Mallinckrodt Lupus Phase 4 Clinical Study for Acthar® Gel (Repository Corticotropin Injection) Completes Enrollment in Difficult-to-Manage Population

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-- Company continues focus on evidence expansion, potential utility of Acthar Gel in appropriate, underserved patients --

STAINES-UPON-THAMES, United Kingdom, April 23, 2019 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a leading global specialty pharmaceutical company, today confirmed it has completed enrollment in the company's Phase 4 clinical study assessing the efficacy and safety of Acthar® Gel in Systemic Lupus Erythematosus (lupus, SLE) patients with persistently active disease. This randomized, double-blind, placebo-controlled trial builds on data from a pilot study of Acthar Gel in patients with active SLE. The trial completed enrollment several months ahead of schedule in this underserved population, with a final count of 172 patients.

Dr. Anca Askanase, the Director of the Columbia University Lupus Center and Principal Investigator for this Phase 4 study, said: "I am delighted that enrollment is completed, and look forward to evaluating the data as it becomes available. Lupus patients are a challenging population to manage medically. We hope that the knowledge from this study will help guide treating physicians and can benefit lupus patients."

Acthar Gel is approved by the U.S. Food and Drug Administration (FDA) for use during an exacerbation or as a maintenance therapy in select patients with SLE.[1]

"This is another exciting milestone in clinical evidence generation for Acthar. The data from our prior lupus pilot clinical study support the use of Acthar to treat lupus patients who have clinically significant disease activity despite receiving corticosteroids," said **Steven Romano, M.D., Chief Scientific Officer and Executive Vice President at Mallinckrodt**. "We look forward to completing the Phase 4 clinical trial later this year with top-line results anticipated by early 2020, providing additional data to help prescribers better understand how Acthar may be utilized in the management of these more difficult-to-manage patients with SLE."

About the Trial

The Phase 4 trial is titled, "A multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of Acthar Gel in subjects with persistently active SLE despite moderate dose corticosteroids." The trial is fully enrolled (n=172). The primary endpoint of the study is to measure reduction in disease activity as reflected by the SLE Responder Index (SRI) at week 16. The SRI is a composite endpoint that includes three different measures of disease activity to reflect response of SLE to therapy.

Find more information about the trial here on the ClinicalTrials.gov website.

About Systemic Lupus Erythematosus

SLE is an autoimmune disease in which the immune system produces antibodies to cells within the body leading to widespread inflammation and tissue damage.[2] It is the most common form of lupus, a condition that impacts an estimated 1.5 million Americans.[3] Ninety percent of those diagnosed with lupus are women, often between the ages of 15-44.[3] Lupus is characterized by periods of illness "flares" and remissions and the disease can affect the joints, skin, brain, lungs, kidneys, and blood vessels. Symptoms may include fatigue, pain or swelling in joints, skin rashes, and fevers.[2]

Acthar Gel (Repository Corticotropin Injection) Indications

Acthar Gel is an injectable drug approved by the FDA for the treatment of 19 indications. Of these, today the majority of Acthar use is in these indications:

- Adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in rheumatoid arthritis (RA), including juvenile RA (selected cases may require low-dose maintenance therapy)
- Monotherapy for the treatment of infantile spasms in infants and children under 2 years of age
- Treatment during an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus
- The treatment of acute exacerbations of multiple sclerosis in adults. Controlled clinical trials have shown Acthar Gel to be

effective in speeding the resolution of acute exacerbations of multiple sclerosis. However, there is no evidence that it affects the ultimate outcome or natural history of the disease
- Inducing a diuresis or a remission of proteinuria in nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus
- Treatment during an exacerbation or as maintenance therapy in selected cases of systemic dermatomyositis (polymyositis)
- The treatment of symptomatic sarcoidosis
- Treatment of severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation

IMPORTANT SAFETY INFORMATION
Contraindications

- Acthar should never be administered intravenously
- Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of Acthar
- Acthar is contraindicated where congenital infections are suspected in infants
- Acthar is contraindicated in patients with scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, uncontrolled hypertension, primary adrenocortical insufficiency, adrenocortical hyperfunction or sensitivity to proteins of porcine origins

