Mallinckrodt Presents New Data on TERLIVAZ® (terlipressin) for Injection at the Society of Critical Care Medicine (SCCM) 2024 Critical Care Congress

January 22, 2024

– Oral presentation of a post hoc analysis of the Phase 3 CONFIRM trial details the therapeutic effect of TERLIVAZ in adult patients with hepatorenal syndrome (HRS) and alcoholic hepatitis (AH)[1] –

DUBLIN, Jan. 22, 2024 /PRNewswire/ -- Mallinckrodt plc, a global specialty pharmaceutical company, today announced the presentation of findings from a post hoc analysis of the Phase 3 CONFIRM clinical trial. In this analysis, treatment with TERLIVAZ® (terlipressin) for injection was associated with improvements in verified hepatorenal syndrome (HRS) reversal and HRS reversal vs. placebo in adult cirrhosis patients with alcoholic hepatitis (AH) and HRS with rapid reduction in kidney function.[1,2] The results will be shared in an oral presentation at the Society of Critical Care Medicine (SCCM) 2024 Critical Care Congress, taking place January 21-23, 2024, in Phoenix, AZ.

TERLIVAZ is the first and only FDA-approved product indicated to improve kidney function in adults with HRS with rapid reduction in kidney function,[2] an acute and life-threatening condition requiring hospitalization.[3] HRS involving rapid reduction in kidney function[2] is estimated to affect more than 42,000 Americans annually and rates of HRS hospitalizations are increasing.[4]

Please see Limitation of Use and Important Safety Information, including Boxed Warning, below.

The post hoc analysis evaluated the efficacy of TERLIVAZ in a subgroup of patients from the CONFIRM trial with HRS, acute-on-chronic liver failure (ACLF) grade 0–2 and serum creatinine (SCr) <5 mg/dL.[1] The incidence of verified HRS reversal – defined as two consecutive SCr values ≤1.5 mg/dL at least two hours apart while on treatment and alive without renal replacement therapy (RRT) for at least 10 days – and HRS reversal – defined as SCr ≤1.5 mg/dL while on treatment – were assessed.[1]

"We are pleased to share the latest data providing valuable insight into the relationship between TERLIVAZ treatment and rates of verified HRS reversal in adult cirrhosis patients with AH compounded by HRS," said **Peter Richardson, MRCP (UK), Executive Vice President & Chief Scientific Officer**. "This research is a reflection of our commitment to provide healthcare providers with the most up-to-date clinical information to support critically ill patients, especially those with AH, and drive the importance of early recognition and treatment of HRS at lower SCr levels and ACLF grades for potentially better outcomes."

A total of 117 patients in the subgroup analysis (N=300) met the criteria for evaluation (TERLIVAZ n=78; placebo n=39).[1] The analysis found that the incidence of verified HRS reversal was significantly higher in patients treated with TERLIVAZ vs. placebo (TERLIVAZ: 32%, n=25; placebo: 8%, n=3: p=0.004), as well as the incidence of HRS reversal (TERLIVAZ: 37%, n=29; placebo: 10.3%, n=4: p=0.002).[1]

This study was sponsored by Mallinckrodt Pharmaceuticals. Presentation details can be found below:

Abstract #1311: Terlipressin Improves Outcomes in Patients with HRS and Alcoholic Hepatitis: The CONFIRM Study[1]

- **Presenter:** Jody C. Olson, MD, FACP, Department of Internal Medicine, Mayo Clinic, Rochester, MN
- **Presentation Date:** Monday, January 22, 2024; 2:30 – 3:30 p.m. MT
- **Location:** Connections Central – RST 04

INDICATION AND LIMITATION OF USE

TERLIVAZ® is indicated to improve kidney function in adults with hepatorenal syndrome with rapid reduction in kidney function.

- Patients with a serum creatinine >5 mg/dL are unlikely to experience benefit.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS OR FATAL RESPIRATORY FAILURE

- **TERLIVAZ may cause serious or fatal respiratory failure. Patients with volume overload or with acute-on-chronic**

liver failure (ACLF) Grade 3 are at increased risk. Assess oxygenation saturation (e.g., SpO_2) before initiating TERLIVAZ.

