Mallinckrodt Presents Data on TERLIVAZ® (terlipressin) for Injection in Patients with Hepatorenal Syndrome (HRS) at the 2024 Digestive Disease Week® (DDW)

May 18, 2024

– Two poster presentations of Mallinckrodt's research for adults with HRS with rapid reduction in kidney function[1] provide further insight into treatment with TERLIVAZ for appropriate patients –

DUBLIN, May 18, 2024 /PRNewswire/ -- Mallinckrodt plc, a global specialty pharmaceutical company, today announced the presentation of two posters on TERLIVAZ® (terlipressin) for injection in patients with hepatorenal syndrome (HRS) with rapid reduction in kidney function[1] at the 2024 Digestive Disease Week® (DDW) taking place in Washington, DC from May 18-21, 2024.

The posters feature a post-hoc analysis of data from the pivotal Phase III CONFIRM trial, analyzing the impact of dose interruptions on treatment response to TERLIVAZ in patients with hepatorenal syndrome-acute kidney injury (HRS-AKI),[2] and a pooled analysis of three Phase III clinical studies assessing the impact of TERLIVAZ treatment on patients with HRS and a baseline serum creatinine (SCr) <5mg/dL.[3]

TERLIVAZ is the first and only FDA-approved product indicated to improve kidney function in adults with HRS with rapid reduction in kidney function,[1] an acute and life-threatening condition requiring hospitalization.[4] HRS involving rapid reduction in kidney function[1] is estimated to affect more than 42,000 Americans annually and rates of hospitalizations are increasing.[5]

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

"We're excited to present our research at DDW. It represents our ongoing commitment to add to the depth and breadth of data on TERLIVAZ and its important role in the treatment of adult patients with HRS with rapid reduction in kidney function,"[1] said **Peter Richardson, MRCP (UK), Executive Vice President & Chief Scientific Officer**. "Collectively, these data support our understanding of those who are most likely to benefit from TERLIVAZ showing the potential impact of use in the real-world, including when the dosing schedule is interrupted."

Abstract #4025396: Treatment Response to Terlipressin is Unaffected by Dose Interruptions in Patients with Hepatorenal Syndrome-Acute Kidney Injury[2]

- **Presenter:** Khalid Mumtaz, MD, The Ohio State University Wexner Medical Center, Columbus, OH
- **Session Type:** Poster Presentation
- **Session Title:** Portal Hypertension and Other Complications of Cirrhosis
- **Session Date and Time:** Saturday, May 18, 2024; 12:30 – 1:30 p.m. EDT

This analysis evaluated the effect of dose interruption on the incidence of HRS reversal for patients with HRS-AKI.[2] The recommended dose regimen includes administering TERLIVAZ 0.85 mg (1 vial) intravenously every six hours on days one to three.[1] On day four, assess SCr versus baseline and if SCr has decreased by at least 30% from baseline continue TERLIVAZ 0.85 mg (1 vial) intravenously every six hours.[1] Patients included in the analysis experienced a dose interruption due to adverse events or any other reason.[2] After a dose interruption, treatment could be restarted at a reduced dose of 0.5 mg or 1 mg every 6-12 hours.[2] The safety and efficacy of this particular use has not been evaluated by FDA.

Abstract #4034883: Terlipressin Treatment Benefits Those Patients with Baseline Serum Creatinine <5 mg/dl: The North American Experience[3]

- **Presenter:** Prasun K. Jalal, MD, Baylor College of Medicine, Houston, TX
- **Session Type:** Poster Presentation
- **Session Title:** Portal Hypertension and Other Complications of Cirrhosis
- **Session Date and Time:** Saturday, May 18, 2024; 12:30 – 1:30 p.m. EDT

This analysis included pooled data from three Phase III, placebo-controlled studies of TERLIVAZ in 608 patients with HRS with rapid reduction in kidney function.[1,3] Patients were dosed with 1 mg terlipressin acetate (equivalent to 0.85 mg terlipressin base) every six hours for ≤14 days.[3] Data was assessed by SCr subgroup (baseline SCr <5 mg/dL or ≥5 mg/dL) for the outcomes of HRS reversal (defined as >/=1 SCr of </=1.5 mg/dL while on

treatment), incidence of renal replacement therapy (RRT), overall survival, and transplant-free survival up to Day 90.[3]

These analyses were sponsored by Mallinckrodt Pharmaceuticals.

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[1] is an acute and life-threatening condition that occurs in people with advanced liver disease.[4] 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.[4] HRS involving rapid reduction in kidney function[1] is estimated to affect more than 42,000 Americans annually and rates of HRS hospitalizations are increasing.[5] If left untreated, HRS with rapid reduction in kidney function[1] has a median survival time of less than two weeks and greater than 80 percent mortality within three months.[6]

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, and 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: 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" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections 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.

CONTACT

Media Inquiries
Green Room Communications
908-577-4531
mediainquiries@grcomms.com

Investor Relations
Derek Belz
Vice President, Investor Relations
314-654-3950
derek.belz@mnk.com

References

---

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

[2] Mumtaz K, Bari K, Reddy G, et al. Treatment Response to Terlipressin is Unaffected by Dose Interruptions in Patients with Hepatorenal Syndrome-Acute Kidney Injury. *Presentation to be shared at the 2024 Digestive Disease Week (DDW).* May 2024.

[3] Jalal P, Verna EC, Rahimi RS, et al. Terlipressin Treatment Benefits Those Patients with Baseline Serum Creatinine <5 mg/dl: The North American Experience. *Presentation to be shared at the 2024 Digestive Disease Week (DDW).* May 2024.

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

[5] 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. 2018-2024 doi.org/10/1080/07853890.

[6] 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. https://doi.org/10.1002/lt.26072.

View original content to download multimedia:https://www.prnewswire.com/news-releases/mallinckrodt-presents-data-on-terlivaz-terlipressin-for-injection-in-patients-with-hepatorenal-syndrome-hrs-at-the-2024-digestive-disease-week-ddw-302148985.html

SOURCE Mallinckrodt plc