containing an antipileptic agent.

27. The formulation of claim 1 further containing a corticosteroid.

28. The formulation of claim 1 further containing a tricyclic antidepressant.

Exhibit B

SUMMARY OF INTERNATIONAL PATENT APPLICATION PCT/FR97/01452, FILED ON 5th AUGUST 1997

This international patent application (PCT/FR97/01452) was filed on August 5, 1997. The invention relates to novel stable paracetamol compositions for use in therapeutic chemistry and specifically galenic pharmacy. The compositions contain a solution of paracetamol in an aqueous solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A water-insoluble inert gas is carefully bubbled through the aqueous solvent to remove oxygen from the medium. Said compositions may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable compositions for relieving pain.

Exhibit C

SUMMARY OF INTERNATIONAL PATENT APPLICATION PCT/FR01/01749, FILED ON 6th JUNE 2001

This international patent application (PCT/FR01/01749) was filed on June 6, 2001. The invention concerns the field of organic chemistry and more particularly that of therapeutic chemistry. More precisely, it concerns a method for obtaining aqueous formulations of easily oxidizable active principles, in particular phenols, stable over a prolonged period, which consists in advanced bubbling deoxygenation with an inert gas and or vacuumizing them, while protecting them against possible oxygen uptake by maintaining them under inert gas atmosphere, by filling under inert gas into bottles previously made air-free by inert gas blowing, then in subjecting them when they are being closed to a vacuum so as to obtain in the bottle a pressure of not more than 65.000 Pa, thereby obtaining solutes having a residual oxygen concentration in the solution, less than 2 ppm, and preferably of the order of 1 ppm and even 0.5 ppm. The invention is useful in particular for preparing injection preparations having an oxygen content in the solution, less than 2 ppm.

Exhibit D-1

AGREEMENT FOR ASSIGNMENT OF PRIORITY RIGHT

between

NEWPHARM, Société Civile de Recherche, registered at the National Trade Book under the serial number 344 260 161 and the place of incorporation of which is situated at 5 rue d'Angiviller 78000 Versailles, represented by Mr DIETLIN François as its manager

Hereinafter designer as the "assignor" on one part,

and

PHARMATOP, Société Civile de Recherche, registered at the National Trade Book under the serial number 407 552 702 and the place of incorporation of which is situated at 5 rue d'Angiviller 78000 Versailles, represented by Mrs FREDJ Danièle as its manager

Hereinafter designer as the "assignee" on the other part.

As the performance of a convention intervened this day between the same parties, it has been set and agreed that follows:

Article 1: Definitions

"Patent" means the French patent application filed on August 5, 1996 with the n°96-09858 under the title "Novel stable liquid formulations based on Paracetamol and their mode of preparation".

"Priority right" means the Unionist priority right stemming from the filing of the said "Patent" in accordance with article 4 of the Convention of Union of Paris dated March 20, 1883.

Article 1: Assignment

The assignor assigns through the present to the assignee which agrees, the full and entire ownership of the priority right.

Article 2 : Applicable law

The law which is applicable for this agreement is the French law.

Article 3 : Advertising

All powers are given to the bearer of an original of these documents for requesting or performing all formalities, registrations, publications, filing and mentioning everywhere and in every administration where need will be.

Made at Versailles in three originals, February 15, 1997.

NEWPHARM
Represented by François DIETLIN

PHARMATOP
Represented by Danièle FREDJ

GEI-062

Exhibit D-2

ASSIGNMENT OF APPLICATION FOR PATENT

WHEREAS, WE, Francois Dietlin & Daniele Fredj citizens of France and residents of France for which Application PCT/FR97/01452 has been filed on 8/5/97 in which the United States has been named as a Designated State, and an app1ication for Letters Patent of the United States thus entitled has been made, said app1ication having been executed on even date herewith and the French priority date of August 5, 1996 of Application Serial No. 96/09858 is hereby claimed.

WHEREAS, SCR Pharmatop a corporation duly organized and existing under the laws of France and having a place of business at 5, rue d'Angiville F-78000 Versailles, France is desirous of acquiring the entire right, title and interest in and to said invention, application and any Letters Patent which may issue thereon;

NOW, THEREFORE, to all whom it may concern, be it known that we, the said François Dietlin & Daniele Fredj for and in consideration of the sum of ONE DOLLAR ($1.00) to us in hand paid by the said SCR Pharmatop and for other good and valuable considerations, the receipt of all of which is hereby acknowledged, do hereby sell, assign, transfer and set over unto the said SCR Pharmatop its successors and assigns, the entire right, title and interest in and to said invention, said application and any Letters Patent that may issue thereon in the United States together with any division or divisions, extension or extensions, reissue or reissues thereof;

AND, we hereby authorize and request the Commissioner of Patents and Trademarks to issue any and all Letters Patent which may issue upon said invention to said SCR Pharmatop as assignee of the entire right, title and interest in and to said invention, application and any Letters Patent that may issue thereupon.

GEI—061

IN WITNESS WHEREOF, We have hereunto set our hands as of the following date:

_____ Date: _____

FRANCOIS DIETLIN

_____ Date: _____

DANIELE FREDJ

_____ _____

_____ Date: _____

_____ Date: _____

_____ Date: _____

:
: ss:
:

On this _____day of _____ before me personally came _____ to me know and known to me to be the individuals described in and who executed the foregoing instrument and fully acknowledged that they executed the same.

_____

UNITED STATES DEPARTMENT OF COMMERCE
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April 19, 1999

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BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:
DIETLIN, FRANCOIS

DOC DATE: 04/20/1998

ASSIGNOR:
FREDJ, DANIELE

DOC DATE: 04/20/1998

ASSIGNEE:
SCR PHARMATOP
5, RUE D'ANGIVILLE
F-78000 VERSAILLES, FRANCE

SERIAL NUMBER: 09051246
PATENT NUMBER:

FILING DATE: 06/05/1998
ISSUE DATE:

KIMBERLY WHITE, EXAMINER
ASSIGNMENT DIVISION
OFFICE OP PUBLIC RECORDS

Exhibit E

Newpharm

Résidence Concorde — 10, square Saint-Florentin 7815 Le Chesnay

BRISTOL MYERS SQUIBB COMPANY
345 Park Avenue
New York NY 10154
USA

Paris, 20 December 2002

Dear Sirs,

We, SCR NEWPHARM, are the owner of the French patent filed on 5 August 1996 under n°96. 09858 and issued under n°2.751.875.

We hereby represent to BMS

- that Mrs Danièle FREDJ and Mr François DIETLIN, inventors, have assigned to us, except for the USA, all their rights,
- that they have assigned their rights for the USA directly to PHARMATOP on 20 April 1998,
- and that we have assigned to SCR PHARMATOP, an affiliated partnership, all priority rights for all countries listed in international patent application PCT/FR97/01452 except USA on 15 February 1997.

We covenant that we will never contest or challenge the rights of PHARMATOP

- on US patent n°6.028.222 issued on 22 February 2000,
- PCT/FR01/01749 filed on 6 June 2001,
- and on any patent or supplementary protection certificate that PHARMATOP may obtain that depends on hereabove stated patent or that is granted based on the hereabove stated patent applications,

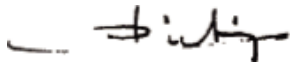
in the United States (including Puerto Rico and all US possessions and territories), Canada and Mexico.

We agree that PHARMATOP will be solely and fully responsible for all and any payments owed by it to us based on said rights and that we shall never claim to you whatsoever amount on these concerns.

Sincerely yours.

Danièle Fredj

François Dietlin



Société Civile de Recherche
Capital 1,341,551.35 € — Siret D 344 260 161 00023
Tel. : 33 1 39 54 55 77 — Telecopy : 33 1 39 66 91 85

APPENDIX 2

TARGET PRODUCT PROFILE

A. Indications at Launch

(a) PRODUCT is indicated for the treatment of post-operative acute pain in adults.

(b) PRODUCT may be administered for up to 3 days.

(a) PRODUCT may be administered concomitantly with morphine.

B. Supporting Clinical Data available for promotion at Launch

(a) Single dose analgesic efficacy in oral surgery pain model. Onset of analgesia: less than 10 minutes. Duration of analgesia: 4 to 6 hours.

(b) Multiple dose analgesic efficacy confirmed in two different pain models: orthopaedic surgery and lower abdominal surgery. Efficacy of proposed dosing regimen, p.r.n. or fixed time, clearly demonstrated. Efficacy in combination with PCA morphine demonstrated.

C. Safety at LAUNCH

(i) No clinically significant drug/drug interactions.

(ii) PRODUCT has comparable tolerance to placebo at the injection site.

(iii) PRODUCT carries no black box warnings.

(iv) PRODUCT has gastrointestinal safety profile comparable to placebo.

(v) PRODUCT has CNS safety profile comparable to placebo.

(vi) PRODUCT has cardiovascular safety profile comparable to placebo.

(vii) In cases of creatinine clearance <10 ml/min, due to the lack of data, infusion should be used with caution.

D. Dosing at LAUNCH

(i) PRODUCT is administered as a 15-minute intravenous infusion of 1gram. May be used every 4 to 6 hours, or up to 4 times per day. Maximum daily dose must not exceed 4 grams.

Assumes conduct of 2 new clinical trials prior to NDA submission

APPENDIX 3

Exceptions to PHARMATOP Representations and Warranties

– international patent application PCT/W002/072080 A2 filed by FRESENIUS KABI DEUTSCHLAND GMBH, a copy of which is attached.

SUMMARY OF INTERNATIONAL PATENT APPLICATION PCT/WO02/072080 A2,
FILED BY FRESENIUS KABI DEUTSCHLAND
GMBH

This international patent application (PCT/WO02/072080 A2) was filed on March 12, 2002 by Fresenius Kabi Deutschland GmbH. The invention relates to parenterally administrable, especially infusible, aqueous paracetamol solutions which are stable in storage and free of particles and discoloration. Said solutions contain a mixture of: a) between 1 and 17 grams of paracetamol per liter, and b) between 0.01 and 0.17 grams of at least one physiologically compatible antioxidant per liter, selected from the group comprising ascorbic acid, N-acetyl-L-cysteine and stabilizer compounds containing SII groups which are different from N-acetyl-L-cysteine. The aqueous solution is free of organic solvents and has a pH value of between 5.5 and 6.5 and an oxygen content of less than 0.5 milligrams per liter. The invention also relates to a method for producing such solutions, and glass or plastic containers containing said solutions.

APPENDIX 4

GUARANTEED PAYMENTS (in US$ millions)

Year 1	Year 2	Year 3	Year 4	Year 5
$[***]	$[***]	$[***]	$[***]	$[***]

Guaranteed Payment amounts shall be payable subject to applicable terms and conditions of the Agreement, shall be payable (when applicable) on a quarterly basis, and shall be due at the same time as a royalty payment would otherwise have been due and payable for such quarter.

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

[Translation] ANNEX 2: PROCEDURES AND PRECAUTIONS RELATING TO THE MANUFACTURE OF THE FORMULATION PMC 0397

These procedures and precautions were established starting from the methods implemented during successive manufacture, at the Delmas Laboratories, of the pilot batches of Perfalgan® whose compositions, dates of manufacture and volumes implemented are indicated hereafter:

[* * *]

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

[* * *]

***Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

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EXHIBIT 10.14

CERTAIN MATERIAL (INDICATED BY AN ASTERISK) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

CLINICAL SUPPLY AGREEMENT

between

LAWRENCE LABORATORIES

and

CADENCE PHARMACEUTICALS, INC.

dated as of February 21, 2006

TABLE OF CONTENTS

EXHIBITS

INDEX OF DEFINED TERMS

CLINICAL SUPPLY AGREEMENT

This Clinical Supply Agreement (the "Agreement") is entered into as of February 21, 2006 (the "Execution Date") by and among Lawrence Laboratories, an indirect wholly-owned subsidiary of Parent (as defined below) and a corporation organized under the laws of Ireland with its registered office at Unit 12, Distribution Centre, Shannon Industrial Estate, Shannon, County Clare, Ireland ("BMS"), Cadence Pharmaceuticals, Inc., a Delaware corporation having an address at 12730 High Bluff Drive, San Diego, California 92130 ("Cadence"), and, solely for the purposes of Section 9.15 hereof, Bristol-Myers Squibb Company, a Delaware corporation having an address at 345 Park Avenue, New York, New York 10154 ("Parent") and is effective as of March 29, 2006 (the "Effective Date"). BMS and Cadence are sometimes collectively referred to herein collectively as the "Parties" and each individually as a "Party."

RECITALS

WHEREAS, Cadence holds certain license rights in intellectual property relating to Parenteral Acetaminophen Products (as defined below) in the United States and Canada pursuant to that certain IV APAP Agreement dated February 21, 2006, between Parent and Cadence (the "IV APAP Agreement"), which sublicenses to Cadence certain intellectual property rights with respect to the United States and Canada under that certain License Agreement dated December 23, 2002 between SCR Pharmatop, a civil law partnership organized under the laws of France, having its head office's address at 10, Square St. Florentin, 78150 Le Chesnay, France, recorded with the Register of Commerce and Companies of Versailles under No. 407552702, and Parent (the "Pharmatop License Agreement") and licenses to Cadence certain rights to use patents and know-how of Parent in the same jurisdictions;

WHEREAS, BMS has arrangements for one of its Affiliates located in Italy to manufacture Clinical Testing Products (as defined below) for supply to Cadence pursuant to this Agreement;

WHEREAS, BMS or its Affiliate holds certain license rights in intellectual property relating to Parenteral Acetaminophen Products (as defined below) in Italy entitling BMS or its Affiliate to use such intellectual property to manufacture Parenteral Acetaminophen Products in Italy for supply to Cadence pursuant to this Agreement;

WHEREAS, BMS or its Affiliates have expertise in manufacturing Parenteral Acetaminophen Products for use in clinical trials and related Placebos (as defined below); and

WHEREAS, Cadence desires to purchase, and BMS desires to supply from its Affiliate's facility in Italy (or such other facility as BMS may determine in accordance with this Agreement), Cadence's requirements for the Clinical Testing Products for use in clinical trials in support of applications for Regulatory Approvals (as defined below) for Parenteral Acetaminophen Products in the Territory.

