Mallinckrodt to Present Data on TERLIVAZ® (terlipressin) for Injection in Adult Patients with Hepatorenal Syndrome (HRS) at the American College of Gastroenterology (ACG) Annual Scientific Meeting

October 22, 2023

– Findings from two clinical studies and one health economic database analysis provide insight into HRS treatment outcomes with TERLIVAZ,[1] patients' cardiac health[2] and association between hospital size and overall outcomes for chronic liver disease patients[3] –

DUBLIN, Oct. 22, 2023 /PRNewswire/ -- Mallinckrodt plc (OTCMKTS: MNKTQ), a global specialty pharmaceutical company, today announced that three posters detailing findings from Mallinckrodt's latest clinical and health economics outcomes research with TERLIVAZ® (terlipressin) for injection for adult patients with hepatorenal syndrome (HRS) with rapid reduction in kidney function[1,2,3,4] will be presented at the American College of Gastroenterology (ACG) Annual Scientific Meeting in Vancouver, British Columbia, taking place October 20-25, 2023.

TERLIVAZ is the first and only FDA-approved product indicated to improve kidney function in adults with HRS with rapid reduction in kidney function,[4] an acute and life-threatening condition requiring hospitalization.[5] TERLIVAZ is not approved in Canada.

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

Paul J. Thuluvath, MD, will present findings from a pooled analysis of Mallinckrodt's three prospective, randomized, placebo-controlled clinical studies in patients with HRS (OT-0401, REVERSE, and CONFIRM) to examine whether there was any impact of race (White vs. non-White) on treatment response to TERLIVAZ.[1] HRS reversal – defined as the proportion of patients achieving a serum creatinine level of ≤ 1.5 mg/dL while on treatment including up to 24 hours after the last dose of study drug – was examined by race and assessed for the potential to predict treatment response.[1]

A post-hoc analysis of the Phase III CONFIRM trial – which evaluated maximum change and time of maximum change in mean arterial pressure (MAP), heart rate (HR) and systolic and diastolic blood pressure (SBP and DBP) with TERLIVAZ treatment – will be presented by Jacqueline G. O'Leary, MD.[2] The data were analyzed to monitor for significant changes in MAP, SBP and DBP between treatment groups, and to determine the associated level of required cardiac monitoring.[2]

Additionally, results from a real-world analysis of the impact of hospital size on patient outcomes among those with chronic liver disease (CLD) and acute kidney injury or HRS will be presented by Ronald J. Wong, MD.[3] This analysis identified nearly 3 million hospitalized patients with CLD (including cirrhosis) from 2016-2022 using the Premier Healthcare Database inclusive of over 1,041 hospitals/health systems in the U.S., to assess overall outcomes of treatment such as in-hospital mortality and comorbidity for patients in hospitals of varying sizes.[3]

Additional information on these studies can be found below.

"These data presentations not only deepen our understanding of how HRS patient baseline characteristics – and their response to therapy – impact treatment outcomes with TERLIVAZ, but also lend insight into how the critical care setting in which patients are hospitalized affects their treatment journey in the real world,"[1,2,3] said **Khurram Jamil, Vice President, Hepatology, Clinical Development & Critical Care.** "We are pleased to share this data with the gastroenterology community and remain steadfast in our mission to conduct clinical and health economic research to better support and inform the care decisions of physicians managing these critically ill patients."

These studies are sponsored by Mallinckrodt Pharmaceuticals and include:

#P0995: The Effect of Race on Treatment Response to Terlipressin in Patients with Hepatorenal Syndrome: A Pooled Analysis of 3 Phase III Clinical Studies[1]

- **Presenter:** Paul J. Thuluvath, MD, Mercy Medical Center & University of Maryland School of Medicine, Baltimore, MD
- **Poster Session:** Liver, Exhibit Hall
- **Session Date and Time:** Sunday, October 22, 3:30 – 7:00 p.m. PDT / 6:30 – 10:00 p.m. EDT

#P2399: The Effect of Terlipressin on Blood Pressure, Mean Arterial Pressure, and Heart Rate in Patients with Hepatorenal Syndrome: A Post Hoc Analysis of the CONFIRM Study[2]

- **Presenter:** Jacqueline G. O'Leary, MD, Dallas VA Medical Center & Baylor University Medical Center, Dallas, TX
- **Poster Session:** Liver, Exhibit Hall
- **Session Date and Time:** Monday, October 23, 10:30 a.m. – 4:15 p.m. PDT / 1:30 – 7:15 p.m. EDT

#P0938: Differences in Patient Characteristics and Outcomes by Hospital Size for Patients with Chronic Liver Disease and Acute Kidney Injury or Hepatorenal Syndrome[3]

- **Presenter:** Robert J. Wong, MD, Stanford University School of Medicine, Palo Alto, CA
- **Poster Session:** Liver, Exhibit Hall
- **Session Date and Time:** Sunday, October 22, 2023, 3:30 – 7:00 p.m. PDT / 6:30 – 10:00 p.m. EDT

Data collected in a retrospective analysis may have errors or omissions. Outcomes may be influenced by therapies not evaluated in the study and the clinical/health economic outcomes may not be solely attributable to TERLIVAZ.

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[4] is an acute and life-threatening condition that occurs in people with

advanced liver disease.[5] 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.[5] HRS involving rapid reduction in kidney function[4] is estimated to affect between 30,000 and 40,000 Americans annually.[6,7] If left untreated, HRS with rapid reduction in kidney function[4] has a median survival time of approximately two weeks and greater than 80 percent mortality within three months.[8]

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; cultured skin substitutes 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 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 impact of Mallinckrodt's pending Chapter 11 cases; 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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[1] Thuluvath PJ, et al. The Effect of Race on Treatment Response to Terlipressin in Patients with Hepatorenal Syndrome: A Pooled Analysis of 3 Phase III Clinical Studies. *Poster to be presented at the American College of Gastroenterology (ACG) Annual Scientific Meeting.* October 20-25, 2023.

[2] O'Leary JG, et al. The Effect of Terlipressin on Blood Pressure, Mean Arterial Pressure, and Heart Rate in patients with Hepatorenal Syndrome: A Post-Hoc Analysis of the CONFIRM Study. *Poster to be presented at the American College of Gastroenterology (ACG) Annual Scientific Meeting.* October 20-25, 2023.

[3] Wong RJ, et al. Differences in Patient Characteristics and Outcomes by Hospital Size for Patients with Chronic Liver Disease and Acute Kidney Injury or Hepatorenal Syndrome. *Poster to be presented at the American College of Gastroenterology (ACG) Annual Scientific Meeting.* October 20-25, 2023.

[4] TERLIVAZ® (terlipressin) for injection. Prescribing Information. Mallinckrodt Hospital Products Inc.

[5] National Organization for Rare Disorders. Hepatorenal Syndrome. Available at: https://rarediseases.org/rare-diseases/hepatorenal-syndrome/. Accessed September 2023.

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[8] 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.

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