Mallinckrodt Announces Data at Kidney Week 2020 Reimagined that Showed A Potential for Reduced Need for Renal Replacement (RRT) Therapy for Patients with Hepatorenal Syndrome Type 1 (HRS-1) Treated with Terlipressin

October 29, 2020

Post-hoc, pooled analyses of three Phase 3 trials found HRS-1 patients treated with terlipressin was associated with less RRT up to Day 90 versus placebo

DUBLIN, Oct. 29, 2020 /PRNewswire/ -- Mallinckrodt plc, a global biopharmaceutical company, today announced results from two post-hoc studies of its investigational agent terlipressin in adults with hepatorenal syndrome type 1 (HRS-1). HRS-1 is an acute and life-threatening syndrome involving acute kidney failure in people with cirrhosis.[1] Results were presented at Kidney Week 2020 Reimagined, the annual meeting of the American Society of Nephrology. The results, based on pooled analyses of three Phase 3 trials including the pivotal CONFIRM study, found that HRS-1 patients treated with terlipressin (N=352) required renal replacement therapy (RRT) (dialysis) less often and had improved RRT-free survival up to Day 90 compared to placebo (N=256).

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

The results shared in an oral presentation titled "Terlipressin Improves Renal Replacement Therapy–Free Survival in Hepatorenal Syndrome Type 1" included a post-hoc analysis to assess the incidence of RRT among patients from the CONFIRM (NCT 02770716), REVERSE (NCT 01143246) and OT-0401 (NCT 00089570) Phase 3 trials. Results from this pooled analysis showed: at Day 30, 26 percent in the terlipressin group (56/218) needed RRT compared with 42 percent of those on placebo (70/166); at Day 60, 27 percent of the terlipressin group (52/193) required RRT versus 45 percent on placebo (64/143); and at Day 90, 29 percent of surviving patients in the terlipressin group (52/182) needed RRT compared with 45 percent in the placebo group (60/133).[2]

The pooled analysis also showed that RRT-free 90-day survival was higher among patients treated with terlipressin versus placebo in all three trials. The pooled RRT-free survival rate for patients treated with terlipressin was 37 percent (130/352) versus 29 percent in the placebo group (73/256) across the three trials (p=0.03).2 The presentation can be accessed **here** on the company's website.

"The findings presented from the post-hoc and pooled analyses support the positive results of the Phase 3 CONFIRM trial among HRS-1 patients, showing the potential for terlipressin to help patients reduce the need for renal replacement therapy and improve RRT-free survival," said presenting author **Juan Carlos Q. Velez, MD, Chair of Nephrology at Ochsner Health System, New Orleans, LA**. "These findings add to the breadth of existing knowledge and data of terlipressin, which has been extensively studied around the world for decades, and are important as HRS-1 is typically fatal and marked by rapid decline within three months if left untreated."

Limitations of a pooled analysis such as this include a reliance on the quality or reporting of the original study results. In addition, the variability of patient populations, the quality of the data and the potential for underlying biases are not addressed.

A second data set was presented in a poster presentation titled, "Treatment of Hepatorenal Syndrome Type 1 with Terlipressin Reduces Need for Renal Replacement Therapy After Liver Transplantation," including a post-hoc analysis of the CONFIRM study which evaluated the need for RRT among patients who had liver transplantation at 90 days. The study found that patients treated with terlipressin had a lower rate of RRT following liver transplantation compared to patients treated with placebo (19.6 percent (9/46) versus 44.8 percent (13/29); p=0.036). The poster also included a pooled analysis which assessed survival rates from the three terlipressin Phase 3 clinical trials for patients following liver transplantation. The analysis found that at Day 90, 50 percent of patients treated with terlipressin (46/92) were alive without receiving RRT compared with 32.2 percent in the placebo group (19/59; p=0.032).[3] The poster can be accessed **here** on the company's website.

"Mallinckrodt remains committed to furthering our understanding of HRS-1 and terlipressin to address HRS-1, where a patient's condition can deteriorate rapidly and treatment options are limited," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**.

Terlipressin is approved in many countries outside the United States, where it has been a standard of care for decades in the treatment of patients with HRS-1.[4,5] Terlipressin, together with albumin, is currently the standard of care for HRS-1 in countries where it is available.[6]

HRS-1 has a median survival time of less than two weeks and greater than 80 percent mortality within three months if left untreated.[7,8] At present, there are no approved drug therapies for HRS-1 in the U.S. or Canada.[9] HRS-1 is estimated to affect between 30,000 and 40,000 patients in the U.S. annually.[10,11]

The studies were funded by Mallinckrodt.

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, hepatology, 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.

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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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