Mallinckrodt Presents Interim Results on Real World Use of Extracorporeal Photopheresis (ECP) in Heart Transplant Patients in a Late-Breaking Presentation at the 20th Congress of the European Society for Organ Transplantation (ESOT)

September 2, 2021

- Analysis from the largest known, ongoing, retrospective, explorative, single-arm, pan-European multicenter study of ECP in heart transplant patients suggests potential for ECP in the treatment of acute cellular rejection, antibody mediated rejection and prevention of rejection –
- Company awards educational grant to advance knowledge of ECP immunomodulation in solid organ transplantation during the Science Slam Symposium at the ESOT Congress 2021 –

DUBLIN – September 2, 2021 – Mallinckrodt plc (OTCMKTS: MNKKQ), a global biopharmaceutical company, announced today interim results[i] from a retrospective, explorative, single-arm, pan-European multicenter study to evaluate the real world use of extracorporeal photopheresis (ECP) and therapy-related outcomes in heart transplant patients. The first results from the largest known study of ECP in heart transplantation patients were reported during a late-breaking oral presentation at the 20th Congress of the European Society for Organ Transplantation (ESOT) in Milan, Italy.

The interim analysis examined data from medical charts of 71 patients who received ECP treatment following heart transplantation at four medical centers in Germany, France and Hungary between 2015 and 2021. Of the 71 patient charts examined, 51 patients (72 percent) were no longer receiving ECP treatment and treatment was ongoing for 20 patients (28 percent). Mean follow up time was two years from the start of ECP treatment to last visit. Median time from heart transplant to start of ECP was eight months, and on average, 26 individual ECP treatments were performed over a mean duration of nine months. The three main reasons to start ECP treatment were: acute cellular rejection (ACR) in 31 patients (44 percent), antibody mediated rejection (AMR) in 15 patients (21 percent) and prevention of rejection (PR) in 16 patients (23 percent).

Forty-eight of the 51 patients had graft function measurements at the start and end of ECP treatment and of these, 29 patients (60 percent) showed improved graft function at the end of ECP treatment. Improvement in graft function was defined as at least 15 percent-point increase in ejection fraction and/or improvement in at least one grade of ACR, AMR, Chronic Allograft Vasculopathy (CAV), or stable CAV, or at least one New York Heart Association (NYHA) class lower, without any worsening in any of the other parameters. The remaining 19 patients (40 percent) showed stable graft function at the end of ECP treatment.

Study limitations include that, as an explorative single-arm study, comparative effectiveness cannot be assessed. The study relied on real world medical charts which could be missing data or may have used site-specific measurement schedules and procedures. There was no source data verification and low patient numbers limited analysis by reason to start ECP treatment. Due to the retrospective nature of this analysis, it is hypothesis-generating; no formal conclusions should be drawn. In addition, the assessments of ECP treatment were completed at different time points. The ECP treatment platform varied based on the treatment center. Dosing and frequency of treatment varied, with no minimum amount of treatment required. Not all benefits from this analysis may be solely attributable to ECP treatment as patients may have been on multiple therapies at the time of ECP treatment.

In a sub-analysis of patients grouped by the three main reasons to start ECP treatment, rejection improvement from the start to end of ECP treatment was demonstrated in 17 of 21 ACR patients (81 percent) and five of seven AMR patients (71 percent). In the PR group, 12 patients (75 percent) remained free from any biopsy-proven rejection after starting ECP over a mean follow-up of 2.8 years. Four patients (25 percent) developed ACR.

Among the 71 patients reviewed, eight (11 percent) had at least one ECP-related safety event. In total, six patients (8 percent) had complications with venous access, two (3 percent) had hypotension events and two (3 percent) had unspecified events. The interim analysis showed overall survival was 93 percent among all 71 patients. Five patients died, three with a functioning graft. No deaths were deemed related to ECP treatment.

The findings from the interim analysis are limited to trends relative to the study's endpoints of efficacy and are not necessarily indicative of the final results to be announced from the completed analysis.

The study was funded by Mallinckrodt.

"These results suggest that ECP has the potential to be an effective treatment for acute cellular rejection, as well as an option for antibody mediated rejection with and without donor specific antibodies, and in rejection prevention in heart transplantation," said presenting author, **Markus Barten, M.D., Surgical Director of Heart Failure Clinic, University Heart Center Hamburg.** "We are encouraged by the results of this multicenter study and believe that additional data around the efficacy and safety of ECP as a potential treatment option may be warranted to help advance the scientific understanding of ECP in heart transplant patients."

Mallinckrodt also awarded a €50,000 educational grant to ESOT supporting its commitment to advancing education and research in transplantation. The 2021 winner, determined by an ESOT jury, was awarded during the Science Slam Symposium at the ESOT Congress 2021 on Tuesday, August

31st. The educational grant award was established to recognize and support researchers who are working to advance the knowledge of ECP immunomodulation in solid organ transplantation within the Europe, Middle East and Africa region.

“As a pioneer in ECP immunomodulation, Mallinckrodt is committed to furthering understanding of the use of ECP in heart transplant patients and its potential to improve clinical outcomes in this patient population,” said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**. “Organ rejection after heart transplantation due to ACR or AMR is a therapeutic challenge for clinicians and patients, and modalities that can improve graft function and prevent rejection are greatly needed.”

About Extracorporeal Photopheresis (ECP)

ECP, a blood based immunomodulatory therapy developed more than 30 years ago, is recommended by the International Society for Heart and Lung Transplantation (ISHLT)[ii] and other clinical societies[iii],[iv],[v] as an adjunctive therapy for the prevention and treatment of ACR after heart transplantation. Additionally, ECP may be considered to treat AMR with or without donor specific antibodies.[vi],[vii] In countries where it is approved, ECP is used to treat a range of immune-mediated diseases, including skin manifestations of cutaneous T-cell lymphoma (CTCL), graft-versus-host disease (GvHD), organ transplant rejection and other autoimmune diseases. During ECP treatment, a small amount of white blood cells is collected and treated with a drug that is activated by ultraviolet light.

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, nephrology, pulmonology and ophthalmology; immunotherapy and neonatal respiratory critical care therapies; analgesics 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 related to an ongoing, retrospective study in ECP. 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: final results of the underlying study; satisfaction of regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; 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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[i] Real World Use and Clinical Impact of Extracorporeal Photopheresis in Heart Transplant Patients – Results From a European Multi-Centre Study. Presented at: European Society for Organ Transplantation (ESOT) Congress 2021; Aug. 29-Sept. 1; Milan, Italy.

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[iv] Padmanabhan et al. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice - Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eighth Special Issue. *J Clin Apher*. 2019;34:171–354.

[v] Knobler et al. European dermatology forum - updated guidelines on the use of extracorporeal photopheresis 2020 - part 2. *Eur Acad Dermatol Venereol*. 2021;35(1):27-49.

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