AGREEMENT

THEREFORE, the Parties, intending to be legally bound, agree as follows:

ARTICLE 1

DEFINITIONS

1.1 Defined Terms. As used in this Agreement, the following terms shall have the following meanings:

"Affiliate" of a Party means any corporation, firm, partnership or other entity that directly or indirectly Controls, is Controlled by or is under common Control with such Party.

"Agreement" has the meaning set forth in the Introductory Paragraph.

"Applicable Law" means any applicable federal, state, local or foreign statute, law, ordinance, rule or regulation, judicial order or industry standard imposed by regulation or law, including without limitation the laws of, and regulations promulgated under, the FDCA or the Canadian equivalent of the FDCA.

"BMS" has the meaning set forth in the Introductory Paragraph.

"BMS Party" has the meaning set forth in Section 6.2.

"Business Day" means any day other than a Saturday, a Sunday or a United States Federal, EU, Irish or Italian holiday.

"Cadence" has the meaning set forth in the Introductory Paragraph.

"Cadence Party" has the meaning set forth in Section 6.1.

"cGMP" means all current good manufacturing practices under 21 C.F.R. 210, as amended from time to time or any successor regulation.

"Claim" means any claim (including without limitation, product liability claims, strict liability or tort claims and intellectual property infringement claims), action, suit, governmental investigation or other proceedings made or brought by or on behalf of a Third Party against any Cadence Party or any BMS Party, as the case may be, including without limitation enforcement actions by the FDA or other applicable Drug Regulatory Authorities and claims for infringement of intellectual property and for bodily injury, death or property damage.

"Clinical Testing Product" means any Parenteral Acetaminophen Products and any related Placebo used in clinical trials to support Regulatory Approval in the Territory of any such Parenteral Acetaminophen Product.

"Clinical Use" means the non-commercial use of any Clinical Testing Product in clinical trials or otherwise, in each case solely to support Regulatory Approval of any Parenteral Acetaminophen Product in the Territory.

"Confidential Information" has the meaning set forth in the IV APAP Agreement.

"Control" means (a) with respect to Technology or technical information, the possession by a Party of the ability to grant a license or sublicense of such Technology or technical information as provided herein without violating the terms of, or requiring a consent under, any agreement or arrangement between such Party and any Third Party and (b) when used with respect to any Person means the power to direct the management and policies of such Person, directly or indirectly, whether through the ownership of voting securities, by contract, or otherwise. "Controlled" and "Controlling" shall have correlative meanings.

"Demand" has the meaning set forth in Section 7.1.

"Dispute" has the meaning set forth in Section 7.1.

"Dollar" or "$" means United States dollars, the lawful currency of the United States.

"Drug Regulatory Authority" means any governmental authority or instrumentality with responsibility for granting any licenses, approvals, authorizations (e.g., NDAs) or granting pricing and/or reimbursement approvals necessary for the marketing and sale of pharmaceutical products in any regulatory jurisdiction.

"Effective Date" has the meaning set forth in the Introductory Paragraph.

"EMEA" means the European Agency for the Evaluation of Medicinal Products, or any successor agency.

"Execution Date" has the meaning set forth in the Introductory Paragraph.

"Facility" has the meaning set forth in Section 3.9.

"FDA" means the United States Food and Drug Administration or any successor agency.

"FDCA" means the Federal Food, Drug & Cosmetics Act, 21 U.S.C. 321 et seq., any amendments or supplements thereto, or any regulations promulgated or adopted thereunder.

"Firm Order" has the meaning set forth in Section 3.2(a).

"Force Majeure" means any circumstances that are not within the reasonable control of the Person affected thereby, including without limitation an act of God, terrorist attack, war, insurrection, riot, strike or labor dispute, shortage of materials, fire, explosion, flood, government requisition or allocation, breakdown of or damage to plant, equipment or facilities (to the extent that, in the event of a breakdown only, such plant, equipment or facilities were reasonably maintained), interruption or delay in transportation, fuel supplies or electrical power, embargo, boycott, order or act of civil or military authority.

"Forecast" has the meaning set forth in Section 3.1.

"Indemnified Party" has the meaning set forth in Section 6.3.

"Indemnifying Party" has the meaning set forth in Section 6.3.

"IV APAP Agreement" has the meaning set forth in the Recitals.

"NDA" means a new drug application or an abbreviated new drug application, including any amendments or supplements thereto, filed with the FDA pursuant to the FDCA or any comparable filing with any Drug Regulatory Authority in Canada and includes any Common Technical Document for the Registration of Pharmaceuticals for Human Use filed with the FDA or any other Drug Regulatory Authority in the Territory.

"Parent" has the meaning set forth in the Introductory Paragraph.

"Parenteral Acetaminophen Product" means the currently validated parenterally administered dosage form of paracetamol: APAP for injection [***] as more particularly set forth in the Specifications.

"Parties" has the meaning set forth in the Introductory Paragraph.

"Party" has the meaning set forth in the Introductory Paragraph.

"Person" means any individual, firm, corporation, partnership, limited liability company, trust, joint venture, governmental authority or other entity.

"Pharmatop License Agreement" has the meaning set forth in the Recitals.

"Placebo" means the currently validated placebo to be used for clinical trials of Parenteral Acetaminophen Products: Placebo APAP for injection [***] as more particularly set forth in the Specifications.

"Quality Agreement" has the meaning set forth in Section 3.8.

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"Regulatory Approval" means with respect to any Parenteral Acetaminophen Products in any regulatory jurisdiction in the Territory, approval from the applicable Drug Regulatory Authority sufficient to market and sell such Parenteral Acetaminophen Products in such jurisdiction.

"Specifications" means with respect to Parenteral Acetaminophen Products and Placebo the specifications set forth on Exhibit A.

"Supply Price" has the meaning set forth in Section 2.2.

"Supply Term" means the period beginning on the Effective Date and terminating on the earlier of (i) the date Cadence receives Regulatory Approval from any Drug Regulatory Authority in any jurisdiction in the Territory; or (ii) the close of business on December 31, 2008.

"Technology" means and includes all inventions, discoveries, improvements, trade secrets, know-how, processes, procedures, research records, records of inventions, test information, formulae, drawings, specifications, instructions, techniques, data, market surveys and other similar proprietary methods, materials or property, whether or not patentable, relating to Parenteral Acetaminophen Products and/or the Placebo, including but not limited to (a) samples of, methods of production or use of, and structural and functional information pertaining to, chemical compounds, proteins or other biological substances, (b) data, formulations, techniques and know-how, and (c) rights under patents, patent applications, and copyrights.

"Territory" means the United States (including Puerto Rico and all U.S. possessions and territories) and Canada.

"Third Party" means a Person who or which is neither a Party nor an Affiliate of a Party.

ARTICLE 2

SUPPLY OF CLINICAL TESTING PRODUCTS

2.1 Supply and Purchase. (a) During the Supply Term and upon the terms and conditions set forth in this Agreement, BMS shall, or shall cause its Affiliates to, manufacture, or cause the manufacture of, and supply to Cadence Clinical Testing Products for Clinical Use, ordered pursuant to Firm Orders hereunder, subject to variations permitted by Section 3.2. Cadence shall purchase from BMS and its Affiliates all of the Clinical Testing Products ordered by Cadence pursuant to Firm Orders hereunder. BMS and its Affiliates shall not have any obligation to supply Clinical Testing Products for commercial sale, and following the expiration of the Supply Term, BMS and its Affiliates shall not have any obligation to supply Clinical Testing Products hereunder, except that if BMS does not timely deliver at the designated port of departure in accordance with Section 3.4 any Clinical Testing Products it is obligated to supply hereunder or if any portion of such Clinical Testing Products is properly rejected in accordance

with Section 3.6, BMS's obligation to supply such quantity of Clinical Testing Products shall remain in effect until conforming Clinical Testing Products are placed at the disposal of Cadence's carrier at the designated port of departure in accordance with this Agreement. BMS's obligation to manufacture, supply and deliver the Clinical Testing Products is conditioned on the execution and delivery of the Quality Agreement contemplated by Section 3.8 not less than four (4) months prior to the scheduled date for placement of the Clinical Testing Products at the disposal of Cadence's carrier, and BMS shall have no obligation to accept any Firm Order that calls for the delivery of any Clinical Testing Product following the end of the Supply Term. BMS shall not be obligated to supply more than [***] each of Parenteral Acetaminophen Products or Placebo over the term of this Agreement.

(b) The Clinical Testing Products shall be in finished dosage forms (in vials in bulk without commercial or clinical labeling) as specified in the Specifications. Cadence shall be responsible for labeling the Clinical Testing Products for Clinical Use.

(c) So that BMS shall be aware of the date of the expiration of the Supply Term, Cadence shall (i) keep BMS informed as to the expected date of any Regulatory Approval with respect to Parenteral Acetaminophen Products in the Territory, (ii) notify BMS within three (3) Business Days after Cadence receives written notice of any such Regulatory Approval and (iii) promptly notify BMS of any determination by Cadence to permanently cease all Clinical Use of the Parenteral Acetaminophen Products in the Territory.

2.2 Purchase Price of Clinical Testing Products. The purchase price to be paid by Cadence for Clinical Testing Products (the "Supply Price") shall be $[***] for the Parenteral Acetaminophen Products and $[***] for the Placebo, in each case as such prices are adjusted as provided below. Such purchase prices shall be adjusted (i) as of the first day of each calendar year to reflect any increase during the [***] period ending on November 30 of the preceding calendar year in the [***] as published by Eurostat or any successor agency that assumes responsibility for the preparation and publication of such index and (ii) from time to time to reflect any increase exceeding [***] percent ([***]%) in the aggregate in the cost of raw materials or supplies.

2.3 Limitation to Clinical Use. Neither Cadence nor any of its Affiliates shall (i) label or relabel (or cause to be labeled or relabeled) any of the Clinical Testing Products for commercial sale or for any use or purpose other than Clinical Use, (ii) sell to any Third Party any Clinical Testing Products supplied hereunder or (iii) use any Clinical Testing Products for any purpose other than Clinical Use.

ARTICLE 3

TERMS AND CONDITIONS OF PURCHASE AND SALE

3.1 Forecasts. Attached as Exhibit B is Cadence's initial non-binding forecast of its requirements for each Parenteral Acetaminophen Product and Placebo for Clinical Use that Cadence expects to order for delivery during the [***] ([***]) [***] following the anticipated

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Effective Date. Prior to the first day of each calendar quarter during the Supply Term, Cadence shall deliver to BMS an updated non-binding forecast setting forth its requirements for each Parenteral Acetaminophen Product and Placebo for Clinical Use that Cadence expects to order for delivery during the [***] ([***]) month period beginning on the first day of such calendar quarter. Each such forecast is referred to herein as, a "Forecast".

3.2 Ordering. (a) Cadence shall submit to BMS a written irrevocable firm purchase order for all Clinical Testing Products to be purchased by it not later than [***] ([***]) [***] prior to the requested shipping date of such Clinical Testing Products (each, a "Firm Order"). Each such Firm Order shall include the quantity of each Clinical Testing Product and the desired time and manner of shipment and the shipping destination. Any Firm Order for any Clinical Testing Product must be for a quantity equal to the minimum batch size for such Clinical Testing Product as in effect from time to time or an integral multiple thereof. The minimum batch size in effect as of the date of this Agreement is [***] of Parenteral Acetaminophen Product and [***] of Placebo. The Parties agree that the actual number of vials successfully manufactured by BMS for any batch of the Clinical Testing Products may be within a range of plus or minus [***] percent (+/-[***]%) of the minimum batch size or of the actual number of vials ordered by Cadence pursuant to a Firm Order. The number of vials of Clinical Testing Products supplied by BMS pursuant to a Firm Order may vary from the amount actually ordered by Cadence within such limits, and BMS may ship to Cadence, and Cadence shall purchase, such greater or lesser number of vials in full satisfaction of such Firm Order, provided that Cadence shall only be required to purchase such number of vials actually supplied to Cadence. BMS shall provide to Cadence no less than [***] ([***]) [***] prior written notice of any change in the minimum batch size. BMS shall not be obligated to fill more than one order for, or to make more than one delivery of, Placebo. If Cadence has submitted to BMS, and BMS has accepted, a Firm Order prior to the Effective Date, the fulfillment of such Firm Order by BMS shall be subject to the execution of the Quality Agreement, and BMS shall not be obligated to place any Clinical Testing Products at the disposal of Cadence's carrier prior to the expiration of [***] ([***]) [***] after the execution of the Quality Agreement.

(b) No terms and conditions contained in any purchase order, acknowledgment, invoice, bill of lading, acceptance or other preprinted form issued by either Party shall be effective to the extent they are inconsistent with or modify the terms and conditions contained herein.

3.3 Shipping Document. Each shipment of Clinical Testing Products shall include a certificate of analysis and a packing slip that describes the Clinical Testing Products, the date of manufacture, traceable lot or batch number(s), quantities, shipment date and destination and such additional information as the Parties may agree in writing from time to time.

3.4 Delivery, Title, and Shipping. (a) Delivery of Clinical Testing Products shall be [***] the designated port of departure (Incoterms 2000) in Italy, which port of departure (maritime or air) shall be specified by Cadence. BMS shall arrange for shipping and insurance in the manner customarily arranged for its own products from the point of manufacture to the port of departure and shall arrange for Italian export clearances, but Cadence shall bear the cost of such shipping and insurance, any special packing expenses and export or customs agents, all of

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which shall be included in BMS's invoice and paid by Cadence in accordance with Section 3.5. Cadence shall arrange for loading, shipment, insurance from the port of departure to the ultimate destination and import customs clearances at the destination country, and Cadence shall be responsible for all loading charges, freight, insurance, import customs clearances and other shipping expenses from such port of departure to the ultimate destination. Title to the Clinical Testing Products and risk of loss, delay or damage in transit for Clinical Testing Products purchased by Cadence shall pass to Cadence when the Clinical Testing Products are placed at the disposal of Cadence's carrier at the port of departure. Cadence shall cause its carrier to inspect all Clinical Testing Products for physical damage prior to shipment, and Cadence shall promptly notify BMS of any such physical damage. Cadence shall bear the cost of all such pre-shipment inspection. BMS and its Affiliates shall not have any responsibility for any loss or damage to any Clinical Testing Products after BMS or its export or customs agent places the Clinical Testing Products at the disposal of Cadence's carrier, nor shall any loss or damage to any Clinical Testing Products following such placement at the disposal of Cadence's carrier obviate Cadence's obligation to purchase and pay for such Clinical Testing Products. Without limiting BMS's right to recover the full invoiced amount for the Clinical Testing Products and as partial security therefor, Cadence shall cause each shipment of Clinical Testing Products to be insured for the full invoiced amount of each shipment. Cadence shall provide to BMS proof, satisfactory to BMS, of such insurance.

