All Primary and Secondary Outcome Targets Met in Mallinckrodt’s Phase 4 Acthar® Gel (Repository Corticotropin Injection) Rheumatoid Arthritis (RA) Clinical Trial (n=259) with Data Presented at the European Congress of Rheumatology 2019 (EULAR)

June 13, 2019

-- Study met primary outcome measure; 63 percent of patients with persistently active RA achieved low disease activity (LDA) as assessed by DAS28-ESR<sup>¹</sup> at Week 12 --

-- Randomized, placebo-controlled, blinded, withdrawal phase of study showed significantly more patients with persistently active RA who met rigorous response criteria at Week 12 maintained LDA results when treated with Acthar Gel (62 percent) versus placebo (43 percent, P<0.05) at Week 24, a substantial difference in this more refractory patient population --

-- Significantly more patients in Acthar Gel group (86 percent) than placebo group (66 percent, P≤0.05) had sustained low disease activity at Week 24 as defined by Clinical Disease Activity Index --

-- Significantly fewer patients in the Acthar Gel continuation group experienced cumulative disease activity flare rate at Week 24 (17 percent) than placebo group (30 percent, P<0.05) --

STAINES-UPON-THAMES, United Kingdom, June 13, 2019 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a global specialty biopharmaceutical company, is reporting that all primary and secondary outcome measures were met in its Phase 4, multicenter study assessing the efficacy and safety of Acthar<sup>®</sup> Gel (repository corticotropin injection, or RCI) in patients with persistently active RA who were previously treated with disease-modifying anti-rheumatic drugs (DMARDs) and corticosteroids. Encouraging topline data<sup>²</sup> from the randomized, placebo-controlled, blinded, withdrawal phase of the study, as well as positive results from the open-label period of the study, were presented in a poster presentation on Thursday, June 13 at the European Congress of Rheumatology 2019 (EULAR) held June 12-15 in Madrid.

The Phase 4 study poster, “A Multicenter Study Assessing the Efficacy and Safety of Repository Corticotropin Injection in Patients With Persistently Active Rheumatoid Arthritis” presented at EULAR 2019 is on the company’s website. As previously announced, both parts of the multicenter study are now complete (open-label portion, n=259; randomized, placebo-controlled, blinded, withdrawal portion, n=154).

Acthar Gel is U.S. Food and Drug Administration (FDA)-approved as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in RA, including juvenile RA (selected cases may require low-dose maintenance therapy). Please see Important Safety Information for Acthar Gel below.

“This is the first reporting of the double-blind portion of the study, and the topline results showed that Acthar Gel has sustained effectiveness in patients with rheumatoid arthritis who were treated previously with multiple standard therapies but continued to have active disease,” said Dr. Roy Fleischmann, Co-Medical Director of the Metroplex Clinical Research Center and Clinical Professor of Medicine at the University of Texas Southwestern Medical Center in Dallas. “We look forward to further reporting of the data in this important study.”

Key Findings:

Randomized, Placebo-Controlled, Blinded, Withdrawal Period

A number of measures were assessed to evaluate sustained improvement:

- Significantly more patients in the Acthar Gel group (62 percent) than in the placebo group (43 percent, P<0.05) had sustained LDA of <3.2 at Week 24, as assessed by the DAS28-ESR, a composite index that measures disease activity in patients with RA.
- Significantly more patients in the Acthar Gel group (86 percent) than in the placebo group (66 percent, P≤0.05) had sustained low disease activity at Week 24, as defined by the Clinical Disease Activity Index (CDAI, Score ≤10), a composite measure of disease activity in patients with RA.
- Significantly fewer patients in the Acthar Gel continuation group experienced cumulative disease activity flare rate at Week
Treatment is aimed at stopping inflammation to put the disease in remission
at Week 24 were 91 percent, 75 percent and
on the ClinicalTrials.gov website.

An estimated 1.5 million U.S. adults are living with RA.

Steven Romano, M.D., Executive Vice President and Chief Scientific Officer
at Mallinckrodt. "We are excited that our ongoing data generation efforts continue to confirm Acthar Gel is indeed an important therapeutic option for
appropriate patients living with difficult-to-treat autoimmune disorders. We look forward to the continued emergence of data from other Acthar Gel
ongoing studies across multiple disease areas."

