Mallinckrodt Presents Results from Two Retrospective Studies on Real World Characteristics and Outcomes of Patients with Hepatorenal Syndrome Type-1 (HRS-1) at The Liver Meeting Digital Experience

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Retrospective medical chart review studies show outcomes based on disease severity and highlight unmet treatment needs in people with HRS-1

DUBLIN, Nov. 12, 2021 /PRNewswire/ -- Mallinckrodt plc, (OTCMKTS: MNKKQ) a global biopharmaceutical company, today announced findings from two retrospective medical chart review studies on real world outcomes of patients hospitalized with hepatorenal syndrome type-1 (HRS-1) treated with terlipressin and other vasopressors. HRS-1, also known as HRS-acute kidney injury (HRS-AKI), is a life-threatening complication in patients with advanced liver disease.[1] The data were highlighted in poster presentations at the Liver Meeting Digital Experience, the annual meeting of the American Association for the Study of Liver Diseases (AASLD), being held virtually from November 12-15. The posters can be accessed **here** on the company's website.

Terlipressin is an investigational product and its safety and effectiveness have not yet been established by the U.S. Food and Drug Administration.

"The work of Dr. Sanyal, Dr. Allegretti and their teams around HRS-1 helps us better understand this complex disease, including more effective diagnosis, and underscores the need for additional treatment options to help clinicians improve care for their patients," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**.

The first poster presentation titled "*Hepatorenal Syndrome Patient Characteristics, Treatment, and Clinical Response by Disease Severity: Real-world Practice Patterns from 11 U.S. Hospitals,"* is a retrospective, observational study based on medical chart data from 132 hospitalized adult patients across 11 hospitals in the U.S. between January 1, 2016, and June 30, 2019. The objective of the study was to describe characteristics of HRS-1 patients in the United States and assess real-world treatment patterns and clinical outcomes based on disease severity. Patients were classified as standard presentation (i.e., baseline serum creatinine [SCr] <5 mg/dL, acute on chronic liver failure [ACLF] grade 0-2, and Model for End-Stage Liver Disease [MELD] score <35) or severe presentation (i.e., baseline SCr ≥5 mg/dL or ACLF >2 or MELD score ≥35). Data were collected from hospital admission up to 90 days post-discharge or until death using an electronic case report form.

A total of 65 patients (49.2 percent) had standard disease severity and 67 (50.8 percent) had severe disease. The analysis showed that initial use of vasopressor therapies was similar between the two groups with midodrine/octreotide monotherapy being the most widely used (89.2 percent in standard cases versus 82.1 percent in severe cases). Overall response to therapy (N=132) was low in patients initiating existing treatment regimens irrespective of disease severity (Complete Response: 13.8 percent versus 17.9 percent and Partial Response: 9.2 percent versus 16.4 percent in the standard and severe groups, respectively, p=0.324).[2]

The limitations of this post hoc analysis of a retrospective chart review may include a more heterogeneous HRS population than those in randomized clinical trials, sampling bias from conveniently selected centers, potential selection bias towards patients with known outcomes to the providers and under reporting of less severe adverse events.

"Hepatorenal syndrome is very difficult to diagnose and typically met with high mortality rates if left untreated.[3,4] Our analysis showed that overall response rate was low in patients initiating existing treatment regimens irrespective of disease severity, indicating a high unmet medical need in people with HRS-1, and need for alternate therapies," said **Arun Sanyal, M.D., lead study investigator and Reno Vlahcevic Professor of Medicine, Physiology and Molecular Pathology at Virginia Commonwealth University.**

The second poster presentation, titled "*Serum Creatinine ≥5 mg/dL is Associated with Decreased Safety and Efficacy in Patients Treated with Terlipressin for Hepatorenal Syndrome-Acute Kidney Injury (HRS-AKI) in the United Kingdom,"* is a post hoc analysis of a medical chart review study with data from 203 hospitalized adult patients treated with terlipressin collected across 26 hospitals in the UK (where terlipressin is approved and available) between January 1, 2013, and December 31, 2017. The objective of the analysis was to describe efficacy and safety outcomes in patients with a SCr ≥5 mg/dL at the time of vasopressor initiation. Data were collected from hospital admission up to 90 days post-discharge or until death using an electronic case report form.

The results showed that among 203 patients who received terlipressin, 181 (89 percent) had a SCr <5 mg/dL at presentation and 22 (11 percent) had

a SCr ≥5 mg/dL. The overall response rate was 74.0 percent in patients with presenting SCr <5 mg/dL and 63.6 percent in patients with presenting SCr ≥5 mg/dL. Patients with a presenting SCr <5 mg/dL were more likely to achieve complete response compared with those with presenting SCr ≥5 mg/dL (54.7 versus 13.6 percent, respectively; P<.001). The overall survival was longer in patients with presenting SCr <5 mg/dL than in patients with presenting SCr ≥5 mg/dL (*P* =.041). Additionally, patients with presenting SCr ≥5 mg/dL were more likely to develop fluid overload or pulmonary edema (27.3 percent) and multi-organ failure (31.8 percent) compared to patients with a SCr <5 mg/dL (14.4 and 6.1 percent, respectively).[5]

The limitations of this post hoc analysis of a retrospective chart review may include a more heterogeneous HRS population than those in randomized clinical trials, sampling bias from conveniently selected centers, potential selection bias towards patients with known outcomes to the providers and under reporting of less severe adverse events.

"Our analysis supports previous studies linking higher presenting SCr to poorer outcomes in patients with HRS-1.[6,7] Importantly, these findings highlight significant unmet need for effective medical therapy for HRS-AKI and suggest that earlier initiation of vasoconstrictors may optimize patient outcomes," said **Andrew Allegretti, M.D. MSc, lead study investigator and Director of Critical Care Nephrology, Massachusetts General Hospital**.

The studies were sponsored by Mallinckrodt.

About Hepatorenal Syndrome

HRS is classified into two distinct types – hepatorenal syndrome type-1 and type-2.[1] HRS-1 is a rapidly progressive condition that leads to renal failure.[1] It is often a challenge to effectively diagnose in a timely manner due to its diagnosis of exclusion.[2] At present, there are no drug therapies approved for the treatment of HRS-1 in the U.S. or Canada.[8] HRS-1 is estimated to affect between 30,000 and 40,000 patients in the U.S. annually.[9,10]

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. It 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 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 terlipressin, including 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: 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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