First Patient Enrolled in Mallinckrodt's Phase 2a Study of Investigational Drug MNK-6106 in Hepatic Cirrhosis and Chronic Hepatic Encephalopathy (HE)

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-- Trial is to Assess Pharmacokinetics, Pharmacodynamics and Safety of the Oral Administration of MNK-6106 in Patients with HE --

STAINES-UPON-THAMES, United Kingdom, Aug. 12, 2019 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a global biopharmaceutical company, today confirmed enrollment of the first patient in the company's Phase 2a study assessing the pharmacokinetics, pharmacodynamics and safety of the oral investigational drug MNK-6106 (L-ornithine phenylacetate) versus rifaximin in patients with hepatic (liver) cirrhosis and hepatic encephalopathy (HE). Study completion is expected by first quarter 2020.

Mallinckrodt acquired MNK-6106 and the intravenous investigational drug MNK-6105 (L-ornithine phenylacetate) when it completed the acquisition of Ocera Therapeutics in December 2017. MNK-6106 is being evaluated for post-discharge continuity of care for patients with cirrhosis and, if approved, may have the potential to reduce the risk of recurrent HE episodes and possibly rehospitalization.

The company expects to begin recruiting by the end of 2019 for a Phase 3 clinical trial investigating MNK-6105 in patients being treated for acute HE in the hospital.

"Enrollment of the first patient in this clinical trial of investigational drug MNK-6106 marks another important milestone in the compound's development program," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer** at **Mallinckrodt**. "The evaluation of the oral formulation will allow us to gain insights into the potential utility of this compound to manage patients whose acute episode of HE has resolved, and who may require longer-term treatment to reduce the likelihood of future episodes and potential complications."

About the Clinical Trial

The clinical study is titled "A Phase 2a Comparator, Randomized, Open-Label Study to Assess the Pharmacodynamics, Safety and Pharmacokinetics of Oral Administration MNK-6106 (L-ornithine Phenylacetate) vs. Rifaximin in Subjects with Hepatic Cirrhosis and a History of Prior Episodes of Hepatic Encephalopathy." The study will include adult men and non-pregnant women with hepatic cirrhosis who have a history of at least two or more documented episodes of HE in the last 12 months – with one in the last six months – and who present with hyperammonemia at the time of screening.

Approximately 48 subjects who meet eligibility criteria will be randomly assigned to one of four groups. Those in three experimental arms will receive MNK-6106 for five days with food, according to different dosing regimens – 2 grams, three times daily; 4 grams, twice daily; and 4 grams, three times daily. The fourth group, the active comparator group, will receive 550 milligrams of rifaximin twice daily for five days with food.

The primary objective of this study is to evaluate the pharmacological effect of this compound through the assessment of plasma ammonia concentration as a pharmacodynamic marker following oral administrations of MNK-6106 with rifaximin as a control in participants with hepatic cirrhosis and a history of prior episodes of HE. The study's endpoints are the absolute and percentage change in plasma ammonia from baseline, in a timeframe from baseline to five days.

Find more information about the U.S. trial here for the U.S. Food and Drug Administration's ClinicalTrials.gov website.

About MNK-6106

MNK-6106 (L-ornithine phenylacetate), an ammonia scavenger, is being studied for treatment of hepatic encephalopathy, a neuropsychiatric syndrome associated with hyperammonemia, a complication of chronic liver disease.

About Hepatic Encephalopathy

Hepatic encephalopathy is a critical neurocognitive complication of chronic liver disease. It is associated with elevated circulating ammonia levels stemming from end stage liver disease (cirrhosis). Symptoms range from mildly altered mental status to coma or death. Severe hepatic encephalopathy in patients with cirrhosis is associated with a mortality of more than 50% in the first year alone.[1,2] Once a patient suffers an acute hepatic encephalopathy episode, prevention of recurrence is critical and may require chronic therapy.

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; analgesics 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, including Mallinckrodt's expectations with regard to the Phase 2a study of the investigational drug MNK-6106 as well as its 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: clinical trial results; 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 Fichet J, Mercier E., Genee O. et al. Prognosis and 1-year mortality of intensive care unit patients with severe hepatic encephalopathy, J Crit Care. (2009) 24:364-370.
2 Garcia-Martinez R, Simon-Talero M, Cordoba J. Prognostic assessment in patients with hepatic encephalopathy. Dis Markers. (2011) 31:171-179.

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