Open-Label Period

- The primary endpoint of the study was the proportion of patients reaching LDA by DAS28-ESR of <3.2 at 12 weeks. The open-label analysis showed there was a decrease in the mean DAS28-ESR scores from baseline through Week 12, with 63 percent of patients who completed the open-label period achieving the LDA target at Week 12.
- Acthar Gel was associated with significant improvements in DAS28-ESR and CDAI scores.
- Significant improvements in additional efficacy measures were seen at Week 12, including fatigue, physical function, swollen joints and tender joints.
- AEs observed were consistent with those in previous trials of Acthar Gel. AEs (n=38) included diabetes mellitus (n=1), increase in glycosylated hemoglobin (n=2), increase in liver function test (n=1), hyperglycemia (n=1) and hypertension (n=2). Three patients reported serious AEs (chest pain, pneumonia and craniocerebral injury).
- Bone turnover markers were assessed as an exploratory endpoint.
- Twenty-four patients discontinued the open-label period of the study.

"We are pleased to report these positive results from the randomized, placebo-controlled, blinded, withdrawal phase of this important Acthar Gel study
in underserved patients with such a debilitating disease," said Steven Romano, M.D., Executive Vice President and Chief Scientific Officer
at Mallinckrodt. "We are excited that our ongoing data generation efforts continue to confirm Acthar Gel is indeed an important therapeutic option for
appropriate patients living with difficult-to-treat autoimmune disorders. We look forward to the continued emergence of data from other Acthar Gel
ongoing studies across multiple disease areas."

Study Limitations

- Sample bias may exist for the open-label phase of the ongoing study, and patients were aware that they were receiving
Acthar Gel.4
- Examiner bias may also exist as the patient had to reach low disease activity in order to enter the second phase of the study.4
- The results cannot be solely attributed to Acthar Gel since patients were on different medications at the start of the trial
and no washout periods were undertaken.4

About the Study

The study was a Phase 4, multicenter, two-part study assessing the efficacy and safety of Acthar Gel in adult patients with RA with persistently active
disease who were previously treated with corticosteroids and conventional synthetic and/or biologic DMARDs. The primary endpoint of the study was
the proportion of patients reaching LDA at 12 weeks.

Part 1 of the study was an open-label period (n=259). After 12 weeks of treatment with Acthar Gel, patients were evaluated for treatment response
using the DAS28-ESR. In Part 2 of the study (n=154), participants who achieved LDA of DAS28-ESR of <3.2 at Week 12 in Part 1 entered a
double-blind withdrawal period, randomized in a 1:1 ratio to receive either Acthar Gel or matching placebo for an additional 12 weeks.

Full results from the randomized, placebo-controlled, blinded, withdrawal phase of the study are targeted for presentation at a research meeting later
this year.

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

About Rheumatoid Arthritis

RA is an autoimmune disease. It is a chronic condition that causes pain, stiffness, and swelling of the joints—all symptoms caused by
inflammation.5 An estimated 1.5 million U.S. adults are living with RA.6 Treatment is aimed at stopping inflammation to put the disease in remission
and relieve symptoms.7 Nonsteroidal anti-inflammatory drugs are used to ease symptoms whereas corticosteroids, disease-modifying anti-rheumatic
drugs and biologics are used to slow down the disease activity.

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
arthritiis, including juvenile rheumatoid arthritis (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 reporting 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; analgesics and gastrointestinal products. Its Specialty Generics reporting segment includes specialty generic drugs and active pharmaceutical ingredients. 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 (SEC) 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 regarding its potential impact on patients and anticipated benefits associated with its use. 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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References

1 Disease Activity Score 28-joint count Erythrocyte Sedimentation Rate
3 American College of Rheumatology (ACR) disease activity response rates that measure the proportion of patients with an improvement of 20/50/70 percent is based on Patient Assessment of Physical Function± criteria and not Patient Global Health≠ as previously reported. ±≠Both criteria based on the ACR Assessment.

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