The ultimate destination country of each shipment hereunder shall be in the Territory. In the event Cadence desires to use any of the Clinical Testing Products for clinical trials in the Clinical Study Countries (as defined in the IV APAP Agreement) in accordance with Section 3.6 of the IV APAP Agreement, Cadence shall ship such Clinical Testing Products to the Territory and Cadence shall be solely responsible for shipping such Clinical Testing Products for the Territory to an appropriate destination in the applicable Clinical Study Country.

(b) BMS shall place the Clinical Testing Products at the disposal of Cadence's carrier at port of departure (maritime or air) for shipment to Cadence or its designee, appropriately labeled with a traceable lot or batch number and packaged for shipping in the standard commercial packaging materials customarily used by BMS not later than the later of (i) [***] ([***]) [***] following the receipt of Cadence's Firm Order or (ii) the shipping date requested by Cadence in its Firm Order. If Cadence requests a shipping date that is less than [***] ([***]) [***] after the delivery to BMS of the applicable Firm Order, BMS shall use reasonable commercial efforts to meet such earlier delivery date, but BMS shall not be in breach of this Agreement for failing to meet such earlier delivery date. If BMS or its Affiliate is unable to place any shipment at the disposal of Cadence's carrier by the date described in the first sentence of this paragraph, in addition to any other remedies available to Cadence pursuant to this Agreement, BMS shall provide Cadence with updated delivery information (including estimated delivery date(s)) in writing on a weekly basis until such shipment has been made available to Cadence's carrier.[***](c) Cadence shall make arrangements with a carrier to pick up each shipment of Clinical Testing Products at the designated port of departure (maritime or air) and to transport such shipment of Clinical Testing Products to Cadence or its designee. Cadence shall notify BMS in advance in writing of the name of the carrier and shall provide such other information as may be necessary for BMS to place the Clinical Testing Products at the disposal of such carrier

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at the port of departure. Cadence shall have sole responsibility for the import of the Clinical Testing Products into the Territory and for obtaining all import and import-related customs permits and clearances.[***](d) In the event of any shortage of supply of Clinical Testing Products due to Force Majeure, BMS shall allocate its available supply of Clinical Testing Products between it and its Affiliates, its and its Affiliates' other customers and Cadence on a pro rata basis based on the aggregate back orders of Clinical Testing Products, which allocation shall be determined by BMS in good faith.

3.5 Invoicing and Payment. (a) BMS shall invoice Cadence for the Clinical Testing Products in Dollars at the time of shipment. Each invoice shall include the invoice number, the Firm Order number (if any), unit price and total price of the Clinical Testing Products contained in the shipment.

(b) Cadence shall pay BMS within [***] ([***]) [***] after the receipt of any invoice. All payments to be made hereunder to BMS shall be made in Dollars by wire transfer of immediately available funds to such bank account as may be designated by BMS in writing from time to time, unless the Parties agree to settle such payments through other means. In the event Cadence disputes any invoice, Cadence shall pay any undisputed amount as and when due hereunder and shall pay the additional amount, if any, owed with respect to such invoice not later than [***] ([***] [***] following the resolution of such dispute, together with interest from the original due date of such invoice at the rate specified in Section 3.5(c).

(c) Any payment not made as and when due shall bear interest at the rate of [***] percent ([***]%) per annum, compounded daily, from the due date to the date of payment. In addition to but without limiting the preceding sentence, BMS shall have the right to suspend future shipments of Clinical Testing Products to Cadence if BMS does not receive payment within [***] ([***]) [***] after the date of any invoice, other than invoices subject to a *bona fide* dispute. BMS shall resume shipments of Clinical Testing Products upon receiving such late payment and, if requested by BMS, reasonable assurances as to payment of future invoices.

3.6 Inspection; Non-Conforming Product. (a) Cadence shall promptly inspect or cause to be inspected all shipments of Clinical Testing Products hereunder and shall test, or cause to be tested, all Clinical Testing Products received by it or its designee within [***] ([***]) [***] after receipt of such shipment at the shipping destination. Within [***] ([***]) [***]s after receipt by Cadence of any shipment of Clinical Testing Products, Cadence may reject any lot or portion thereof that failed to conform to the Specifications or the terms of this Agreement at the time BMS placed the Clinical Testing Products at the disposal of Cadence's carrier by sending BMS notice of the lot or batch numbers of the rejected Clinical Testing Products, together with an indication of the specific basis for rejection and a sample of the rejected goods. Notwithstanding the foregoing, if the discovery of the non-conformity of any Clinical Testing Product could not reasonably have been discovered until after such [***] ([***]) [***] period, Cadence shall notify BMS of such non-conformity promptly (and in any event not less than [***] ([***]) [***]) following the discovery thereof. Cadence shall not be entitled to reject any shipment or any portion thereof on account of damage incurred following the time that BMS

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placed the Clinical Testing Products at the disposal of Cadence's carrier, and Cadence's sole remedy shall be against the carrier or under any applicable insurance. BMS shall have the right to examine and test any Clinical Testing Product that Cadence claims to be non-conforming. If it is determined that there is any such failure to conform to Specifications at the time that BMS placed the Clinical Testing Products at the disposal of Cadence's carrier, BMS and Cadence shall cooperate to determine the cause of the non-conformity.

(b) In the event that BMS and Cadence do not resolve such issue within [***] ([***]) Business Days after BMS notifies Cadence that BMS disagrees with Cadence's belief as to the non-conformity of any Clinical Testing Product at the time that BMS places the Clinical Testing Products at the disposal of Cadence's carrier, such Parties shall submit a sample of the disputed Clinical Testing Product to an independent laboratory, mutually selected by the Parties, for testing, and the results of such testing shall be binding upon the Parties, absent manifest error. The Party whose assertion as to the conformity or nonconformity of the Clinical Testing Product in question is not supported by the results of the testing of the independent laboratory shall bear all costs and expenses of such testing. If the results of such testing by such independent laboratory are inconclusive, then (i) all costs and expenses of such testing shall be borne by the Parties in equal shares and (ii) the Parties shall share the Supply Price of such Clinical Testing Products and the freight, insurance and other shipping expenses, fees, duties, taxes and levies incurred by the Parties in connection therewith, and Cadence shall pay to BMS one-half of such Supply Price and other items within [***] ([***]) [***] after the receipt of such inconclusive results; and (iii) BMS shall promptly replace any such Clinical Testing Products and deliver FCA in accordance with Section 3.4 replacement conforming Clinical Testing Products (even if such replacement entails shipping Clinical Testing Products subsequent to the Supply Term), which shall be purchased and paid for by Cadence in accordance with Article 2 and Section 3.5 of this Agreement.

(c) Cadence shall, as requested by BMS in its sole discretion: (i) return promptly to BMS at BMS's expense all properly rejected Clinical Testing Products or (ii) destroy such non-conforming Clinical Testing Products in accordance with FDA guidelines or send such non-conforming Clinical Testing Products to a destruction facility of BMS's choice for destruction at BMS's expense. Cadence shall not be required to pay BMS for any Clinical Testing Product that has been properly rejected, and BMS shall reimburse or credit Cadence for the freight, insurance and other shipping expenses, fees, duties, taxes and levies for any shipment of Clinical Testing Products that is properly rejected. BMS shall promptly replace any properly rejected Clinical Testing Products and supply to Cadence conforming Clinical Testing Products (even if such replacement entails shipping Clinical Testing Products subsequent to the Supply Term). Cadence shall pay the Supply Price and all shipping costs (which shall include the cost of returning the Clinical Testing Products to BMS and reshipping such Clinical Testing Products to Cadence or its designee) for any Clinical Testing Products improperly rejected.

3.7 Obsolescence Charge. To the extent that BMS purchases inventories of raw materials, components or other supplies to meet Cadence's Forecast, Cadence shall reimburse BMS for any such inventories that were purchased but unused and cannot reasonably be used by BMS.

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3.8 Quality Control. Not later than [***] ([***]) [***] after the Execution Date, BMS (and/or one of its Affiliates) and Cadence shall enter into a quality agreement (the "Quality Agreement") containing quality terms consistent with Applicable Law and such other terms as are mutually satisfactory to the Parties and not inconsistent with this Agreement. When the Quality Agreement is finalized and executed, a copy of the definitive Quality Agreement shall be attached hereto as Exhibit C to this Agreement. In the event of any conflict between the terms of this Agreement and the Quality Agreement, the terms of the Quality Agreement shall control.

3.9 Change of Supplier or Facility. BMS may in its sole discretion upon [***] ([***]) [***] written notice to Cadence change the manufacturing facility used in the manufacturing of the Clinical Testing Products (the "Facility").

3.10 Recalls. Each Party shall notify the other by telephone within [***] ([***]) [***] after receiving any information, request or directive giving rise to a good faith belief that a recall of any Clinical Testing Product is required under Applicable Law or is otherwise necessary to avoid risk of injury or liability. In the event that a Drug Regulatory Authority in the Territory issues or requests a recall or takes similar action in connection with the Clinical Testing Products, or in the event that either Party in good faith, believes that a recall is required under Applicable Law or is otherwise necessary to avoid risk of injury or liability, it may initiate a recall by providing written notice thereof to the other Party specifying in reasonable detail, the nature of the recall and the affected products. Within [***] ([***]) Business Days following such written notification (or sooner if exigent circumstances exist or otherwise are required in order to comply with Applicable Law), the Parties shall discuss the circumstances giving rise to such notification and the content of such notification, and, if so required, the timing and breadth of the recall, the customers to which the recall shall extend, the strategies and notifications to be used, and other related issues. BMS and Cadence each shall maintain such traceability records as are sufficient and as may be necessary to permit a recall, product withdrawal or field correction of any Clinical Testing Product. Each Party shall provide full cooperation and assistance to the other Party in connection with any recall as may be reasonably requested by the other Party. In the event that the Parties cannot agree on any such decision regarding the manner of a recall and such recall relates solely to a failure of BMS and its Affiliates to manufacture the Clinical Testing Product in accordance with Applicable Law or the Specifications, the issue shall be resolved by BMS in good faith. In the event that the Parties cannot agree on any such decision regarding the manner of a recall and such recall relates to a matter other than a failure of BMS and its Affiliates to manufacture the Clinical Testing Product in accordance with Applicable Law or the Specifications, the issue shall be resolved by Cadence in good faith. Cadence shall be responsible for collecting and shipping any recalled Clinical Testing Product to a location determined by BMS. BMS shall be responsible for disposing of any recalled Clinical Testing Product in accordance with Applicable Law. The costs of the recall (including all costs of collecting, shipping and disposing of the recalled Clinical Testing Product) shall be borne by Cadence, except that such costs shall be borne by BMS to the extent it results from a breach of any of BMS's representations, warranties or covenants under this Agreement.

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3.11 Representations, Warranties and Covenants.

(a) BMS represents, warrants and covenants that the Clinical Testing Products when delivered FCA at the designated port of departure (Incoterms 2000) in accordance with Section 3.4 shall (i) conform to the Specifications; (ii) be manufactured, packaged, tested, stored and handled by it and its Affiliates in compliance with the Specifications, the Quality Agreement, cGMP and any Applicable Laws; and (iii) at the time of that BMS places the Clinical Testing Products at the disposal of Cadence's carrier, not be adulterated or misbranded within the meaning of the FDCA. Notwithstanding the foregoing, BMS does not represent, warrant or covenant against any Clinical Testing Product becoming adulterated or misbranded within the meaning of the FDCA or ceasing to conform to the Specifications as a result of an act or omission or damage caused by Cadence or any Third Party (including any carrier of Cadence) after placement of the Clinical Testing Products at the disposal of Cadence's carrier pursuant to Section 3.4. BMS represents, warrants and covenants that BMS or its Affiliate shall transfer to Cadence good and marketable title to the Clinical Testing Products free from any and all liens, mortgages or encumbrances of any kind created by BMS and its Affiliates and its and their suppliers and creditors.

(b) BMS represents, warrants and covenants that it and its Affiliates hold and will continue to hold during the Supply Term sufficient rights in all manufacturing processes and Technology necessary for the manufacture and supply of the Clinical Testing Products.

(c) BMS represents, warrants and covenants that as of the date hereof it has not received written notice of any pending or threatened Claim that would interfere with BMS's performance under this Agreement or that materially and adversely affects the rights and interests of Cadence hereunder.

(d) Each Party represents, warrants and covenants that the execution and delivery of this Agreement and the performance of its obligations hereunder: (i) has been authorized to enter into this Agreement by all necessary corporate action on the part of it and its shareholders, (ii) does not conflict with or violate any requirement of Applicable Law or any of its charter documents and (iii) does not conflict with, violate or breach or constitute a default or require any consent (which has not been obtained) under, any contractual obligation, license or court or administrative order by which it is bound.

(e) EXCEPT AS EXPRESSLY PROVIDED IN THIS SECTION 3.11, NEITHER BMS NOR ANY OF ITS AFFILIATES MAKES ANY REPRESENTATION OR WARRANTY OF ANY KIND, EXPRESS OR IMPLIED, WRITTEN OR ORAL, STATUTORY OR OTHERWISE WITH RESPECT TO THE CLINICAL TESTING PRODUCTS (WHETHER USED ALONE OR IN COMBINATION WITH OTHER SUBSTANCES) OR ANY MANUFACTURING PROCESS USED TO MANUFACTURE ANY CLINICAL TESTING PRODUCTS, INCLUDING WITHOUT LIMITATION (i) ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE; (ii) ANY IMPLIED WARRANTIES ARISING FROM COURSE OF PERFORMANCE, COURSE OF DEALING OR USAGE IN THE TRADE; (iii) ANY WARRANTIES OF DESIGN OR DESCRIPTION OR ANY WARRANTY OTHERWISE CREATED BY ANY AFFIRMATION OF FACT OR

PROMISE OR SAMPLE OR MODEL; AND ALL SUCH REPRESENTATIONS AND WARRANTIES WHETHER IN CONTRACT, WARRANTY, NEGLIGENCE, TORT, STRICT LIABILITY OR OTHERWISE, ARE HEREBY DISCLAIMED.