Warnings and Precautions

- The adverse effects of Acthar are related primarily to its steroidogenic effects
- Acthar may increase susceptibility to new infection or reactivation of latent infections
- Suppression of the hypothalamic-pituitary-axis (HPA) may occur following prolonged therapy with the potential for adrenal insufficiency after withdrawal of the medication. Adrenal insufficiency may be minimized by tapering of the dose when discontinuing treatment. During recovery of the adrenal gland patients should be protected from the stress (e.g. trauma or surgery) by the use of corticosteroids. Monitor patients for effects of HPA suppression after stopping treatment
- Cushing's syndrome may occur during therapy but generally resolves after therapy is stopped. Monitor patients for signs and symptoms
- Acthar can cause elevation of blood pressure, salt and water retention, and hypokalemia. Blood pressure, sodium and potassium levels may need to be monitored
- Acthar often acts by masking symptoms of other diseases/disorders. Monitor patients carefully during and for a period following discontinuation of therapy
- Acthar can cause GI bleeding and gastric ulcer. There is also an increased risk for perforation in patients with certain gastrointestinal disorders. Monitor for signs of bleeding
- Acthar may be associated with central nervous system effects ranging from euphoria, insomnia, irritability, mood swings, personality changes, and severe depression, and psychosis. Existing conditions may be aggravated
- Patients with comorbid disease may have that disease worsened. Caution should be used when prescribing Acthar in patients with diabetes and myasthenia gravis
- Prolonged use of Acthar may produce cataracts, glaucoma and secondary ocular infections. Monitor for signs and symptoms
- Acthar is immunogenic and prolonged administration of Acthar may increase the risk of hypersensitivity reactions. Neutralizing antibodies with chronic administration may lead to loss of endogenous ACTH activity
- There is an enhanced effect in patients with hypothyroidism and in those with cirrhosis of the liver
- Long-term use may have negative effects on growth and physical development in children. Monitor pediatric patients
- Decrease in bone density may occur. Bone density should be monitored for patients on long-term therapy
- Pregnancy Class C: Acthar has been shown to have an embryocidal effect and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

Adverse Reactions

- Common adverse reactions for Acthar are similar to those of corticosteroids and include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain
- Specific adverse reactions reported in IS clinical trials in infants and children under 2 years of age included: infection, hypertension, irritability, Cushingoid symptoms, constipation, diarrhea, vomiting, pyrexia, weight gain, increased appetite, decreased appetite, nasal congestion, acne, rash, and cardiac hypertrophy. Convulsions were also reported, but these may actually be occurring because some IS patients progress to other forms of seizures and IS sometimes mask other seizures, which become visible once the clinical spasms from IS resolve

Other adverse events reported are included in the full Prescribing Information.
Please see full Prescribing Information.

ABOUT MALLINCKRODT
Mallinckrodt is a global business consisting of multiple wholly owned subsidiaries that develop, manufacture, market and distribute specialty pharmaceutical products and therapies. The company's Specialty Brands reportable segment's areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, nephrology, pulmonology and ophthalmology;

immunotherapy and neonatal respiratory critical care therapies; and analgesics. Its Specialty Generics and Amitiza reportable segment includes specialty generic drugs, active pharmaceutical ingredients and AMITIZA® (lubiprostone). To learn more about Mallinckrodt, visit www.mallinckrodt.com.

Mallinckrodt uses its website as a channel of distribution of important company information, such as press releases, investor presentations and other financial information. It also uses its website to expedite public access to time-critical information regarding the company in advance of or in lieu of distributing a press release or a filing with the U.S. Securities and Exchange Commission disclosing the same information. Therefore, investors should look to the Investor Relations page of the website for important and time-critical information. Visitors to the website can also register to receive automatic e-mail and other notifications alerting them when new information is made available on the Investor Relations page of the website.

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS

This release includes forward-looking statements concerning Acthar Gel including expectations with regard to the study described in this release, as well as future research plans and potential impact on patients. The statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those in the forward-looking statements: satisfaction of regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; issues with product quality, manufacturing or supply, or patient safety issues; and other risks identified and described in more detail in the "Risk Factors" section of Mallinckrodt's most recent Annual Report on Form 10-K and other filings with the SEC, all of which are available on its website. The forward-looking statements made herein speak only as of the date hereof and Mallinckrodt does not assume any obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law.

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[1] Acthar® Gel (repository corticotropin injection) [prescribing information]. Mallinckrodt ARD, Inc.

[2] Systemic lupus erythematosus (SLE or lupus), The Centers for Disease Control and Prevention, Available at: https://www.cdc.gov/lupus/facts/detailed.html. Accessed March 21, 2019.

[3] Lupus Foundation of America Press Kit, About Us. Available at: http://www.lupus.org/about/statistics-on-lupus. Accessed March 21, 2019.

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