Mallinckrodt to Present Data on TERLIVAZ® (terlipressin) for Injection in Adult Patients with Hepatorenal Syndrome (HRS) at the American Society of Nephrology (ASN) Kidney Week 2022 Scientific Meeting

November 1, 2022

– Three scientific abstracts highlighting clinical research of terlipressin treatment for adults with HRS involving rapid reduction in kidney function[1] will be presented at the ASN Scientific Meeting, reinforcing Mallinckrodt's ongoing commitment to critically ill patients –

DUBLIN, Nov. 1, 2022 /PRNewswire/ -- Mallinckrodt plc (NYSE American: MNK), a global specialty pharmaceutical company, today announced that three scientific abstracts on clinical research on treatment with TERLIVAZ® (terlipressin) for adult patients with hepatorenal syndrome (HRS) involving rapid reduction in kidney function,[1] will be presented at the American Society of Nephrology (ASN) Kidney Week 2022 Scientific Meeting in Orlando, Florida, from November 3-6. TERLIVAZ is the first and only FDA-approved product indicated to improve kidney function in adults with hepatorenal syndrome (HRS) involving 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.

The findings from a pooled analysis across the OT-0401, REVERSE, and CONFIRM clinical trials, presented by Dr. Juan Carlos Q. Velez, MD, Ochsner Health Network LLC, New Orleans, Louisiana, suggest that initiating treatment with terlipressin plus albumin in patients with HRS Type 1 (HRS-1) at lower serum creatinine (SCr) levels and Model for End-stage Liver Disease (MELD) scores is associated with greater probability of avoiding renal replacement therapy (RRT) through 90 days of treatment.[3] Additional information on Dr. Velez' study and the full list of Mallinckrodt's presentations can be found below.

"We are eager to share data from our latest studies assessing treatment paradigms in the management of HRS and examining the clinical benefits of patients treated with terlipressin among the broader healthcare professional community. These findings provide critical insight into the importance of patient characteristics at baseline and reducing the time to therapeutic intervention in potentially improving long-term outcomes and the avoidance of renal replacement therapy, such as dialysis, in adults with HRS," said **Khurram Jamil, Vice President, Hepatology, Clinical Development & Critical Care.** "Following the recent FDA approval of TERLIVAZ, we are encouraged by the growing body of evidence that continues to support Mallinckrodt's commitment to improving the care for critically ill patients with unmet needs."

These studies are sponsored by Mallinckrodt Pharmaceuticals and include:

Abstract TH-PO034: Initiation of Terlipressin at Lower Serum Creatinine Levels Is Associated With Avoidance of Dialysis in Patients With Hepatorenal Syndrome Type 1[3]

- **Presenter:** Juan Carlos Q. Velez, MD
- **Presentation Date:** November 3, 2022; 10AM – 12PM ET
- **Location:** Exhibit Hall, Orange County Convention Center, West Building

Abstract TH-PO035: Impact of Terlipressin on Serum Sodium Levels in Patients with HRS – the North American Experience[4]

- **Presenter:** Shehzad Nawaz Merwat, MD
- **Presentation Date:** November 3, 2022; 10AM – 12PM ET
- **Location:** Exhibit Hall, Orange County Convention Center, West Building

Abstract TH-PO037: Impact of HRS Reversal on the Need for Renal Replacement Therapy – Analysis from 3 Phase III Terlipressin Studies[5]

- **Presenter:** Muhammad Ahmad Mujtaba, MD
- **Presentation Date:** November 3, 2022; 10AM – 12PM ET
- **Location:** Exhibit Hall, Orange County Convention Center, West Building

Find more information on the American Society of Nephrology (ASN) Kidney Week 2022 website.

Terlipressin is one of the most studied pharmacological agents in HRS with more than 70 published manuscripts and presented abstracts on clinical data to date.[6] It has been approved outside the U.S. for more than 30 years and is available on five continents for its indications in the countries where it is approved.[7,8]

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.[9,10] 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.[11]

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 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 includes forward-looking statements with regard to TERLIVAZ, including 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 October 13, 2022.

[3] JC Q. Velez. Initiation of Terlipressin at Lower Serum Creatinine Levels Is Associated With Avoidance of Dialysis in Patients With Hepatorenal Syndrome Type 1. *To be Presented at the American Society of Nephrology Kidney Week 2022 (ASN) Scientific Meeting.* November 2022.

[4] SN Merwat. Impact of Terlipressin on Serum Sodium Levels in Patients with HRS – the North American Experience. *To be Presented at the American Society of Nephrology Kidney Week 2022 (ASN) Scientific Meeting.* November 2022.

[5] MA Mujtaba. Impact of HRS Reversal on the Need for Renal Replacement Therapy – Analysis from 3 Phase III Terlipressin Studies. *To be Presented at the American Society of Nephrology Kidney Week 2022 (ASN) Scientific Meeting.* November 2022.

[6] Data on File – Ref-05488. Mallinckrodt Pharmaceuticals.

[7] Data on File – Ref-05482. Mallinckrodt Pharmaceuticals.

[8] FDA Cardiovascular and Renal Drugs Advisory Committee. Mallinckrodt Pharmaceuticals Terlipressin Advisory Committee Briefing Document NDA #022231. July 2020.

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

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