3.12 Force Majeure. No Party shall be considered to be in breach of, nor shall any Party be liable for any failure to perform its obligations under, this Agreement (other than obligations to make payments of money) by reason of Force Majeure. A Party affected by Force Majeure shall give the other Party prompt notice of any interruption of performance on account of Force Majeure, and of the resumption of such performance, and shall keep the other Party informed on a current basis as to the steps being taken to remove, and the anticipated time of removal of, the circumstances resulting in such Force Majeure. The time for performance of any obligation hereunder that is affected by Force Majeure shall be extended by the actual time of delay caused by such Force Majeure, provided that the Party affected by such Force Majeure uses commercially reasonable efforts to mitigate any such delay. Notwithstanding the foregoing, nothing in this Section 3.12 shall excuse or suspend the obligation to make any payment due under this Agreement in the manner and at the time provided herein.

ARTICLE 4

REGULATORY MATTERS

4.1 Record Retention. Any books and records relating to the receipt, manufacture, storage, handling or testing of any Clinical Testing Product shall be maintained under this Agreement by a Party or its Affiliates in accordance with Applicable Law.

4.2 Regulatory Matters. At all times during the Term, BMS shall maintain the production facility, equipment and processes (including, without limitation, the process used in producing the Clinical Testing Products and in performing BMS's other obligations under this Agreement in compliance with all Applicable Laws (including, without limitation, cGMP, the FDA and, to the extent applicable, the EMEA guidelines, employment and labor law requirements, electrical, fire and safety at work codes and regulations and guidelines issued by any applicable Drug Regulatory Authorities in the Territory. BMS shall make available for inspection, upon the request of Cadence, all documentation relating to such compliance. Upon reasonable prior notice and subject to BMS's customary rules and restrictions with respect to site visits by non-BMS personnel, BMS shall permit representatives of Cadence to conduct inspections at all Facilities utilized by BMS and its Affiliates hereunder, pursuant to the Quality Agreement, to confirm such compliance; provided that such inspections may not be made more than once in any twelve-month period (not including Cadence's initial visit to the Facility, to be made prior to February 28, 2006) and each such inspection shall be limited to no more than [***] ([***]) [***]; provided, further, that if material corrective measure are necessary, Cadence may conduct an additional inspection to verify the implementation of such corrective measures, which additional inspection shall be limited to [***] ([***]) [***]. BMS shall promptly provide to Cadence copies of all material communications received from and sent to any Drug Regulatory Authority which relate solely to the Clinical Testing Products and which is reasonably likely to cause BMS to be unable to make timely delivery of Clinical Testing Products in accordance with this

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Agreement. BMS shall consult with Cadence regarding its response to any such communication from a Drug Regulatory Authority. Cadence understands and agrees that any inspection, other than inspections to verify corrective measures, will be charged against the time allocated for tech transfer pursuant to Section 2.12 of the IV APAP Agreement. Cadence's initial preparatory tour of BMS's Facility, which shall take place prior to February 28, 2006, and shall last not more than one (1) Business Day, shall not be charged against such time allocated for tech transfer and shall not be counted as Cadence's annual visit.

ARTICLE 5

CONFIDENTIALITY

5.1 Confidentiality. Any Confidential Information of the Parties exchanged hereunder shall be governed by, and shall be maintained in confidence pursuant to, the confidentiality provisions set forth in Section 5.2 and Section 5.3 of the IV APAP Agreement.

ARTICLE 6

INDEMNIFICATION

6.1 By BMS. BMS shall indemnify, defend and hold harmless Cadence, its Affiliates and its and their employees, subcontractors, agents, officers and directors (each a "Cadence Party") from and against all losses, liabilities, damages, fees (including, until such time as BMS assumes control of a given Claim, reasonable attorneys' fees and costs of litigation pertaining to such Claim), and expenses paid or payable by a Cadence Party to a Third Party that result from or arise out of any Claim against a Cadence Party to the extent such Claim or any losses, liabilities, damages or fees, cost and expenses in connection therewith is alleged to be or is in fact caused by, or is alleged to or in fact arises from or is based on the breach of any warranty of BMS contained in Section 3.11 or any material breach of BMS's covenants contained elsewhere in this Agreement; provided, however, that BMS shall not be obligated to indemnify a Cadence Party under this Agreement for any losses, liabilities, damages, fees or expenses incurred by such Cadence Party to the extent attributable to (i) any breach of this Agreement or the Quality Agreement by Cadence or a Cadence Party or (ii) negligence, gross negligence or willful misconduct on the part of Cadence or a Cadence Party.

6.2 By Cadence. Cadence shall indemnify, defend and hold harmless BMS, its Affiliates and its and their employees, subcontractors, agents, officers and directors (each, a "BMS Party"), from and against all losses, liabilities, damages, fees (including, until such time as Cadence assumes control of a given Claim, reasonable attorneys' fees and costs of litigation pertaining to such Claim), and expenses paid or payable by a BMS Party to a Third Party that result from or arise out of any Claim against a BMS Party to the extent such Claim or any losses, liabilities, damages or fees, cost and expenses in connection therewith is alleged to be or is in fact caused by, or is alleged to or in fact arises from or is based on (i) infringement of a Third Party's intellectual property in connection with the use or sale of the Clinical Testing Products or

(ii) any handling, storage, consumption, administration, injection, infusion, ingestion or other use or misuse of or exposure to the Clinical Testing Products after the placement thereof at the disposal of Cadence's carrier at the designated port of departure, except to the extent that the Claim or any losses, liabilities, damages or fees, cost and expenses in connection therewith results from or arises out of (A) a failure of the Clinical Testing Products to conform to the Specifications when placed at the disposal of Cadence's carrier in accordance with Section 3.4; (B) any breach of this Agreement or the Quality Agreement by BMS; (C) the negligence, gross negligence or willful misconduct on the part of BMS; or (D) any other matter for which BMS is expressly obligated to indemnify Cadence pursuant to Section 6.1. Cadence shall be solely responsible for any handling, storage, consumption, administration, injection, infusion, ingestion or other use or misuse of or exposure to, the Clinical Testing Products after placement at the disposal of Cadence's carrier, except as provided in the immediately preceding sentence.

6.3 Conditions to Indemnification. A Party seeking indemnification under this Article 6 (the "Indemnified Party") shall give prompt notice of the Claim to the other Party (the "Indemnifying Party") and, provided that the Indemnifying Party is not contesting the indemnity obligation, shall permit the Indemnifying Party to control and assume the defense of any litigation relating to such Claim and disposition of any such Claim unless the Indemnifying Party is also a party (or likely to be named a party) to the proceeding in which such Claim is made and the Indemnified Party gives notice to the Indemnifying Party that it may have defenses to such Claim or proceeding that are in conflict with the interests of the Indemnifying Party, in which case the Indemnifying Party shall not be so entitled to assume the defense of the case. If the Indemnifying Party does assume the defense of any Claim or proceeding, it (i) shall act diligently and in good faith with respect to all matters relating to the settlement or disposition of any Claim as the settlement or disposition relates to Parties being indemnified under this Article 6, (ii) shall cause such defense to be conducted by counsel reasonably acceptable to the Indemnified Party, or (iii) shall not settle or otherwise resolve any Claim without prior notice to the Indemnified Party and the consent of the Indemnified Party (which consent shall not be unreasonably withheld, conditioned or delayed) if such settlement involves anything other than the payment of money by the Indemnifying Party. The Indemnified Party shall cooperate with the Indemnifying Party in its defense of any Claim for which the Indemnifying Party has assumed the defense in accordance with this Section 6.3, and shall have the right (at its own expense) to be present in person or through counsel at all legal proceedings giving rise to the right of indemnification.

6.4 Limitation of Liability. IN NO EVENT SHALL EITHER PARTY (OR ANY OF ITS AFFILIATES OR SUBCONTRACTORS) BE LIABLE TO THE OTHER PARTY FOR, NOR SHALL ANY INDEMNIFIED PARTY HAVE THE RIGHT TO RECOVER, ANY SPECIAL, INDIRECT, INCIDENTAL, PUNITIVE OR CONSEQUENTIAL DAMAGES (INCLUDING LOST PROFITS OR DAMAGES FOR LOST OPPORTUNITIES), WHETHER IN CONTRACT, WARRANTY, NEGLIGENCE, TORT, STRICT LIABILITY OR OTHERWISE (WHETHER IN ANY CLAIM FOR INDEMNIFICATION PURSUANT TO THIS ARTICLE 6 OR OTHERWISE), ARISING (x) OUT OF THE MANUFACTURE, USE OR SALE OF ANY CLINICAL TESTING PRODUCT SOLD HEREUNDER OR (y) OUT OF ANY BREACH OF OR FAILURE TO PERFORM ANY OF THE PROVISIONS OF THIS AGREEMENT OR (z) ANY REPRESENTATION OR WARRANTY CONTAINED IN OR MADE PURSUANT TO THIS AGREEMENT, EXCEPT THAT SUCH LIMITATION SHALL

NOT APPLY TO PUNITIVE OR CONSEQUENTIAL DAMAGES PAID OR PAYABLE TO A THIRD PARTY BY AN INDEMNIFIED PARTY FOR WHICH THE INDEMNIFIED PARTY IS ENTITLED TO INDEMNIFICATION HEREUNDER.

ARTICLE 7

DISPUTE RESOLUTION

7.1 Arbitration. Except as otherwise provided in this Agreement, any dispute, difference or question arising between the Parties or any of their Affiliates or Indemnified Parties in connection with this Agreement or the Quality Agreement, the formation, interpretation, construction thereof or the rights, duties or liabilities of any Party or any of its Affiliates (a "Dispute") shall be resolved by binding arbitration in accordance with this Section 7.1. Any Party or any such Affiliate or Indemnified Party may require resolution of any such Dispute by arbitration hereunder by sending a written notice to the other Party demanding arbitration of the Dispute (the "Demand"). In that event, the Dispute shall be finally resolved by arbitration in accordance with the United States Arbitration Act and the Commercial Arbitration Rules of the American Arbitration Association. The venue for the arbitration shall be New York, New York. The arbitration shall be conducted in the English language before a panel of three (3) arbitrators. Each Party shall name one arbitrator, and the two so named shall name the third arbitrator, who shall act as chairman. If the two party arbitrators cannot agree on a third arbitrator within thirty (30) days after the Demand, then at the request of either Party the President of the Association of the Bar of the City of New York shall appoint the third arbitrator. The arbitrators shall promptly meet, fix the time, date and place of the hearing and notify the Parties. All documents, exhibits, testimony or other information that is not in the English language shall be translated into the English language at the expense of the Party proffering the evidence requiring translation. The decision of the arbitrators may (depending on the equities of the case) include an award of legal fees, costs of arbitration and interest. The panel of arbitrators shall promptly transmit an executed copy of its decision to the Parties. The decision of the arbitrators shall be final, binding and conclusive upon the Parties. Judgment on the award rendered by the arbitrators may be entered in any court having jurisdiction thereof. Each Party retains the right to seek from a court any interim or provisional relief that may be necessary to protect the rights or property of that Party as permitted by Section 9.3 hereof pending the establishment of the arbitrators' determination of the merits of the controversy, and any such action shall not be deemed incompatible with this Agreement to arbitrate or a waiver of the right to arbitration. The obligations of the Parties under this Section are specifically enforceable and shall survive any termination of this Agreement. Unless the decision of the arbitrators provides otherwise, the Parties shall bear their own costs in preparing for the arbitration and the costs of the arbitrators shall be equally divided between the Parties.

ARTICLE 8

TERM; TERMINATION

8.1 Term; Termination. (a) This Agreement shall commence on the Effective Date and shall continue for the Supply Term and until BMS has supplied in accordance with this Agreement all the Clinical Testing Products ordered by Cadence pursuant to Firm Orders prior to the end of the Supply Term that BMS is obligated to supply under this Agreement unless earlier terminated as provided below. This Agreement shall terminate upon the occurrence of any of the following events:

(i) the written consent of each of BMS and Cadence to terminate this Agreement;

(ii) Cadence's permanent cessation of the Clinical Use of the Parenteral Acetaminophen Products in the Territory;

(iii) the termination of the IV APAP Agreement; or

(iv) the dissolution or termination of Cadence, other than in connection with or following an assignment of this Agreement in accordance with Section 9.7.

(b) Either Party may, by written notice to the other Party, terminate this Agreement in the event of a material breach of this Agreement by the other Party, which remains uncured by such other Party for a period of sixty (60) days.

8.2 Consequences of Termination. Termination of this Agreement pursuant to this Article 8 shall be without prejudice to any rights which shall have accrued to the benefit of any Party prior to such termination. Such termination shall not relieve any Party from its obligations which are expressly indicated to survive the termination of this Agreement. All of the Parties' rights and obligations under the immediately proceeding sentence and under Sections 2.3, 3.6, 3.7, 3.10, 3.11 and 8.2 and Articles 4, 5, 6, 7and 9 hereof shall survive such termination for the applicable period. In the event of the termination or expiration of this Agreement (other than for an uncured material breach by BMS), Cadence will reimburse BMS and its Affiliates for the cost of any inventory of Placebos or the inventory of raw materials and supplies purchased by BMS for producing the Placebos to the extent (i) BMS or its Affiliates reasonably acquired and held such inventory consistent with Cadence's Forecasts, (ii) BMS and its Affiliate that holds such inventory is unable reasonably to utilize such inventory for other customers or for itself or any other BMS Affiliate and (iii) BMS delivers such inventory to Cadence.