- **Do not initiate TERLIVAZ in patients experiencing hypoxia (e.g., SpO_2 <90%) until oxygenation levels improve. Monitor patients for hypoxia using continuous pulse oximetry during treatment and discontinue TERLIVAZ if SpO_2 decreases below 90%.**

Contraindications

TERLIVAZ is contraindicated:

- In patients experiencing hypoxia or worsening respiratory symptoms.
- In patients with ongoing coronary, peripheral, or mesenteric ischemia.

Warnings and Precautions

- **Serious or Fatal Respiratory Failure:** Obtain baseline oxygen saturation and do not initiate TERLIVAZ in hypoxic patients. Monitor patients for changes in respiratory status using continuous pulse oximetry and regular clinical assessments. Discontinue TERLIVAZ in patients experiencing hypoxia or increased respiratory symptoms.

  Manage intravascular volume overload by reducing or discontinuing the administration of albumin and/or other fluids and through judicious use of diuretics. Temporarily interrupt, reduce, or discontinue TERLIVAZ treatment until patient volume status improves. Avoid use in patients with ACLF Grade 3 because they are at significant risk for respiratory failure.

- **Ineligibility for Liver Transplant:** TERLIVAZ-related adverse reactions (respiratory failure, ischemia) may make a patient ineligible for liver transplantation, if listed. For patients with high prioritization for liver transplantation (e.g., MELD ≥35), the benefits of TERLIVAZ may not outweigh its risks.

- **Ischemic Events:** TERLIVAZ may cause cardiac, cerebrovascular, peripheral, or mesenteric ischemia. Avoid use of TERLIVAZ in patients with a history of severe cardiovascular conditions or cerebrovascular or ischemic disease. Discontinue TERLIVAZ in patients who experience signs or symptoms suggestive of ischemic adverse reactions.

- **Embryo-Fetal Toxicity:** TERLIVAZ may cause fetal harm when administered to a pregnant woman. If TERLIVAZ is used during pregnancy, the patient should be informed of the potential risk to the fetus.

Adverse Reactions

- The most common adverse reactions (≥10%) include abdominal pain, nausea, respiratory failure, diarrhea, and dyspnea.

Please click here to see full Prescribing Information, including Boxed Warning.

About Hepatorenal Syndrome (HRS)

Hepatorenal syndrome (HRS) involving rapid reduction in kidney function[2] is an acute and life-threatening condition that occurs in people with advanced liver disease.[3] HRS is classified into two distinct types – a rapidly progressive type that leads to acute renal failure where patients are typically hospitalized for their care and a more chronic type that progresses over weeks to months.[3] HRS involving rapid reduction in kidney function[2] is estimated to affect more than 42,000 Americans annually and rates of HRS hospitalizations are increasing.[4] If left untreated, HRS with rapid reduction in kidney function[2] has a median survival time of less than two weeks and greater than 80 percent mortality within three months.[5]

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, ophthalmology, and oncology; 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.

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS

This release contains forward-looking statements, including with regard to TERLIVAZ®, its potential to improve health and treatment outcomes, its potential impact on patients, and the planned presentation regarding the TERLIVAZ trial. 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: the effects of Mallinckrodt's recent emergence from bankruptcy; satisfaction of, and compliance with, 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 or adverse side effects or adverse reactions associated with TERLIVAZ; 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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References

[1] Olson JC, et al. Terlipressin Improves Outcomes in Patients with HRS and Alcoholic Hepatitis: The CONFIRM Study. *Oral presentation to be shared at the Society of Critical Care Medicine (SCCM) 2024 Critical Care Congress*. January 2024.

[2] TERLIVAZ® (terlipressin) for Injection. Prescribing Information. Mallinckrodt Hospital Products Inc. 2023.

[3] National Organization for Rare Disorders. Hepatorenal Syndrome. Available at: https://rarediseases.org/rare-diseases/hepatorenal-syndrome/. Accessed January 2024.

[4] Singh J, Dahiya DS, Kichloo A, Singh G, Khoshbin K, Shaka H. Hepatorenal Syndrome: A Nationwide Trend Analysis from 2008 to 2018. *Annals of Med*. 2021;53:1. doi.org/10/1080/07853890.

[5] Flamm, S.L., Brown, K., Wadei, H.M., et al. The Current Management of Hepatorenal Syndrome–Acute Kidney Injury in the United States and the Potential of Terlipressin. *Liver Transpl*. 2021;27:1191-1202. doi.org/10.1002/lt.26072.

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