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 24, 2022

– Five scientific abstracts spanning clinical and health economic outcomes research will be presented at the ACG Scientific Meeting, showcasing the breadth of Mallinckrodt's commitment to HRS patients with rapid reduction in kidney function[1] –

DUBLIN, Oct. 24, 2022 /PRNewswire/ -- Mallinckrodt plc (OTCMKTS: MNKPF), a global specialty pharmaceutical company, today announced that five scientific abstracts on the clinical and health economic outcomes of treatment with TERLIVAZ® (terlipressin) for adult patients with hepatorenal syndrome (HRS) involving rapid reduction in kidney function,[1] will be presented at the American College of Gastroenterology (ACG) Annual Scientific Meeting in Charlotte, North Carolina from October 21-26. 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.

The findings from one of the abstracts, presented by Dr. R. Todd Frederick, Department of Transplant, California Pacific Medical Center, CA, provide insight into the effect of terlipressin on renal and circulatory dysfunction in patients with HRS, relative to placebo.[3] Additional information on Dr. Frederick's study and the full list of Mallinckrodt's presentations can be found below.

"We look forward to sharing a range of new data, among those an ACG Award-Winning abstract that has received Presidential Poster recognition, highlighting the importance of additional treatment options for patients with HRS, like terlipressin. These findings not only have important implications for morbidity and mortality, but also help to shine a light on the persistent clinical and economic burden HRS patients in the U.S. face, and their need for additional options," said **Khurram Jamil, Vice President, Hepatology, Clinical Development & Critical Care.** "With the recent FDA approval of TERLIVAZ, we are hopeful that we are one step closer to improving outcomes for these critically ill patients."

These studies are sponsored by Mallinckrodt Pharmaceuticals and include:

Abstract D0501: Clinical and Economic Burden of Patients With HRS-AKI Treated With Current Standard of Care: Retrospective Analysis of Real World Data[4]

- **Presenter:** Xingyue Huang, PhD
- **Presentation Dates:**
  - October 23, 2022; 5 – 7PM ET
  - October 24, 2022; 10AM – 12PM ET & 3 – 5PM ET
  - October 25, 2022; 10AM – 12PM ET & 3 – 5PM ET
- **Location:** Crown Ballroom
- **Presidential Poster Recognition & ACG Award-Winning Abstract**

Oral Abstract 22: Terlipressin Treatment of Patients With Hepatorenal Syndrome Type 1 Decreased the Need for Renal Replacement Therapy in Transplant Recipients: A 12-Month Follow-Up of the CONFIRM Study[5]

- **Presenter:** K. Rajender Reddy, MD, FACG
- **Presentation Date:** October 25, 2022; 9AM – 9:10AM ET
- **Location:** Hall C2

Abstract D0499: Treatment Response to Terlipressin Plus Albumin Varies by Precipitating Factor in Patients with Hepatorenal Syndrome Type 1[3]

- **Presenter:** R. Todd Frederick, MD

- **Presentation Date:** October 25, 2022; 10AM – 12PM ET
- **Location:** Crown Ballroom

Abstract D0474: Impact of Terlipressin on Serum Sodium Levels in Patients With Hepatorenal Syndrome Type 1 (HRS-1): CONFIRM Study[6]

- **Presenter:** Nikolaos Pyrsopoulos, MD, MBA, PhD, FACG
- **Presentation Date:** October 25, 2022; 10AM – 12PM ET
- **Location:** Crown Ballroom

Abstract D0505: Increasing Burden of Hepatorenal Syndrome and Acute Kidney Injury Among Hospitalized Patients With Chronic Liver Disease is Associated With High In-Hospital Mortality and Increased Healthcare Resource Utilization[7]

- **Presenter:** Robert Wong, MD, MD, FACG
- **Presentation Date:** October 25, 2022; 10AM – 12PM ET
- **Location:** Crown Ballroom

Find more information on the American College of Gastroenterology (ACG) Annual Scientific Meeting 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.[8] 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.[9,10]

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 is estimated to affect between 30,000 and 40,000 Americans annually.[11,12] If left untreated, HRS with rapid reduction in kidney function has a median survival time of approximately two weeks and greater than 80 percent mortality within three months.[13]

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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[6] N Pyrsopoulos. Impact of Terlipressin on Serum Sodium Levels in Patients with Hepatorenal Syndrome Type 1 (HRS-1): CONFIRM Study. *Presented at American College of Gastroenterology (ACG) Scientific Meeting.* October 2022.
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[8] Data on File – Ref-05488. Mallinckrodt Pharmaceuticals.
[9] Data on File – Ref-05482. Mallinckrodt Pharmaceuticals.
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