ARTICLE 9

MISCELLANEOUS

9.1 Notices. All notices, consents, requests, demands and other communications required or permitted under this Agreement: (a) shall be in writing in the English language;

(b) shall be sent by messenger, a reliable express delivery service or facsimile (with a copy sent by one of the foregoing means), charges prepaid as applicable, to the appropriate address(es) or number(s) set forth below; and (c) shall be deemed to have been given on the date of receipt by the addressee (or, if the date of receipt is not a Business Day, on the first Business Day after the date of receipt), as evidenced by (i) a receipt executed by the addressee (or a responsible person in his or her office), the records of the Person delivering such communication or a notice to the effect that such addressee refused to claim or accept such communication, if sent by messenger or express delivery service, or (ii) a receipt generated by the sender's fax machine showing that such communication was sent to the appropriate number on a specified date, if sent by facsimile. All such communications shall be sent to the following addresses or numbers, or to such other addresses or numbers as any Party may inform the others by giving five Business Days' prior notice:

If to Cadence:

Cadence Pharmaceuticals, Inc.
12730 High Bluff Drive, Suite 410
San Diego, CA 92130
Attn: President & CEO
Fax No.: (858) 436-1401

With a copy to:

Cadence Pharmaceuticals, Inc.
12730 High Bluff Drive, Suite 410
San Diego, CA 92130
Attn: VP of Business Development
Fax No.: (858) 436-1401

If to BMS:

Lawrence Laboratories
Unit 12 Distribution Centre
Shannon Industrial Estate
County Clare
Ireland
Attn: General Manager
Fax No.: 011-35-3-61-47-1396

With a copy to:

Bristol-Myers Squibb Company
1 Squibb Drive
New Brunswick, NJ
Attn: Senior Counsel Technical Operations
Fax No.: 732-227-3874

If to Parent:

Bristol-Myers Squibb Company
1 Squibb Drive
New Brunswick, NJ
Attn: Director, Contract Manufacturing
Fax No.: 732-227-3960

With a copy to:

Bristol-Myers Squibb Company
1 Squibb Drive
New Brunswick, NJ
Attn: Senior Counsel Technical Operations
Fax No.: 732-227-3874

9.2 Governing Law. This Agreement is a contract under the laws of the State of New York and for all purposes shall be governed by, and construed and enforced in accordance with, the laws of said State, without giving effect to any conflict of law rules.

9.3 Equitable Relief. The Parties acknowledge and agree that each would be irreparably damaged in the event that any provision of this Agreement is not performed by the other in accordance with its specific terms or is otherwise breached. Accordingly, it is agreed that each Party is entitled to an injunction or injunctions to prevent breaches of this Agreement by the other and shall have the right to specifically enforce this Agreement and the terms and provisions hereof against the other without the posting of any bond or other security, in addition to any other remedy to which such aggrieved Party may be entitled at law or in equity; provided, however, that the powers of the arbitrators under Section 7.1 shall be limited to enforcing the obligations provided for in this Agreement as drafted.

9.4 Headings. All titles or captions contained in this Agreement are for convenience of reference only and shall not limit or affect in any way the meaning or interpretation of this Agreement.

9.5 No Third Party Beneficiaries. This Agreement shall be binding upon, and inure solely to the benefit of, the Parties and their permitted assigns, and nothing herein, express or implied, is intended to, or shall confer upon, any other Person any legal or equitable right, benefit or remedy of any nature whatsoever.

9.6 Severability. If any term or other provision of this Agreement is held to be invalid, illegal or incapable of being enforced by any Applicable Law or public policy, all other terms and provisions of this Agreement shall nevertheless remain in full force and effect so long as the economic or legal substance of the transactions contemplated hereby is not affected in any manner materially adverse to any Party. Upon such determination that any term or other provision is invalid, illegal or incapable of being enforced, the Parties shall negotiate in good faith to modify this Agreement so as to effect the original intent of the Parties as closely as possible in an acceptable manner in order that the transactions contemplated hereby are consummated as originally contemplated to the greatest extent possible.

9.7 Assignment and Subcontracting. (a) Except as set forth below in this Section 9.7 neither this Agreement, nor any right, interest or obligation hereunder, may be assigned, pledged or otherwise transferred by any Party, whether by operation of law or otherwise, without the prior consent of the other Party, except that BMS may assign any of its rights or delegate any of its obligations hereunder to any of its Affiliates, provided, that BMS shall provide Cadence with written notice of any such assignment or delegation. Cadence acknowledges that BMS will delegate the manufacturing of the Clinical Testing Products to its Affiliate, Bristol-Myers Squibb S.R.L., in Italy and that delegation to such Affiliate shall not require any further notice to Cadence.

(b) Either Party may assign or transfer all of its rights and obligations hereunder without the prior consent of the other Party to a successor in interest by reason of merger, consolidation or sale of substantially all of the assets of the assigning Party (and so long as such assignment or transfer includes, without limitation, all Approvals, all manufacturing assets relating to the IV APAP Agreement, and all rights and obligations under the IV APAP Agreement); provided, that such successor in interest shall have agreed prior to such assignment or transfer to be bound by the terms of this Agreement in a writing provided to the other Party.

(c) BMS may subcontract any or all of its obligations under this Agreement to a Third Party, with the prior written consent of Cadence, which shall not be unreasonably withheld, delayed, or conditioned.

(d) Not withstanding anything to the contrary herein, any assignment, delegation or subcontracting by a Party of any of its rights or obligations under this Agreement shall not relieve such Party from any of its obligations hereunder.

(e) Any assignment or transfer in violation of the foregoing shall be null and void and wholly invalid, the assignee or transferee in any such assignment or transfer shall acquire no rights whatsoever, and the non-assigning non-transferring Party shall not be required to recognize, such assignment or transfer.

(f) Subject to the foregoing, this Agreement shall inure to the benefit of and be binding on the Parties' successors and permitted assigns.

9.8 Consents. Any consent or approval to any act or matter required under this Agreement shall be in writing and shall apply only with respect to the particular act or matter to which such consent or approval is given, and shall not relieve any Party from the obligation to obtain the consent or approval, as applicable, wherever required under this Agreement to any other act or matter.

9.9 Entire Agreement. This Agreement contains the entire agreement of the Parties with respect to the subject matter of this Agreement and supersedes all prior written and oral agreements, and all contemporaneous oral agreements, relating to such subject matter.

9.10 Exhibits. The Exhibits attached to this Agreement are an integral part hereof and all references to this Agreement include such Exhibits.

9.11 Waivers and Amendments. No modification of or amendment to this Agreement shall be valid unless in a writing signed by all Parties referring specifically to this Agreement and stating the Parties' intention to modify or amend the same. Any waiver of any term or condition of this Agreement shall be in a writing signed by the Party sought to be charged with such waiver referring specifically to the term or condition to be waived, and no such waiver shall be deemed to constitute the waiver of any other breach of the same or of any other provision hereof.

9.12 No Partnership or Joint Venture. This Agreement is not intended to create, and nothing contained herein shall be construed to create, an association, joint venture, trust or partnership, or to impose a trust or partnership covenant, obligation or liability on or with regard to the other Party. Each Party shall be severally responsible for its own covenants, obligations and liabilities as herein provided. No Party shall be under the control of, or shall be deemed to control any other Party; no Party is the legal representative, agent, joint venturer or employee of the other Party with respect to this Agreement for any purpose whatsoever; no Party shall have the right or power to bind the other Party; and no Party has the right or authority to assume or create any obligations of any kind or to make any representation or warranty on behalf of any other Party, whether express or implied, or to bind any other Party in any respect whatsoever.

The provisions of this Agreement are intended only for the regulation of relations between the Parties.

9.13 Absence of Presumption. With regard to each and every term and condition of this Agreement and any and all agreements and instruments subject to the terms hereof, the Parties hereto understand and agree that the same have or has been mutually negotiated, prepared and drafted, and if at any time the Parties hereto desire or are required to interpret or construe any such term or condition or any agreement or instrument subject hereto, no consideration shall be given to the issue of which Party hereto actually prepared, drafted or requested any term or condition of this Agreement or any agreement or instrument subject hereto.

9.14 Counterparts; Facsimile Execution. This Agreement may be executed in any number of counterparts, and by each of the Parties on separate counterparts, each of which, when so executed, shall be deemed an original, but all of which shall constitute but one and the same instrument. Delivery of an executed counterpart of this Agreement by facsimile shall be equally as effective as delivery of a manually executed counterpart of this Agreement.

9.15 Guarantee. In consideration for Cadence entering into this Agreement and for other good and valuable consideration the sufficiency of which is hereby acknowledged, Parent hereby absolutely and unconditionally guarantees to Cadence the timely performance of each and all of the obligations (including, without limitation, any obligation to make payments under this Agreement) of BMS (or any of its permitted assignees), subject to the terms and conditions of this Agreement. Parent agrees that its guarantee is a continuing obligation which shall not be terminated unless and until all of the obligations hereunder of BMS (or any of its permitted assignees) are fully performed and that Cadence may enforce this guarantee without exhausting any and all remedies available against BMS (or any of its permitted assignees).

SIGNATURE PAGE TO CLINICAL SUPPLY AGREEMENT

IN WITNESS WHEREOF, the Parties have duly executed this Agreement as of the day and year first above written.

LAWRENCE LABORATORIES

By: /s/ Barry Sexton
Name: Barry Sexton
Title: General Manager

CADENCE PHARMACEUTICALS, INC.

By: /s/ Theodore R. Schroeder
Name: Theodore R. Schroeder
Title: President and CEO

And with respect to Section 9.15 only:

BRISTOL-MYERS SQUIBB COMPANY

By: /s/ Bernard F. Leclere
Name: Bernard F. Lecler
Title: VP Supply Chain

EXHIBIT A

SPECIFICATIONS

Specifications for Parenteral Acetaminophen Products

The Specifications are the same as those for BMS's currently marketed product, which are set forth below, except that the Specifications for the Clinical Testing Products do not include a trade name. The Clinical Testing Products will be provided in vials in bulk, without commercial or clinical labeling.

[***]

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

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*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

EXHIBIT B

INITIAL FORECAST

For the first [***] period after the Effective Date:

[***] (at minimum batch size) of Parenteral Acetaminophen Product

[***] (at minimum batch size) of Placebo

in each case to be placed at the disposal of Cadence's carrier not later than the later of (i) [***] ([***]) [***] after the Effective Date or (ii) [***] ([***]) months after the execution of the Quality Agreement.

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

EXHIBIT C

QUALITY AGREEMENT

Bristol-Myers Squibb Company
Cadence Pharmaceuticals

QUALITY AGREEMENT — Intravenous Acetaminophen

Parties to this Agreement:

Cadence Pharmaceuticals (the Contracting Company)	-	**Company A**
Bristol-Myers Squibb Srl, BMS Anagni (the Contract Acceptor)	-	**Company B**

1. GUIDING PRINCIPLES

This quality agreement (written in accordance with the principles defined in Chapter 7 of the EU/PIC Guide to Good Manufacturing Practice and the US Food and Drug Administration regulations 21 CFR part 211) specifies the relationship between the quality organizations of Cadence Pharmaceuticals and Bristol-Myers Squibb Srl BMS Anagni, for the Products listed in Appendix A. These Products are manufactured and/or packaged and QC tested by BMS Anagni Company B (hereafter referred to as BMS Anagni) and released and used for clinical trials by Cadence Pharmaceuticals Company A (hereafter referred to as Cadence).

The abbreviation "BMS Anagni" is used throughout the remainder of this document to refer to "Bristol-Myers Squibb Srl located in Anagni, Italy" represented by its affiliates or agents who are signatories to this document. The abbreviation "BMS" refers to Bristol-Myers Squibb Company.

Quality contacts are listed in Appendix B.

A glossary of terms used in this document is shown in Appendix C.

2. PRIMARY RESPONSIBILITIES

2.1 The Cadence Pharmaceuticals Pharmaceutical Development and Quality Assurance Departments have the responsibility to provide sufficient information to BMS Anagni to ensure that Products can be manufactured, packaged and tested in accordance with cGMPs, the Product specifications and Cadence requirements. The governing document for these requirements shall be the US Investigational New Application (IND) number 58,362 which has been transferred from BMS to Cadence Pharmaceuticals. Cadence will provide the manufacturing, specification and quality sections of IND 58,362 directly to BMS Anagni with a letter authorizing the use of these documents as the governing compliance document. The letter will be sent from the Vice President of Regulatory Affairs and Quality Assurance at Cadence within 30 days of receipt of the full IND from BMS. All manufacturing procedures, QC testing and release specifications shall be in conformance with this IND application.

2.2 Lawerence Laboratories, a Bristol-Myers Squibb Company wholly-owned subsidiary located in Shannon, Ireland, has the responsibility to purchase and to ship to BMS Anagni, the API, acetaminophen.

2.2 BMS Anagni has the responsibility to purchase, test and release material, perform sampling, maintain in-process controls and to ensure that the Products are manufactured, packaged, QC tested and released for shipment in compliance with cGMPs and the Product registrations. Anagni has also the responsibility to, test and release the API sent by Lawrence Laboratories

2.3 Final certification and release of the bulk packaged Product to Cadence is the responsibility of a BMS Anagni Qualified Person who will ensure that the Products have been manufactured, packaged, and QC tested and in compliance with cGMPs and the IND application requirements.

2.4 Final certification and release of the final labeled Product to clinical sites is the responsibility of a Cadence Authorized Person who will ensure that the Products have been handled, labelled and released to clinical sites in compliance with cGMPs and the IND application requirements.

2.5 Changes to the manufacturing process, QC testing, release specifications or stability testing requirements as outlined in IND 58,362 shall be approved by Cadence Quality Assurance and Pharmacetical Development groups prior to implementation for any clinical batch of Product intended for use by Cadence in clinical trials.

2.6 A summary of responsibilities is included in Appendix D.

3. CHANGE CONTROL

All changes will be completed in accordance with standard BMS Anagni procedures. This will ensure that all the parties to this agreement are notified and their approval obtained, as required, prior to the execution of the change. A change is defined as any alteration from the process, QC testing, Specifications or other cGMP requirements outlined in IND 58,362. These changes require approval by Cadence Quality Assurance and Pharmaceutical Development prior to implementation.

4. MATERIAL RELEASE PROCEDURES

4.1 Starting Materials

API is supplied by Laurence Labs to BMS Anagni. BMS Anagni is responsible for inspecting and testing starting materials according to approved in-house procedures and technical specifications, which are in compliance with IND 58,362.

4.2 Bulk Product / Bulk Nested Product / Finished Product

4.2.1 Product testing, batch record review and batch release of Product will be performed by BMS Anagni to ensure the Product meets specification listed in Attachment E, and was manufactured in compliance with cGMPs, the Product IND 58,362 and other BMS, Anagi or Cadence requirements.

