Data on Impact of Revised Consensus Recommendations on Time to Treatment and Serum Creatinine (SCr) at Treatment Start for Patients with Hepatorenal Syndrome Type 1 (HRS-1) Presented at the 2019 International Liver Congress™ (EASL)

April 15, 2019

-- Retrospective analysis showed applying latest International Club of Ascites (ICA) diagnostic criteria would be estimated to result in earlier time to treatment at a lower SCr level and potentially improved outcomes --

STAINES-UPON-THAMES, United Kingdom, April 15, 2019 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a leading global specialty pharmaceutical company, is reporting data from a retrospective analysis of data from the Phase 3 REVERSE trial to estimate the impact of applying the revised International Club of Ascites (ICA) diagnostic criteria for Hepatorenal Syndrome Type 1 (HRS-1) on timing of treatment and serum creatinine (SCr) at treatment start. The data were shared on April 13 at the 2019 International Liver Congress™ of the European Association for the Study of the Liver (EASL) in Vienna, Austria.

HRS-1 is a rare and acute disease characterized by the development of rapid kidney failure in patients with advanced chronic liver disease.[1] Prior to 2015, the traditional definition of HRS-1 was a twofold increase of SCr to a level greater than 2.5 mg/dL during a period of less than two weeks. In 2015, the ICA revised consensus recommendations for the diagnosis of HRS-1 based on a dynamic change in SCr in patients with cirrhosis, in order to support earlier treatment of HRS-1.

"HRS-1 has an extremely poor prognosis if left untreated and patients often do not live beyond a few weeks after diagnosis," said Florence Wong, M.D., Professor, GI Division, Department of Medicine, University of Toronto, Toronto General Hospital. "This analysis is important because serum creatinine level has been shown to be a predictor of HRS reversal and potentially improved outcomes. Therefore, it is imperative that time to treatment be as short as possible after diagnosis before progression of HRS, i.e., a higher pre-treatment serum creatinine level."

The poster, "The Diagnosis of Hepatorenal Syndrome (HRS): How Much Does Use of the 2015 Revised Consensus Recommendations Affect Earlier Treatment and Serum Creatinine (SCr) at Treatment Start?" [Poster #SAT-141] can be accessed here.

The study is a retrospective analysis of pre-enrollment serial SCr data from 141 of the 196 patients enrolled in the REVERSE trial for which data were available for this analysis. Researchers assessed the mean number of days between diagnosing HRS-1 using the revised and the traditional criteria. SCr at diagnosis was compared using the revised and the traditional criteria to estimate the effect of the revised criteria on SCr at the potential start of vasoconstrictor therapy.

**Study Highlights:**

- Applying revised ICA Acute Kidney Injury-HRS diagnostic criteria rather than traditional HRS-1 diagnostic criteria would be estimated to result in:
  - Earlier treatment by approximately **four days**
  - SCr level at initiation of treatment would be on average approximately **1 mg/dL lower**
  - Almost half (47 percent) of patients would receive treatment before a further ≥ 1.5-fold increase in SCr

The retrospective study was supported by Mallinckrodt.

**Study Limitations:**

This study is a retrospective analysis of a previously completed clinical trial. Results were based on a statistical model that was not specified or measured in the original clinical trial. Results do not imply cause and effect and may be incomplete.

"HRS-1 is a diagnosis of exclusion; initiating treatment takes time. This analysis underscores the need for urgency in utilizing the newer diagnostic criteria in facilitating earlier treatment for HRS-1 patients in order to facilitate potentially better outcomes for patients," said Tunde Otulana, M.D., Senior Vice President and Chief Medical Officer at Mallinckrodt. "We are committed to supporting best practices for patients with HRS-1, including diagnostic criteria that can potentially improve the treatment paradigm."

**About Hepatorenal Syndrome Type 1**

Hepatorenal Syndrome Type 1 (HRS-1) is a rare and acute disease characterized by the development of rapid kidney failure in patients with advanced chronic liver disease. 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 treatment in the U.S. or Canada.[4]

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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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