Mallinckrodt Announces Positive Top-Line Results from its Pivotal Phase 3 CONFIRM Trial of Terlipressin in Patients with Hepatorenal Syndrome Type 1 (HRS-1)

August 15, 2019

-- Study met primary endpoint, verified HRS-1 reversal including three components: renal function improvement, avoidance of dialysis and short-term survival --

-- CONFIRM is the largest-ever prospective study (n=300) conducted in patients with HRS-1, an acute and rare disease with high unmet needs and poor prognosis, with no approved therapies in the U.S. or Canada --

STAINES-UPON-THAMES, United Kingdom, Aug. 15, 2019 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a global biopharmaceutical company, today announced positive top-line results from its pivotal Phase 3 CONFIRM clinical study evaluating the efficacy and safety of terlipressin in 300 adults with hepatorenal syndrome type 1 (HRS-1). The study met its primary endpoint of verified HRS-1 reversal (p=0.012). Verified HRS-1 reversal includes three components: renal function improvement, avoidance of dialysis and short-term survival. The company plans to present the data at an upcoming medical meeting.

HRS-1 is a life-threatening, rare and acute disease characterized by complications of liver disease that lead to kidney failure.[1] HRS-1 has a very poor prognosis, with a median survival time of less than two weeks and greater than 80 percent mortality within three months.[2,3] At present, there are no approved drug therapies for HRS-1 in the U.S. or Canada.[4] HRS-1 is estimated to affect between 30,000 and 40,000 patients in the U.S.[5,6] annually.

The company plans to submit a New Drug Application to the U.S. Food and Drug Administration (FDA) in early 2020. Terlipressin is an investigational product and its safety and effectiveness have not yet been established by the FDA or Health Canada.

"The initial results from the Phase 3 CONFIRM study are very encouraging in that they demonstrate terlipressin reversed the course of HRS-1 as measured by improvement in renal function, avoidance of dialysis and short-term survival. The study met nearly all of the pre-specified secondary endpoints," said lead investigator **Arun Sanyal, M.D., Z. Reno Vlahcevic Professor of Medicine, Physiology and Molecular Pathology at Virginia Commonwealth University**. "HRS-1 is a life-threatening disease that is extremely difficult to treat. We anticipate the complete results will continue to help inform the effectiveness and safety profile of terlipressin in this patient population with urgent unmet medical needs."

About the Pivotal Phase 3 CONFIRM Study (multi-center, randomized, placebo-controlled, double-blind trial in the U.S. and Canada):

- Designed to confirm efficacy and safety of terlipressin to treat HRS-1
- Largest prospective trial ever conducted (n=300) in HRS-1 patients
- Eligibility criteria included adults with liver cirrhosis and ascites with rapidly worsening renal function and no response to diuretics or albumin
- Primary endpoint of verified HRS reversal was intended to evaluate renal function improvement, avoidance of dialysis and short-term survival

In 2016, Mallinckrodt and the FDA reached agreement on the CONFIRM protocol design and data analysis under the agency's special protocol assessment (SPA) process. A SPA is an advanced agreement with the FDA for the acceptability of the clinical design, endpoints and statistical data analyses for a Phase 3 trial before the start of the trial.

"At Mallinckrodt, we are committed to advancing therapies that treat underserved patients with severe and critical conditions, including patients with this devastating condition. We are pleased and encouraged by the positive top-line results of the CONFIRM trial, the largest-ever prospective trial in HRS-1," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**. "The CONFIRM trial will support regulatory submissions of terlipressin as a treatment for HRS-1 in the U.S and Canada, and we look forward to sharing full results soon."

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

About Terlipressin

Terlipressin is a potent, vasopressin analogue selective for V1 receptors being investigated for the treatment of HRS-1 in the U.S. and Canada. Terlipressin is an investigational product in these countries as the safety and efficacy have not been established with, nor has approval been granted by regulatory authorities in either country. Terlipressin is approved for use outside the U.S. and Canada.

About Hepatorenal Syndrome Type 1 (HRS-1)

HRS-1 is a life-threatening, rare, and acute disease characterized by complications of liver disease that leads to kidney failure.[1] HRS-1 has a very poor prognosis, with a median survival time of less than two weeks and greater than 80 percent mortality within three months.[7,8] At present, there are no approved drug therapies for HRS-1 treatment in the U.S. or Canada.[9]

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 with regard to the study described in this release, including the 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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