New Retrospective Data on African Americans with Advanced Symptomatic Sarcoidosis Treated with Acthar® Gel (Repository Corticotropin Injection) Presented at the American Thoracic Society Annual International Conference

May 17, 2022

Retrospective medical chart review subgroup analysis showed Acthar Gel was associated with overall symptom improvement and reduction in use of concomitant medications in African Americans

DUBLIN , May 17, 2022 /PRNewswire/ -- Mallinckrodt plc, (OTCMKTS: MNKKQ) a global biopharmaceutical company, today announced results of a retrospective, observational medical chart review subgroup analysis assessing real-world treatment outcomes among African Americans with advanced symptomatic sarcoidosis who initiated therapy with Acthar Gel (repository corticotropin injection). Investigators presented the findings during a poster presentation at the American Thoracic Society Annual International Conference, taking place in San Francisco, CA. from May 13-18. The poster is available here on the company's website. The full study results, from which this subgroup analysis was pulled, were previously published in *Therapeutic Advances in Respiratory Disease*, an online, open-access peer-reviewed journal.

Acthar Gel is a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides. Acthar Gel is approved by the U.S. Food and Drug Administration (FDA) for the treatment of symptomatic sarcoidosis and is only commercially available in the U.S.[1] Acthar Gel is also referenced in the European Respiratory Society (ERS) treatment guidelines—which list Acthar Gel among the various anti-inflammatory treatments for pulmonary sarcoidosis and note it can be used on a case-by-case basis when other therapies are ineffective or not tolerated—and the U.S. Sarcoidosis Expert Panel Consensus Statement recommendations for sarcoidosis.[2,3] **Please see Important Safety Information for Acthar Gel below.**

This ad hoc subgroup analysis was based on data from medical charts of 168 (77 male and 91 female) adult African Americans with symptomatic sarcoidosis who had completed a course of Acthar Gel or received Acthar Gel for at least six months at the time of data collection. Patients had a mean of 5.2 years since initial diagnosis of sarcoidosis and 121 (72 percent) patients had at least one comorbidity. The mean duration of Acthar Gel treatment was 31.7 weeks and 105 (62.5 percent) patients continued Acthar Gel therapy for at least six months.

Sarcoidosis is a chronic condition that causes inflammation in the body.[4,5] There are health disparities that exist in the U.S. as African Americans are more likely to develop sarcoidosis compared with Caucasians and are also more severely affected.[4,7] In particular, African American women experience the highest prevalence of sarcoidosis compared to any other group.[6]

"It's critical that ongoing sarcoidosis research highlights the disparities that exist for African Americans with regards to diagnosis, severity of illness and response to treatments. More studies are required that deepen our understandings of these differences and provide meaningful strategies to improve outcomes among this community," said **Mary McGowan of The Foundation for Sarcoidosis Research (FSR)**. FSR is the leading international organization dedicated to finding a cure for sarcoidosis and improving care for sarcoidosis patients through research, education and support. To learn more about how sarcoidosis impacts African American women and FSR's #IgnoreNoMore Campaign sponsored by Mallinckrodt Pharmaceuticals, visit www.stopsarcoidosis.org/aaws-campaign/.

The data analysis found a significant reduction in use of any co-medication after Acthar Gel initiation ($p<0.0001$) and the percentage of patients who used glucocorticoids decreased significantly from 59.5 percent during the three months before initiation of Acthar Gel to 11.9 percent three months after Acthar Gel therapy ($p<0.0001$). According to physicians' assessments of change in patients' health status after Acthar Gel therapy, most patients (N=160, 95 percent) had improved and 83 patients (49 percent) had at least two types of improvements in sarcoidosis symptoms. The most commonly reported types of sarcoidosis symptom improvements were overall symptoms (N=122, 73 percent), inflammation (N=57, 34 percent), improved patient quality of life (N=53, 32 percent), improved lung function (N=51, 30 percent) and reduction or discontinuation of glucocorticoid (N=48, 29 percent).

"We believe the results of this retrospective medical chart review subgroup analysis support Acthar Gel's role as a viable treatment option for African Americans with advanced symptomatic sarcoidosis and support the importance of continued collection of real-world data to help inform patients' treatment options," said **George J. Wan, Ph.D., M.P.H., Vice President Health Economics and Outcomes Research at Mallinckrodt**.

The limitations of this retrospective chart review include that the study relied on real-world medical charts which could be missing data or may have used site-specific measurement schedules and procedures. Additionally, outcomes may be influenced by therapies not documented in the chart as

most patients were on multiple therapies; the clinical outcomes may not be solely attributable to Acthar Gel. Patient outcomes and safety were not quantified, and physician assessment of patient outcomes may be subjective. Due to the retrospective nature of this analysis, it is hypothesis-generating; no formal conclusions should be drawn.

