Mallinckrodt Presents Data on TERLIVAZ® (terlipressin) for Injection in Patients with Hepatorenal Syndrome (HRS) at the 2024 American Association for the Study of Liver Diseases (AASLD) Annual Meeting

November 18, 2024

– Poster evaluates potential impact of waiting until Day 4 (and after 12 doses of TERLIVAZ) before assessing outcomes in adult patients with HRS with rapid reduction in kidney function[1] –

DUBLIN, Nov. 18, 2024 /PRNewswire/ -- Mallinckrodt plc, a global specialty pharmaceutical company, today announced a poster presentation on TERLIVAZ® (terlipressin) for injection in patients with hepatorenal syndrome (HRS) with rapid reduction in kidney function[1] at The Liver Meeting, the annual meeting of the American Association for the Study of Liver Diseases (AASLD), taking place in San Diego, CA, from November 15-19, 2024.

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.[2] HRS involving rapid reduction in kidney function[1] is estimated to affect more than 42,000 Americans annually, approximately 0.01% of the U.S. population,[3] making it a very rare condition; and rates of hospitalizations are increasing.[4]

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

The poster presentation includes a pooled patient cohort analysis from the CONFIRM, REVERSE, and OT-0401 Phase 3 studies of TERLIVAZ.[5] The research evaluated HRS reversal among patients on Day 4 after 12 doses of TERLIVAZ.[5] TERLIVAZ treatment is recommended at a dose of 1 mg every six hours for up to 14 days, which can be escalated on Day 4 to 2 mg every six hours if the patient's serum creatinine (SCr) has decreased from baseline but by less than 30%.[5] In the analysis, most patients who achieved HRS reversal by the end of treatment required continuation of therapy beyond Day 4.[5]

- The rate of HRS reversal by the end of treatment was 33.6% (117/348) in the TERLIVAZ group and 16.8% (42/250) in the placebo group.[5]
- Most patients who achieved HRS reversal with TERLIVAZ received >12 doses (94.9%, 111/117), and 5.1% (6/117) received ≤12 doses before discontinuation.[5]
- There appeared to be significantly more patients who achieved HRS reversal in the TERLIVAZ group who received >12 doses, but not among those who received ≤12 doses; however, based on the design of the analysis, statistical methodology did not control for confounding variables, thus the p-values are nominal.[5]

The limitations of this study include, but are not limited to, small sample sizes, variables in methodology, and possible errors and omissions within the data sets.[5]

"We are pleased to share research which evaluated HRS reversal among patients after 12 doses or on Day 4 of treatment," said **Peter Richardson, MRCP (UK), Executive Vice President & Chief Scientific Officer**. "This research further suggests the need to deliver the recommended treatment duration before assessing the patient's response."

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

Poster #4094: Patience is a Virtue: Evidence for Waiting Until Day 4 and After 12 Doses of Terlipressin Before Evaluating Treatment Response in Patients with HRS-AKI[5]

- **Presenter**: Manhal J. Izzy
- **Session Type:** Poster Presentation
- **Session Title:** Portal Hypertension and Other Complications of Cirrhosis
- **Session Date and Time:** Monday, November 18, 2024; 8:00 a.m. – 5:00 p.m. PST

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[2] 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.[2] HRS involving rapid reduction in kidney function[1] is estimated to affect more than 42,000 Americans annually, approximately 0.01% of the U.S. population,[3] making it a very rare condition; and rates of hospitalizations are increasing.[4] 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 of Mallinckrodt's most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, 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] National Organization for Rare Disorders. Hepatorenal Syndrome. Available at: https://rarediseases.org/rare-diseases/hepatorenal-syndrome/. Accessed November 2024.

[3] United States Census Bureau: Quick Facts. Available at: https://www.census.gov/quickfacts/fact/table/US/PST045218. Accessed November 2024.

[4] Singh J., Dahiya D.S., Kichloo A., et al. Hepatorenal Syndrome: A Nationwide Trend Analysis from 2008 to 2018. *Annals of Med*. 2021;53:1. 2018-2024 doi.org/10/1080/07853890.

[5] Izzy, M.J., Gonzalez, S.A., Jalal, P.K., and Cardoza, S. Patience is a Virtue: Evidence for Waiting Until Day 4 and After 12 Doses of Terlipressin Before Evaluating Treatment Response in Patients with HRS-AKI. *Abstract to be presented in a poster presentation at the American Association for the Study of Liver Diseases – The Liver Week Meeting.* November 2024.

[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-american-association-for-the-study-of-liver-diseases-aasld-annual-meeting-302308532.html

SOURCE Mallinckrodt plc