Mallinckrodt Presents Clinical Data for TERLIVAZ® (terlipressin) for Injection in Adults with Hepatorenal Syndrome (HRS) at the American Transplant Congress (ATC) 2023

June 1, 2023

– Findings from two clinical studies in adults with HRS involving rapid reduction in kidney function[1] provide insight into the use of terlipressin among patients with comorbidities and varying baseline characteristics[2,3] –

DUBLIN, June 1, 2023 /PRNewswire/ -- Mallinckrodt plc (NYSE American: MNK), a global specialty pharmaceutical company, today announced the presentation of results from two clinical studies in adults with hepatorenal syndrome (HRS) with rapid reduction in kidney function[1] treated with TERLIVAZ® (terlipressin) for injection at the American Transplant Congress (ATC) 2023, taking place in San Diego, Calif. from June 3-7, 2023. The results of the two studies – a pooled analysis of two Phase III terlipressin trials (REVERSE, CONFIRM) and a retrospective analysis of the Phase III CONFIRM trial – will be presented in oral lecture sessions on June 5, 2023, at 4:30 p.m. and 4:40 p.m. PT, respectively.[2,3]

TERLIVAZ (terlipressin) for injection is a synthetic vasopressin analogue indicated to improve kidney function in adults with HRS with rapid reduction in kidney function.[1] Patients with a serum creatinine >5 mg/dL are unlikely to experience benefit.[1]

Please see Important Safety Information, including Boxed Warning, below.

TERLIVAZ is the first and only FDA-approved product indicated for the treatment of adults with HRS involving rapid reduction in kidney function,[1] an acute and life-threatening condition requiring hospitalization.[4] Terlipressin is recommended by the American Association for the Study of Liver Diseases (AASLD) guidance[5] and the American College of Gastroenterology (ACG) guidelines.[6]

The findings from the pooled analysis of the Phase III REVERSE and CONFIRM studies, presented by Adnan Said, University of Wisconsin Hospital and Clinics, Madison, Wis., provide insight into clinical outcomes following terlipressin therapy compared with placebo in patients with HRS type 1 (HRS-1) and systemic inflammatory response syndrome (SIRS).[2] Furthermore, the results of the retrospective analysis of the Phase III CONFIRM trial, presented by Fredric Gordon, Tufts Medical Center, Boston, Mass., offer perspective into terlipressin's therapeutic potential to reduce renal replacement therapy (RRT) requirements post-liver transplant in HRS-1 patients with acute-on-chronic liver failure (ACLF) grade 0-2 and serum creatinine (SCr) levels <5 mg/dL.[3]

Renal failure requiring hemodialysis post-liver transplant is a major risk factor for death in liver transplant recipients.[7] Patients who require post-transplant dialysis also have significantly worse graft survival compared with those without post-transplant dialysis.[8]

"We are excited to share findings from our latest clinical research that not only support the use of terlipressin to improve kidney function for appropriate patients with HRS involving rapid reduction in kidney function,[1,3] but also aim to generate increased awareness and understanding among healthcare professionals of the treatment considerations and goals for HRS patients with burdensome comorbidities, like systemic inflammatory response syndrome,[2]" said **Khurram Jamil, Vice President & Head, Hepatology, Clinical Development & Critical Care at Mallinckrodt.** "This research reflects Mallinckrodt's ongoing commitment to serve the needs of both critically ill patients and the physicians responsible for their care by expanding our collective understanding of the progression and clinical management of HRS."

Liver transplantation is the only definitive treatment for patients with HRS with rapid reduction in kidney function,[1] yet the majority of HRS patients still face access challenges.[9] In light of these ongoing challenges, improving transplant outcomes – and conducting research that provides insight into the clinical management of these critically ill patients – is essential to addressing the scarcity of available liver transplants and other prominent unmet needs.[7]

These studies were sponsored by Mallinckrodt Pharmaceuticals:

Presenting Monday, June 5, 2023; 4:30 p.m. PT

- **Oral Presentation 321: Terlipressin Improves Clinical Outcomes in Patients with Hepatorenal Syndrome Type 1 and Systemic Inflammatory Response Syndrome: A Pooled Analysis of the Phase III REVERSE and CONFIRM Studies**[2]
  - **Presenter:** Adnan Said, University of Wisconsin Hospital and Clinics, Madison, Wis.

Presenting Monday, June 5, 2023; 4:40 p.m. PT

- **Oral Presentation 322: Liver transplant rates and clinical outcomes in patients with hepatorenal syndrome type 1 and ACLF grade 0−2 and serum creatinine (SCr) <5 mg/dL at baseline**[3]
  - **Presenter:** Fredric Gordon, Tufts Medical Center, Boston, Mass.

Find more information on the American Transplant Congress 2023 Meeting website.

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.[4] 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.[4] HRS involving rapid reduction in kidney function[1] is estimated to affect between 30,000 and 40,000 Americans annually.[10,11] 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.[12]

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 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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