Mallinckrodt to Present Data on TERLIVAZ® (terlipressin) for Injection in Adult Patients with Hepatorenal Syndrome (HRS) at the European Association for the Study of the Liver (EASL) Congress 2023

June 15, 2023

– Two scientific poster presentations at EASL 2023 will detail findings of Mallinckrodt's latest research providing insight into the therapeutic effect of TERLIVAZ® from baseline, and the clinical management of adults with HRS with rapid reduction in kidney function[1] –

DUBLIN, June 15, 2023 /PRNewswire/ -- Mallinckrodt plc (NYSE American: MNK), a global specialty pharmaceutical company, today announced that two scientific posters detailing Mallinckrodt's latest research findings on the clinical outcomes of treatment with TERLIVAZ® (terlipressin) for injection and clinical management criteria for adult patients with hepatorenal syndrome (HRS) will be presented at the European Association for the Study of the Liver (EASL) Congress 2023 in Vienna, Austria, taking place June 21-24, 2023. Both posters will be presented on June 24, 2023, 9:00 a.m. – 5:00 p.m. CEST / 3:00 a.m. – 11:00 a.m. EDT.

TERLIVAZ is the first and only FDA-approved product indicated to improve kidney function in adults with hepatorenal syndrome (HRS) with rapid reduction in kidney function,[1] an acute and life-threatening condition requiring hospitalization.[2]

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

R. Todd Frederick, MD, Department of Transplant, California Pacific Medical Center, will present findings from a retrospective analysis of the CONFIRM Phase III trial. The CONFIRM trial is the largest-ever prospective, randomized clinical trial of terlipressin compared to placebo in patients with HRS type 1 (HRS-1). The study evaluated if the application of updated 2015 International Club of Ascites (ICA) diagnostic criteria for HRS- acute kidney injury (HRS-AKI), which recommends earlier treatment at lower serum creatinine (SCr) levels, has the potential for better clinical outcomes.[3]

Additionally, results from a pooled analysis from three North American placebo-controlled Phase III trials (OT-0401, REVERSE, CONFIRM) of terlipressin in patients with HRS-1 will be presented by Prof. Kevin Moore, BSc, PhD, UCL Institute of Liver and Digestive Health, Royal Free Hospital, University College London. This analysis provides insight into the efficacy of terlipressin in patient subgroups based on their precipitating factors (PFs) leading to HRS, and the associated impact on HRS reversal and clinical outcomes.[4]

Additional information on these studies can be found below.

"We look forward to sharing data on the real-world impact of TERLIVAZ® through the lens of patients with precipitating factors, as well as the potential impact that applying the updated diagnostic criteria can have on improving the timely diagnosis of HRS patients and earlier treatment with available therapies, such as TERLIVAZ.[3,4]" said **Khurram Jamil, Vice President, Hepatology, Clinical Development & Critical Care.** "These findings not only help to support the use of TERLIVAZ for appropriate patients with HRS, but also have important implications for how the medical community approaches the diagnosis and clinical management of this critical condition."

These studies are sponsored by Mallinckrodt Pharmaceuticals and include:

Poster 1139: Earlier diagnosis of hepatorenal syndrome-acute kidney injury with updated guidelines – review of the CONFIRM trial[3]

- **Presenter:** R. Todd Frederick, MD, Department of Transplant, California Pacific Medical Center, San Francisco, Calif.
- **Poster Session:** Cirrhosis and its Complications: Portal Hypertension
- **Session Date and Time:** Saturday, June 24, 2023; 9:00 a.m. – 5:00 p.m. CEST / 3:00 a.m. – 11:00 a.m. EDT

Poster 22: The effect of precipitating factors for hepatorenal syndrome on response to terlipressin treatment: A subgroup analysis of a pooled North American database[4]

- **Presenter:** Kevin Moore, BSc, PhD, UCL Institute of Liver and Digestive Health, Royal Free Hospital, University College London, London, UK
- **Poster Session:** Cirrhosis and its Complications: Portal Hypertension
- **Session Date and Time:** Saturday, June 24, 2023; 9:00 a.m. – 5:00 p.m. CEST / 3:00 a.m. – 11:00 a.m. EDT

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 between 30,000 and 40,000 Americans annually.[5,6] If left untreated, HRS with rapid reduction in kidney function[1] has a median survival time of approximately two weeks and greater than 80 percent mortality within three months.[7]

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 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: 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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References

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

[2] National Organization for Rare Disorders. Hepatorenal Syndrome. Available at: https://rarediseases.org/rare-diseases/hepatorenal-syndrome/. Accessed March 28, 2023.

[3] Frederick RT, Wong F, Vargas HE, Pappas SC, Jamil K. Earlier diagnosis of hepatorenal syndrome-acute kidney injury with updated guidelines – review of the CONFIRM trial. *Abstract to be presented at the European Association for the Study of the Liver (EASL) 2023 Liver Congress*. June 2023.

[4] Moore K, Zafar Z, Pyrsopoulos NT, Jamil K. The effect of precipitating factors for hepatorenal syndrome on response to terlipressin treatment: A subgroup analysis of a pooled North American database. *Abstract to be presented at the European Association for the Study of the Liver (EASL) 2023 Liver Congress*. June 2023.

[5] C Pant, B S Jani, M Desai, A Deshpande, Prashant Pandya, Ryan Taylor, R Gilroy, M OIyaee. Hepatorenal [DA1] syndrome in hospitalized patients with chronic liver disease: results from the Nationwide Inpatient Sample 2002-2012. *J of Investig Med.* 2016; 64:33-38.

[6] United States Census Bureau: Quick Facts. Available at: https://www.census.gov/quickfacts/fact/table/US/PST045218. Accessed May 3, 2023.

[7] 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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