4.2.2 For each batch of Product, BMS Anagni will send Cadence a Certificate of Analysis, a copy of the Product Batch Record, a copy of all deviation reports and conclusions, a copy of any out-of-specification reports and conclusions, other investigations conducted as a result of deviations from production requirements and a Certificate of Conformance/Manufacture (CoC/M). The CoC/M will include a statement that the batch has been manufactured and packaged according to the master production documents in compliance with cGMPs and IND 58,362 and that any deviations have been investigated as per BMS Anagni Standard Operating Procedures. In addition, it will include the following information:

- Product name, lot number, date of manufacture and expiry date (bulk nested Products/Finished Products only)
- Total quantity of bulk Product released (Number of units)
- Notification if and when the batch was reprocessed or reworked using a validated procedure
- Signature of BMS Anagni Product Release Authority

4.3 Final certification and release of Product to clinical sites will be the responsibility of Cadence Quality Assurance, who will act in accordance with applicable regulations and filings.

5. BATCH RECORD RETENTION

5.1 Originals of all batch and laboratory documentation (including raw data) will be retained by BMS Anagni according to regulatory and BMS Anagni requirements.

5.2 BMS Anagni will provide a copy of the complete batch documents to Cadence Quality Assurance.

6. RETAIN SAMPLES

This requirement applies to bulk nested Product or Finished Product only. Bulk nested Products are indicated by the abbreviation (BN) in Appendix A; Finished Products are indicated by (FP) and bulk Product by (B).

BMS Anagni will ensure that retain samples of Product are kept under proper storage conditions, as required to comply with retain sample requirements and/or registration commitments. However, in no case should the number of retained samples be less than the amount needed to perform twice the necessary tests for Finished Product release, with the exception of sterility and bacterial endotoxin testing for which only one complete retest quantity need be retained. Testing of retain samples may be initiated with approval of Cadence Quality Assurance. Retain samples will be visually inspected on an annual basis as per cGMP and BMS Anagni, requirements. Any issues will be immediately notified to Cadence Quality Assurance.

7. STABILITY FOR FINISHED PRODUCT AND PLACEBO

This requirement applies to bulk nested Product and placebo or Finished Product and placebo only. Bulk nested Products are indicated by the abbreviation (BN) in Appendix A; Finished Products are indicated by (FP) and bulk Product by (B).

7.1 BMS Anagni will ensure the completion of appropriate stability studies on Products and placebo in their primary packaging containers according to the stability protocol outlined in IND 58,362, Attachment E, that will conform to current ICH and cGMP guidelines.

7.2 For each lot of Product or placebo, representative samples must be collected for stability testing according to the stability protocols. Stability to be performed on the clinical trial lots according to the approved stability protocols, Attachment E.

7.3 If a confirmed result indicates a Product or placebo lot has failed to remain within specifications, BMS Anagni is required to notify the Cadence Quality Assurance representatives immediately.

7.4 In all cases BMS Anagni must investigate any confirmed out-of-specification result and forward a copy of the completed investigation report within 30 days to Cadence Quality Assurance**.**

8. COMPLAINTS

8.1 Product complaint reports received by BMS Anagni from its customers will be handled in accordance with standard BMS Anagni policies and guidelines.

8.2 When requested, BMS Anagni will investigate all Product complaints and provide Cadence Quality Assurance with a written report within thirty (30) days after receipt of the complaint or complaint sample as appropriate.

9. RECALL

Recalls will be handled in accordance with applicable regulations and standard BMS Anagni guidelines. The designated group that manages Product recalls is responsible for making all Product recall decisions. Within certain jurisdictions, this group must include an Authorized Person from Cadence Quality Assurance.

10. ANNUAL PRODUCT REVIEW — Not Applicable

11. AUDITS

Audits of BMS Anagni will be performed by Cadence auditors prior to release of the first clinical production lot by Cadence (only one audit is anticipated) and audit reports will be available to the Anagni Quality group upon request.

12. VENDOR QUALIFICATION

This will be completed in accordance with appropriate Regulatory requirement and standard BMS Anagni policies and guidelines.

13. STORAGE

BMS Anagni will ensure that pharmaceutical Products (bulk Product, bulk nested Product or Finished Product) are stored within the Product label storage range defined in IND 58,362. Excursions in temperature and/or relative humidity (if applicable) during storage must be investigated. Any such excursion impacting on Product quality will be reported to the Authorized Person.

14. SUBCONTRACTING

Where BMS Anagni proposes to subcontract any services related to the Products supplied, BMS Anagni change control procedures will apply. Cadence Pharmaceutical Development and Quality Assurance shall be notified of any intention to subcontract manufacturing or testing activities to gain agreement prior to implementing any transfer activities.

15. MICROBIOLOGICAL MONITORING

BMS Anagni will maintain an appropriate microbiological monitoring program to ensure acceptable microbiological quality and compliance with applicable regulations.

16. TRAINING

Each person engaged in the manufacturing, processing, packaging, testing or holding of a drug Product shall have education, training, and experience, or any combination thereof, to enable that person to perform the assigned functions. Training shall be in the particular operations that the employee performs and in current applicable manufacturing regulations as they relate to the employee's functions. Training in applicable manufacturing regulations shall be conducted by qualified individuals on a continuing basis and with sufficient frequency to assure that employees remain familiar with requirements applicable to them. This training must be documented in a training record for each employee.

17. QUALIFICATION & VALIDATION PROGRAMS

This will be completed in accordance with appropriate Regulatory expectations and standard BMS Anagni policies and guidelines.

18. COMPLIANCE WITH LOCAL REGULATIONS

BMS Anagni undertakes to obtain and maintain the appropriate authorisation to manufacture the Products. BMS Anagni shall inform the Cadence Quality Assurance person responsible about any change or withdrawal of such authorisation without undue delay.

19. SHIPPING PROTOCOL AND RESPONSIBILITIES FOR RECEIPT OF PRODUCT AND PLACEBO

Shipping and resolution of product defects shall be managed as specified in the Clinical Supply Agreement between Lawrence Laboratories and Cadence Pharmaceuticals, dated 21 February 2006.

Cadence shall evaluate the shipping protocols and any available data supplied by BMS for both the product and placebo to determine the suitability of this information to support the shipping of product by Cadence. If the BMS shipping data does not support the Cadence proposed shipping conditions and procedures, Cadence shall conduct a shipping study for the drug product and/or placebo to demonstrate the acceptability of the shipping conditions. The Cadence shipping protocol and study results shall be shared with BMS.

20. HISTORY SECTION

Version Number	Comment	Issue Date
1	First issue of the Quality Agreement between Cadence and BMS Anagni for Products listed in Appendix A	**June 2006**

Issue date: This is defined as the date the document received final signature

Cadence Approval:

Signed: _____ _____

Richard E. Lowenthal, MSc,
Vice President Regulatory Affairs and Quality Assurance,
Cadence Pharmaceuticals

Lawrence Laboratories:

Signed: _____ _____

Gillian O'GHara
QA Director, Lawrence Labs

BMS Anagni Approval:

Signed: _____ _____

Eugenio Cusimano
QC/QA Director & Qualified Person
Bristol-Myers Squibb BMS Anagni

APPENDIX A:

Products:

Acetaminophen (Perfalgan) Injection [Active Product] (FP)

Acetaminophen (Perfalgan) Injection Placebo (FP)

(BN) indicates this is a bulk nested Product

(B) indicates this is a bulk Product

(FP) indicates this is a Finished Product

APPENDIX B:

Cadence Quality Assurance

Quality Contacts — Richard E. Lowenthal, MSc

Phone: 858-335-1300
Fax: 858-436-1401
e-mail: rlowenthal@cadencepharm.com

Cadence Pharmaceutical Development

Product Development Contact — William Craig, PhD

Phone: 858-354-0847
Fax: 858-436-1401
e-mail: wcraig@cadencepharm.com

Bristol-Myers Squibb BMS Anagni

Quality Contact — Qualified Person

Eugenio Cusimano

QC/QA Director,

Phone: ++39 0775 762210
Fax: ++39 0775 762285
e-mail: eugenio.cusimano@bms.com

APPENDIX C:

Glossary of Terms

Pharmaceutical Product	Any Product that may be defined as a Bulk Product or a Finished Product
Bulk Product	Any Product which has completed all processing stages up to, but not including, packaging in a primary container (e.g., blister, bottle).
Finished Product	Any Product that has completed all processing stages and is in its final pack for release to Cadence.
Authorized Person	The person or persons charged with final release of the batch for clinical studies outside of the European Union (EU).
Qualified Person	The person or persons charged with certification and batch release of medicinal Products within the European Union (EU) or European Economic Area (EEA).
cGMP	Current Good Manufacturing Practices for Pharmaceuticals as described in regulations promulgated by the FDA or equivalent regulatory agency in a foreign country or jurisdiction.
Governmental Authority	Any (i) national, state, provincial, local or any foreign or supranational government; (ii) governmental, regulatory or administrative authority, agency or commission; or (iii) any court, tribunal or judicial or arbitral body.

APPENDIX D:

Division of pharmaceutical responsibilities*

Contract Giver: Cadence Pharmaceuticals, Inc.

Contract Acceptor: Bristol Myers Squibb, Anagni

	Contract Giver	Contract Acceptor
Agreement with the registration documents	☑	☑
Active ingredient(s):		
Specification	☑	☑ Note 1
Supply/Procurement	☑	☑
Testing	o	☑
Release	☑	☑
Excipients:		
Specification	o	☑ Note 1
Supply/Procurement	o	☑
Testing	o	☑
Release	o	☑
Primary packaging: (Note 2)		
Specification	☑	☑ Note 1
Supply/Procurement	o	☑
Testing	o	☑
Release	o	☑
Secondary packaging (Note 3):		
Specification	☑	☑ Note 1
Supply/Procurement	o	☑
Testing	o	☑
Release	o	☑
Package leaflet: N/A		
Specification	o	o
Clearance for printing/proof —reading	o	o
Supply/Procurement	o	o
Testing	o	o
Release	o	o

* This list is not necessarily all inclusive and is intended only as a summary of the highlights contained within the body of the Quality Agreement.

Cont’d

Bulk product/bulk nested Product:				
Manufacturing directions		o		☑ Note 1
In-process control		o		☑
Manufacture		o		☑
Manufacturing record completion		o		☑
Review of manufacturing documentation		o		☑
Testing directions		o		☑ Note 1
Quality control/test record		o		☑
Release		☑		☑
Certificate of manufacture/conformance		o		☑
Certificate of analysis		o		☑
Release for dispatch		o		☑
Assignment of batch number		o		☑
Assignment of expiration date		o		☑ Note 4
Retain Samples		☑		☑ see Section 6
Stability Testing		☑		☑ see Section 7
Transportation to Contract Giver		o		☑
Review of manufacturer certificates		☑		o
Authorized or Qualified Person release of Finished Product		☑		o
Finished Product (Note 5)				
Specification		☑		o Note 1
Packaging directions		☑		o Note 1
In-process control		☑		o
Packaging		☑		o
Packaging record completion		☑		o
Review of packaging documentation		☑		o
Testing directions		☑		o Note 1
Quality control/test record		☑		☑
Certificate of analysis		☑		☑
Certificate of manufacture/conformance		o		☑
Assignment of batch number		☑		o
Assignment of expiration date		☑		o
Retain Samples		☑		o
Stability Testing		o		o
Transportation to warehouse (compliance with GDP)		o		o
Review of manufacturer certificates		☑		o
Authorized or Qualified Person release of Finished Product		☑		o

Note 1: This refers to documents prepared internally by BMS Anagni. Any such documentation must be in accordance with the appropriate Product registration. BMS Anagni is responsible for the bulk finished product and all requirements for release and documentation. Cadence is responsible for labeling of the product and final packaging to produce the clinical finished product.

Note 2: This applies to bulk nested Product and Finished Product only — see Appendix A

Note 3: This applies to Finished Product only — see Appendix A (Secondary packaging will occur at both BMS Anagni for shipment to the United States and also at a 3rd party clinical packaging site for shipment to clinical sites)

Note 4: This applies to bulk nested Product only — see Appendix A

APPENDIX E:

Testing Standards & Stability Protocols (attached)

[Note: Attached IND Stability Protocol as currently written]

EXHIBIT 10.15

CERTAIN MATERIAL (INDICATED BY AN ASTERISK) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

Execution Copy

CLEAR VIEW PROJECTS

May 19, 2005

Mr. Ted Schroeder
President and CEO

By Mail:
Cadence Pharmaceuticals
12730 High Bluff Drive, Suite 410
San Diego, CA 93130

By Email:
tschroeder@CadencePharm.com

Dear Ted:

Thank you for offering Clearview Projects, Inc, ("Clearview") the opportunity to provide Cadence Pharmaceuticals ("Cadence" or "Company") with consulting services ("Services"). This engagement letter ("Engagement Letter") sets forth the terms and conditions under which Clearview will perform such Services. Subsequent sections of this Engagement Letter are organized as follows:

- Background
- Services
- Fees and Expenses
- Other Terms

Background

Cadence is a privately held, venture capital backed specialty pharmaceutical company focusing on the hospital channel segment. Since its inception, the company has assembled an experienced team of executives to fill out the senior management infrastructure. With this senior management team in place, the company believes it is poised to scale up both its pipeline and commercial launch activity.

Cadence's first product, CPI-226, is a topical antimicrobial currently undergoing confirmatory Phase III clinical trials. The primary endpoint for the CPI-226 Phase III trial is related to so-called ***local catheter site infections***. Management believes that confirmation of this endpoint will lead to an FDA approval.

With CPI-226 as a starting base, the company seeks to acquire or in-license additional clinical candidates or commercial products in order to fully develop the growth business model of the company. Clearly, a key driver for scaling the initial growth curve of the company is this product-level acquisition activity. To that end, you have identified three (3) late-stage

development program(s)/product(s) ("Three Targets") for which you are in varying stages of discussion with the current owner. Our understanding of the transaction situations associated with each of the Three Targets is:

- Phase III Pain Management development-stage program. The rights to this late-stage development program are currently owned by a "Big Pharma" and you anticipate the need to structure an offer in the very near future for exclusive US rights.
- [***].
- [***].