The study was funded by Mallinckrodt.

About Sarcoidosis

Sarcoidosis is a challenging, yet manageable, rare multisystem disease.[4,5] In some cases the symptoms may come and go throughout one's lifetime. This is referred to as symptomatic sarcoidosis. In people living with sarcoidosis, the immune system overreacts, forming clumps of cells called granulomas that result in inflammation of the body's tissues.[7] The disease can impact any organ but most often impacts the lungs, lymph nodes, eyes, and skin.[4] Over 90 percent of people with sarcoidosis suffer lung problems.[8] Concomitant involvement of organs outside of the lungs is common, occurring in as many as half of all sarcoidosis cases.[8]

IMPORTANT SAFETY INFORMATION

Contraindications

Acthar is contraindicated:

- For intravenous administration
- In infants under 2 years of age who have suspected congenital infections
- With concomitant administration of live or live attenuated vaccines in patients receiving immunosuppressive doses of Acthar
- 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 origin

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-adrenal (HPA) axis 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 axis 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. Monitor blood pressure and sodium and potassium levels
- 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 gastrointestinal (GI) bleeding and gastric ulcer. There is also an increased risk for perforation in patients with certain GI disorders. Monitor for signs of perforation and bleeding
- Acthar may be associated with central nervous system effects ranging from euphoria, insomnia, irritability, mood swings, personality changes, and severe depression to 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. Cases of anaphylaxis have been reported in the post marketing setting. Neutralizing antibodies with chronic administration may lead to loss of endogenous ACTH and Acthar activity
- There may be 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 in patients on long-term therapy

Adverse Reactions

- Commonly reported post marketing adverse reactions for Acthar include injection site reaction, asthenic conditions (including fatigue, malaise, asthenia, and lethargy), fluid retention (including peripheral swelling), insomnia, headache, and blood glucose increased
- The most common adverse reactions for the treatment of infantile spasms (IS) are increased risk of infections, convulsions, hypertension, irritability, and pyrexia. Some patients with IS progress to other forms of seizures; IS sometimes masks these seizures, which may become visible once the clinical spasms from IS resolve

Pregnancy

- Acthar may cause fetal harm when administered to a pregnant woman

Please see full Prescribing Information for additional Important Safety 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, ophthalmology, and oncology; immunotherapy and neonatal respiratory critical care therapies; analgesics; cultured skin substitutes and gastrointestinal products. Its Specialty Generics reportable 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 its potential impact on patients and anticipated benefits associated with its use, as well as related on-going studies. 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; 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.

CONTACT

Media Inquiries
Heather Guzzi
Senior Vice President, Green Room Communications
973-524-4112
hguzzi@greenroompr.com

Investor Relations
Daniel J. Speciale
Global Corporate Controller & Chief Investor Relations Officer
314-654-3638
daniel.speciale@mnk.com

Derek Belz
Vice President, Investor Relations
314-654-3950
derek.belz@mnk.com

References

---

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

[2] Baughman RP, Valeyre D, Korsten P, et al. ERS clinical practice guidelines on treatment of sarcoidosis. *Eur Respir J*. 2021; in press (https://doi.org/10.1183/13993003.04079-2020).

[3] Rahaghi FF, Sweiss NJ, Saketkoo LA, et al. Management of repository corticotrophin injection therapy for pulmonary sarcoidosis: a Delphi study. *Eur Respir Rev*. 2020; 29:190147. https://doi. org/10.1183/16000617.0147- 2019.

[4] Judson MA. The clinical features of sarcoidosis: a comprehensive review. *Clin Rev Allerg Immunol*. 2015;49:63-78.

[5] Baughman RP, Field S, Costabel U, et al. Sarcoidosis in America. Analysis based on health care use. *Ann Am Thorac Soc*. 2016;13:1244-1252.

[6] Hena, K. M. Sarcoidosis Epidemiology: Race Matters. *Front Immunol*. 2020;11:1-5.

[7] Baughman RP, Culver DA, Judson MA. A concise review of pulmonary sarcoidosis. *Am J Respir Crit Care Med*. 2011;183:573-581.

[8] Shigemitsu H, Patel HV, Schreiber MP. Extrapulmonary sarcoidosis. In: Judson MA, ed. Pulmonary Sarcoidosis: A Guide for the Practicing Clinician. Vol 17. New York, NY: Springer; 2014:149-186.

View original content to download multimedia:https://www.prnewswire.com/news-releases/new-retrospective-data-on-african-americans-with-advanced-symptomatic-sarcoidosis-treated-with-acthar-gel-repository-corticotropin-injection-presented-at-the-american-thoracic-society-annual-

international-conference-301548351.html

SOURCE Mallinckrodt plc