Services

Clearview will provide analytical and execution advice for all aspects of your efforts to acquire rights associated with the Three Targets. These services will include:

- Assistance in accessing the appropriate decision making process within the current corporate owners' organization. This will include interaction with management at all levels in the company's organization structure.
- Advice and support in developing a strategic business case for the implied investment required for the acquisition/in-licensing of these products/programs. This would include any interaction you may require with the Cadence Board of Directors.
- Advice and support in structuring an offer and in executing all aspects of the transaction process — including business due diligence and negotiations (alongside counsel and other functional experts).
- Other related tasks that you may reasonably require in furthering the acquisition initiatives.

As with the vast majority of our engagements, we will utilize a team structure to perform the engagement services. This approach enables Clearview to emphasize particularly specialized expertise depending on the underlying task at hand. [***], Vice President and leader of Clearview's partnering/alliance client activities, will oversee day-to-day aspects of the engagement and will ensure that any mix of the professionals identified in Exhibit I are involved as appropriate. In addition, other Clearview professional staff may be involved to effectively carry out a variety of analytical and project management work activities.

During the term of this Engagement Letter, neither Cadence nor its Board will retain any other firm to provide similar services to those being performed by Clearview and described herein ("Competitive Firm"). A Competitive Firm, however, shall not include consultants providing

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

specific expertise, support or advice — not in competition with the Services — relating to one or more of the Three Targets.

The Services will be carried out for the specific use of Mr. Ted Schroeder, CEO of Cadence, and the Board of Cadence. Commencement of the Services will be initiated upon the execution of this Engagement Letter.

Fees and Expense

In consideration for our Services, Cadence will pay Clearview a cash monthly retainer ("Monthly Retainer") in the amount of $[***]. Should Cadence choose to stop its efforts for pursuing a transaction for one or two of the Three Targets ("Lapsed Target") and the parties do not agree on a Substitute Target for each such Lapsed Target, then Clearview's Monthly Retainer would be reduced to $[***] payable in cash. "Substitute Target" shall be a commercial or late-stage development program/product which, upon mutual agreement between Cadence and Clearview, becomes a constituency of the Three Targets. In addition to this Monthly Retainer, upon the closing of each individual transaction involving the acquisition/in-licensing of rights associated with any one of the Three Targets ("Success Fee Transaction"), Cadence will pay Clearview, or an affiliate, $[***] ("Success Fee"). The consideration for the Success Fee shall be composed of $[***] paid in cash ("Cash Success Fee") and $[***] paid in the form of either issued Cadence common equity ("Equity Success Fee") or cash, the choice of which shall be at the discretion of Cadence ("Fee Choice"). Cadence shall make its Fee Choice within [***] days of closing a Success Fee Transaction. The number of common shares related to the Equity Success Fee shall be determined by dividing $[***] by the price-per-share associated with the equity financing round completed by Cadence within [***] days of closing a Success Fee Transaction. If no equity financing round is completed by Cadence within [***]days of closing a Success Fee Transaction, then the number of common shares related to the Equity Success Fee shall be determined by dividing $[***] by the price-per-share associated with the most recent equity financing round completed by Cadence.

The Monthly Retainer and Success Fee payments shall not include direct out-of-pocket expenses incurred by Clearview in carrying out the Services ("Expenses"). We will invoice you separately for Expenses, which for this engagement, should be principally travel-related and any purchased third party market research that both Cadence and Clearview mutually agree to be appropriate. Expenses incurred by Clearview shall be reimbursed by the Company in cash upon receipt of reasonable documentation.

All Monthly Retainer and Expense payments shall be remitted to Clearview within [***] business days of the Company's receipt of an invoice for such amounts. Success Fee payments shall be remitted to Clearview at the closing of each such Success Fee Transaction. The Equity Success Fee, however, shall be paid at the earlier of [***] days from closing a Success Fee Transaction or within [***] business days of closing a Cadence equity financing round subsequent to closing a Success Fee Transaction.

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All remittances to Clearview shall be wire-transferred in accordance with the following instructions:

Bank: [***]
Account name: [***]
Account number: # [***]
SWIFT number: # [***]
SWIFT address: [***]

Other Terms

With no less than two weeks notice, (1) either party may terminate this Engagement Letter or (2) Cadence may designate a Lapsed Target. In addition, (1) should Cadence terminate the Engagement Letter and subsequently consummate a Success Fee Transaction within the [***] period after such termination, then Clearview shall be entitled to a Success Fee for each such transaction occurrence and (2) should Cadence consummate a Lapsed Success Fee Transaction within the [***] period after such Lapsed Target designation, then Clearview shall be entitled to a Success Fee for each such transaction occurrence. "Lapsed Success Fee Transaction" shall be the closing of an individual transaction involving the acquisition/in-licensing of rights associated with a Lapsed Target.

Clearview agrees that for the [***] period following either the termination of this Engagement Letter, or as applicable, designation of a Lapsed Target, it shall not attempt or assist in the attempt to enter into a partnership ("Partnership") related to any one of the Three Targets or a Lapsed Target without the prior written consent of Cadence. Partnership shall include a program/product-level licensing or acquisition transaction, BUT, shall specifically exclude the acquisition of a division or company whose assets include any one of the Three Targets or a Substitute Target as a minority subset.

Either the Company or Clearview may terminate this Engagement Letter upon written notice to the other party in the event of the dissolution, liquidation, insolvency of the other party or in the event of a voluntary or involuntary bankruptcy or reorganization petition involving such other party.

IN NO EVENT SHALL EITHER PARTY BE LIABLE TO THE OTHER PARTY FOR ANY SPECIAL, INCIDENTAL, CONSEQUENTIAL, INDIRECT, PUNITIVE OR EXEMPLARY DAMAGES (INCLUDING BUT NOT LIMITED TO LOST DATA, LOST PROFITS OR SAVINGS, LOSS OF BUSINESS OR OTHER ECONOMIC LOSS) ARISING OUT OF, OR IN CONNECTION WITH, THE SERVICES, WHETHER OR NOT SUCH PARTY HAS BEEN ADVISED OR KNEW OF THE POSSIBILITY OF SUCH DAMAGES, AND REGARDLESS OF THE NATURE OF THE CAUSE OF ACTION OR THEORY ASSERTED. Clearview's liability for costs or damages allegedly incurred by Company arising out of, or in connection with, Clearview's performance of the Services pursuant to this Engagement Letter shall be limited to the aggregate amount of Fees paid to Clearview pursuant to this Engagement Letter.

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Without limiting any other rights or remedies of Clearview under this Engagement Letter, and regardless of any investigation made at any time by or on behalf of Clearview or any information Clearview may have, the Company shall indemnify and save harmless Clearview, its directors, officers, employees, agents and assigns from and against any liability, damages (including punitive damages), injury (including property damage, personal injury or death), loss, claim, cost, debt, expense, obligation, public charge, lawsuit, contract, agreement, undertaking or deficiency of any kind or nature, whether known or unknown, fixed, actual, accrued, or contingent, liquidated or unliquidated (including, but not limited to, reasonable attorneys' fees and other costs and expenses incident to proceedings or investigations or the defense of any claim whether or not litigation is commenced), arising out of, resulting from, or relating to, any act or omission (other than gross negligence or willful misconduct) of Clearview, its employees, agents, associates or assigns that occurs during the term of this Engagement Letter. This indemnification shall survive the termination of this Engagement Letter.

Cadence indemnifies and releases Clearview from all liability relating to any access to, or use of, information prepared in any form whatsoever by Clearview in carrying out the Services ("Clearview Information") by any other party. The Company acknowledges and agrees that the duties of Clearview under this Engagement Letter are owed solely to the Company. The advice (oral or written) rendered by Clearview pursuant to this Engagement Letter is intended solely for the benefit and use of the management of the Company and its Board in considering such matters to which this Engagement Letter relates and the parties agree that such advice may not be relied upon by any other person.

The Company also acknowledges that any projections or forward-looking statements contained in Clearview Information involve risks, uncertainties and other factors that may cause actual results to differ materially from those expressed or implied in such projections or forward-looking statements and that it is likely that actual results will differ materially from those contemplated by such projections or forward-looking statements, and that Clearview gives no representations or warranties, express or implied, that any such projections or forward-looking statements will be realized.

Neither party may transfer or assign any of its rights or obligations under this Engagement Letter without the prior written consent of the other party.

All notices or communications hereunder shall be sent in by facsimile transmission (if available) or email (if available), followed by a signed copy sent by commercial mail or courier, and shall be deemed to have been given two days after being transmitted.

Notice to Clearview shall be addressed to:

Clearview Projects, Inc.
100 Overlook Center
Princeton, NJ 08540
609-580-3600

FAX: 609-580-0047
Attn: Chief Executive Officer

Notice to Company shall be addressed to:

Cadence Pharmaceuticals
12730 High Bluff Drive, Suite 410
San Diego, CA 93130
858-436-1400
FAX: 858-436-1401
Attn: Chief Executive Officer

Written notification of change in address, telephone, fax, email or contact person is required to be provided by either party to the other party in the same manner as notices.

This Engagement Letter shall be governed by, construed and enforced in accordance with the laws of the State of Delaware, excluding its choice of law provisions. Any suit, action or proceeding seeking to enforce any provision of, or based on any matter arising out of or in connection with, this Engagement Letter or the transactions contemplated hereby may be brought in the courts of the State of New Jersey and the federal courts of the United States of America located in New Jersey. Each of the parties (a) consents to the exclusive jurisdiction of such courts (and of the appropriate appellate courts therefrom) in any such suit, action or proceeding, (b) irrevocably waives, to the fullest extent permitted by law, any objection which it may now or hereafter have to the laying of the venue of any such suit, action or proceeding in any such court or that any such suit, action or proceeding which is brought in any such court has been brought in an inconvenient forum, (c) will not attempt to deny or defeat such personal jurisdiction by motion or other request for leave from any such court, and (d) will not bring any action relating to this Engagement Letter or any of the transactions contemplated by this Engagement Letter in any other court. Process in any such suit, action or proceeding may be served on any party anywhere in the world, whether within or without the jurisdiction of any such court. Without limiting the foregoing, each party agrees that service of process on such party as provided in this paragraph will be deemed effective service of process on such party.

This Engagement Letter contains all of the understandings and agreements of the parties with respect to the subject matter hereof and any and all prior understandings and agreements between the parties are superseded by this Engagement Letter. This Engagement Letter may not be modified unless the modification is in writing and executed by both parties.

We look forward to working with you on this exciting project. If this Engagement Letter is satisfactory, please execute one copy below and return it to me by facsimile or in the envelope provided.

Very truly yours,

Clearview Projects, Inc.:

Name	Jan S. Wolpert
Title	CEO
Signature	/s/ Jan S. Wolpert
Date	5/20/05

Accepted and Agreed:

Cadence Pharmaceuticals:

Name	Theodore R. Schroeder
Title	President and CEO
Signature	/s/ Theodore R. Schroeder
Date	5/20/05

Exhibit I. Clearview Bios

[***]

[***]

[***]

[***]

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

[***]

[***]

[***]

*** Certain information on this page has been omitted and filed separately with the Commission. Confidential treatment has been requested with respect to the omitted portions.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” and to the use of our report dated April 21, 2006, in Amendment No. 2 to the Registration Statement (Form S-1 No. 333-135821) and related Prospectus of Cadence Pharmaceuticals, Inc. for the registration of its shares of common stock.

/s/ Ernst & Young LLP

San Diego, California
September 19, 2006

LATHAM & WATKINS LLP

12636 High Bluff Drive, Suite 400
San Diego, California 92130-2071
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www.lw.com

File No. 038916-0007

September 25, 2006

Jeffrey Riedler
Assistant Director
Division of Corporation Finance
Securities and Exchange Commission
100 F Street, N.E.
Mail Stop 7010
Washington, D.C. 20549

Re: Cadence Pharmaceuticals, Inc.
Amendment No. 2 to Registration Statement on Form S-1
Filed September 25, 2006
SEC File No. 333-135821

Dear Mr. Riedler:

We are in receipt of the Staff's letter dated September 13, 2006 with respect to the above-referenced Registration Statement. We are responding to the Staff's comments on behalf of Cadence Pharmaceuticals, Inc. ("***Cadence***" or the "***Company***") as set forth below. Simultaneously with the filing of this letter, Cadence is submitting (by EDGAR) Amendment No. 2 to its Registration Statement on Form S-1 (the "***Amendment***"), responding to the Staff's comments. Courtesy copies of this letter and the Amendment (specifically marked to show the changes thereto) are being submitted to the Staff by hand delivery.

Cadence's responses set forth in this letter are numbered to correspond to the numbered comments in the Staff's letter. All terms used but not defined herein have the meanings assigned to such terms in the Amendment. For ease of reference, we have set forth the Staff's comments and Cadence's response for each item below.

Form S-1

Prospectus Summary, page 1

1. *We note that in response to comments 6 and 17, you disclose in the "Risk Factors" discussion on page 4 the information our comments requested. Although we do not object to your including this information in the "Risk Factors" discussion, it should also appear on page 2, where you first discuss those issues.*

- *Please state in the first full paragraph on page 2 that there are no patents for the drug acetaminophen and that your patents for IV APAP relate only to the specific formulation of the drug.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment to include a statement that there is no patent protection for acetaminophen and that Cadence's patents for IV APAP relate only to the specific formulation of the drug. Please refer to the revisions on page 2 of the Amendment.

- *Please state in the second full paragraph on page 2 that the FDA might require you to perform additional trials for IV APAP, and you might not ever obtain approval for this drug in the United States.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 2 of the Amendment.

2. *We note your response and revisions pursuant to comment 5. However, the issue does not appear to be resolved, so we reissue the comment. You state in the second full paragraph on page 2 that IV APAP has undergone six Phase III trials. Please discuss any difficulties or other issues that have necessitated six Phase III trials rather than just one. If the number of trials is caused only by multiple indications, disclose that fact.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment to clarify that the number of trials was driven by the multiple indications sought by Cadence's licensor, Bristol-Myers Squibb Company ("BMS"). Please refer to the revisions on page 2 of the Amendment. Cadence supplementally advises the Staff that there were no other difficulties that necessitated the multiple Phase III trials conducted by BMS.

Risk Factors

If any of our product candidates for which we receive regulatory approval . . . , page 12

3. *We note your response to comment 10, and we reissue the comment. The fact that you know of a trend that is actually occurring that could reduce the marketing impact of any superiority claims you make regarding omiganan appears to warrant a separate risk factor discussing the situation in detail. Please revise.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment to include a new risk factor discussing the decreasing use of 10% povidone-iodine in favor of chlorhexidine. Please refer to the revisions on page 13 of the Amendment.

Our product candidates may have undesirable side effects . . . , page 14

4. *We note your response to comment 11, and we reissue the comment. Please note that we are not requesting simply what acetaminophen "has the potential to cause." Also,*

your disclosure should be more specific than the statement that the adverse events "have all been related to the skin." Please identify and describe the side effects and adverse events that have been observed in the clinical trials of your products to date.

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment to include a description of the drug-related adverse events that have been observed in the clinical trials to date. Please refer to the revisions on page 15 of the Amendment.

We will need to increase the size of our organization . . . ,page 18

5. *We note your response to comment 14. Please revise the risk factor to state your best estimate as to the approximate number of employees you will need to hire in the next 12 months and the approximate cost of doing so. State, if true, that you do not currently know how many employees you will need beyond that timeframe.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 19 of the Amendment.

We may not be able to manage our business effectively if we are unable . . . , page 18

6. *We note your response to comment 15, and we reissue the comment. Since you state the loss of "one or more of the members of [your] senior management team or other key employees" would harm your business, you should identify the individuals to whom you are referring. Please revise to identify the members of your senior management team and the other employees you consider to be "key."*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 19 of the Amendment.

Special Note Regarding Forward-Looking Statements, page 32

7. *Please delete from the last paragraph of this section the statement that investors "should not place undue reliance on these forward-looking statements." Although we do not object to the other cautionary statements in this section, this statement appears to disclaim responsibility for information in your document.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 34 of the Amendment.

Use of Proceeds, page 34

8. *We note your response to comment 21. We reissue the comment because 20% of the proceeds still appears to be a material amount. Please identify with more specificity the uses currently described as "working capital, capital expenditures and other general corporate purposes," and state an approximate amount for each use.*

Cadence's Response: Cadence has revised the Amendment to provide approximate dollar amounts of the net proceeds intended to be used to: (i) fund clinical trials for its two product candidates and other research and development activities and (ii) fund capital expenditures. Please refer to page 35 of the Amendment. Cadence supplementally advises the Staff that these amounts total $62 million and represent approximately 95% of the anticipated net proceeds from the offering, which Cadence, at this time, estimates will be approximately $65 million. Accordingly, Cadence respectfully submits to the Staff that no further detail is necessary to adequately inform investors of the material anticipated use of proceeds from the offering.

Management's Discussion and Analysis of Financial Condition and Results . . . , page 41

Critical Accounting Policies and Estimates, page 43

Stock-Based Compensation, page 44

9. *Regarding the disclosures that you provided in response to prior comments 39 and 40, please expand them to:*

   a. *Qualitatively and quantitatively discuss the specific significant factors and assumptions utilized in your asset-based approach and current value method in determining the fair value of your common stock at a $0.10 per share prior to March 2006, as per paragraph 182(a) of the AICPA Practice Aid.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 46 of the Amendment.

   b. *Qualitatively and quantitatively elaborate on how the licensing of IV APAP and the advancement of our business model primarily contributed to the difference between the $0.10 per share prior to March 2006 and the $0.34 per share between March and June 2006. See paragraph 182(b) of the AICPA Practice Aid.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 46 of the Amendment.

   c. *Qualitatively and quantitatively discuss the significant factors, assumptions and methodologies used in the contemporaneous valuations of $0.34 and $0.80 per share, including how the enterprise value was estimated and changed.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 46 of the Amendment.

   d. *Qualitatively and quantitatively elaborate on how the prospect of an IPO alone primarily contributed to the difference between the $0.34 per share between March and June 2006 and the $0.80 per share since June 2006. See paragraph 182(b) of the AICPA Practice Aid.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 46 of the Amendment.

e. Qualitatively and quantitatively describe how and why the significant factors, assumptions and methodologies changed between the valuations of $0.10, $0.34 and $0.80 per share.

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 46 of the Amendment.

f. Qualitatively and quantitatively explain how each valuation considered the probability of ultimately being successful with your product candidates or not and the probability of ultimately completing an IPO or not.

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment. Please refer to the revisions on page 46 of the Amendment.

g. Once you can reasonably estimate the IPO price, qualitatively and quantitatively discuss each significant factor contributing to the difference between each valuation and the estimated IPO price. See paragraph 182(b) of the AICPA Practice Aid.

Cadence's Response: Cadence acknowledges the Staff's comment and will qualitatively and quantitatively discuss each significant factor contributing to the difference between each valuation and either (i) the estimated offering price, or (ii) if a contemporaneous valuation by an unrelated valuation specialist was obtained subsequent to the grants but prior to the IPO, the fair value as determined by that valuation. Cadence respectfully advises the Staff that it will provide such information in a pre-effective amendment to the Registration Statement prior to circulating the preliminary prospectus for the offering.

Business

Our Product Development Programs, page 54

10. We note your response to comment 25, and we reissue the comment in part. Given that BMS "completed Phase III trials" for IV APAP in the United States, please explain why BMS's trials were not sufficient to support a new drug application. The "Clinical Development Plan" discussion on page 60, which you reference in your response, does not appear to address this issue; it focuses on your plans going forward.

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment to clarify that because the Phase III clinical trial requirements differ in the United States compared to Europe, Cadence is required to complete additional Phase III trials to support a New Drug Application. Please refer to the revisions on page 56 of the Amendment.

Manufacturing, page 68

11. *We note that in response to comment 13, you state the agreement with Lawrence Laboratories for the manufacture of IV APAP "involves no long-term commitment by either party." However you disclose the agreement extends until the earlier of regulatory approval or December 31, 2008, which appears to be long-term. Please reconcile these statements so it is clear how the agreement is not a long-term agreement. Alternatively, file the agreement as an exhibit. We may have further comments.*

Cadence's Response: Cadence has filed the Clinical Supply Agreement with Lawrence Laboratories as an exhibit to the Registration Statement. Please refer to Exhibit 10.14 of the Amendment.

Certain Relationships and Related Party Transactions, page 98

12. *We note your response to comment 30.*

- *Please state how many shares of Series A-1 preferred stock you issued to Windamere III, LLC to settle the $500,000 advance.*

Cadence's Response: Cadence has revised the Amendment in accordance with the Staff's comment to refer to the amount of shares issued to Windamere III, LLC in settlement of the $500,000 advance. Please refer to the revisions on page 103 of the Amendment.

- *Please file as exhibits your agreements with Windamere III and Clearview Projects. Given the amount of consideration in these two transactions, the transactions appear to have been material.*

Cadence's Response: Cadence has filed as an exhibit the agreement with Clearview Projects. Please refer to Exhibit 10.15 of the Amendment. Cadence advises the Staff that the $500,000 advance to Cadence from Windamere III, LLC was made pursuant to an oral agreement at the time of Cadence's inception. Accordingly, there is no written agreement with Windamere III, LLC to be filed. However, Cadence has described the material terms of this advance in the Registration Statement. Please refer to the "Certain Relationships and Related Party Transactions — Other Transactions" section on page 103 and the "Notes to Financial Statements — Related Party Transactions" section on page F-13 of the Amendment.

13. *Please refer to your response to our prior comment number 37. Please qualitatively and quantitatively demonstrate how you concluded that any alternative accounting would not have a material impact on your financial statements. See SAB Topic 1.M. (SAB 99).*

Cadence's Response: Based on our telephone discussion with Oscar Young and Tabatha Akins of the Staff on September 18, 2006, regarding this comment we will separate our response into two parts. First, we address additional information surrounding our accounting applied, and second, we address the materiality of any impact on the financial statements if Cadence would have applied SFAS 115, *Accounting for Certain Investments in Debt and Equity Securities.*

Additional information regarding the accounting applied

Cadence chose, with the approval of its audit committee, not to apply the provisions of SFAS 115 because it did not acquire the shares of Migenix stock for the purpose of investing its available funds. Instead the shares were acquired solely as a condition of the licensor to complete the transaction to acquire the rights to Omigard. Since Cadence would be receiving unregistered stock that was thinly traded, and with the understanding that it would be held through the development period, Cadence concluded that the stock should be carried at its expected net realizable value, which was estimated to be minimal. The difference between the cost of $500,000 and expected future value, or $400,000, was recognized as part of the cost to license the product and recorded as in process technology in Cadence's 2004 results of operations.

In reviewing the provisions of SFAS 115, paragraph 3.c. states that "restricted stock does not meet that definition" of an equity security and therefore SFAS 115 would not apply. Restricted stock is defined for the purpose of SFAS 115, as follows:

> *"[E]quity securities for which sale is restricted by governmental or contractual requirement (other than in connection with being pledged as collateral) except if that requirement terminates within one year or if the holder has the power by contract or otherwise to cause the requirement to be met within one year. Any portion of the security that can be reasonably expected to qualify for sale within one year, such as may be the case under Rule 144 or similar rules of the SEC, is not considered restricted."*

While the contract does not specifically restrict the sale of the shares, the shares were not registered for immediate re-sale. Furthermore, it was the clear understanding between the parties that Cadence would not immediately re-sell the shares, and the nature of the shares acquired in substance created the same condition.

Cadence acknowledges that had it acquired the Migenix shares as an investment, the shares would meet the definition of an equity security under SFAS 115 and its provisions would have been applied.

Materiality considerations under SAB 99

Cadence is a development stage company founded in May 2004. It has had no revenues and since inception has primarily been dedicated to research activities. Had Cadence recorded the shares as an investment in equity securities, the difference between the accounting applied and the accounting under SFAS 115 would be as follows (in thousands):

	2004	2005	2006	Total
Write-down, as currently recorded	$ 400	$ —	$ —	$ 400
Write-down, assuming application of SFAS 115	$ 95	$ 183	$ 1	$ 279
Over (under)	$ 305	$ (183)	$ (1)	$ 121
Net loss, as reported	$ (3,142)	$ (7,523)	$ (34,870)	$ (45,535)
Equity, as reported	$ 4,422	$ 14,623	$ 34,428	N/A

SEC Staff Accounting Bulletin No. ("SAB 99") provides guidance on assessing materiality as follows:

> *"[Q]uantifying, in percentage terms, the magnitude of a misstatement is only the beginning of an analysis of materiality; it cannot appropriately be used as a substitute for a full analysis of all relevant considerations. Materiality concerns the significance of an item to users of a registrant's financial statements. A matter is material if there is a substantial likelihood that a reasonable person would consider it important. In its Concepts Statement 2, the FASB stated the essence of the concept of materiality as follows:*
>
> *The omission or misstatement of an item in a financial report is material if, in the light of surrounding circumstances, the magnitude of the item is such that it is probable that the judgment of a reasonable person relying upon the report would have been changed or influenced by the inclusion or correction of the item."*

The users of Cadence's financial statements have historically been its investors, who generally were also represented on its board of directors. To date, Cadence's financial results have been secondary to realizing Cadence's potential through the successful development and commercialization of its product candidates. Cadence is confident in representing to the Staff that the impact of not applying the alternative accounting under SFAS 115 to the Migenix shares would not have altered any of the investors' decisions regarding their investment or in making strategic decisions.

SAB 99 also states that:

> *"Evaluation of materiality requires a registrant and its auditor to consider all the relevant circumstances, and the staff believes that there are numerous circumstances in which misstatements below 5% could well be material. Qualitative factors may cause misstatements of quantitatively small amounts to be material; as stated in the auditing literature:*

As a result of the interaction of quantitative and qualitative considerations in materiality judgments, misstatements of relatively small amounts that come to the auditor's attention could have a material effect on the financial statements.

Among the considerations that may well render material a quantitatively small misstatement of a financial statement item are:

- *whether the misstatement arises from an item capable of precise measurement or whether it arises from an estimate and, if so, the degree of imprecision inherent in the estimate,*
- *whether the misstatement masks a change in earnings or other trends,*
- *whether the misstatement hides a failure to meet analysts' consensus expectations for the enterprise,*
- *whether the misstatement changes a loss into income or vice versa*
- *whether the misstatement concerns a segment or other portion of the registrant's business that has been identified as playing a significant role in the registrant's operations or profitability,*
- *whether the misstatement affects the registrant's compliance with regulatory requirements,*
- *whether the misstatement affects the registrant's compliance with loan covenants or other contractual requirements,*
- *whether the misstatement has the effect of increasing management's compensation for example, by satisfying requirements for the award of bonuses or other forms of incentive compensation, and*
- *whether the misstatement involves concealment of an unlawful transaction."*

With the exception to the first consideration listed above where the difference is "capable of precise measurement," none of the considerations would apply to Cadence.

In summary, Cadence believes that the accounting applied to the Migenix shares was appropriate based on the facts and circumstances under which the shares were acquired. However, if the Staff concludes that an alternative accounting under SFAS 115 should have been applied, Cadence, for the reasons described above, believes that the impact of the alternative accounting would not be material to the users of its financial statements.

Finally, Cadence supplementally advises the Staff that it has revised its unaudited balance sheet at June 30, 2006 and its unaudited results of operations for the six months ended June 30, 2006 and for the period from May 26, 2004 through June 30, 2006 to reflect an adjustment to increase accrued liabilities (clinical trial accrual) and research and development expenses by $1.2 million. In reviewing the clinical trial activity after June 30, 2006, Cadence discovered that it was not receiving data from its investigator sites timely. The process to ensure that Cadence has all the information to estimate the clinical trial accrual has been rectified.

* * *

Any comments or questions regarding the foregoing should be directed to the undersigned at (858) 523-5435. Thank you in advance for your cooperation in connection with this matter.

Very truly yours,

/s/ Cheston J. Larson
Cheston J. Larson
of LATHAM & WATKINS LLP

Enclosures

cc: Theodore R. Schroeder, *Cadence Pharmaceuticals, Inc.*
William R. LaRue, *Cadence Pharmaceuticals, Inc.*
David A. Socks, *Cadence Pharmaceuticals, Inc.*
Faye H. Russell, *Latham & Watkins LLP*
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