Mallinckrodt and Terumo Blood and Cell Technologies Announce Positive Recommendations in Australia for Public Funding of UVADEX® (methoxsalen) for ECP Administration with the THERAKOS® CELLEX® Photopheresis System for Chronic Graft Versus Host Disease (cGvHD) in Adults

– In a dual-review process, two independent advisory committees to the Australian Minister for Health recommended reimbursement based on a favorable clinical and cost-effectiveness comparison –

DUBLIN, Ireland and LAKEWOOD, Colo. USA – October 28, 2021 – Mallinckrodt plc (OTCMKTS: MNKKQ), a global biopharmaceutical company, and Terumo Blood and Cell Technologies, a global leader in blood component, therapeutic apheresis and cellular technologies, and the exclusive distributor of the Therakos extracorporeal photopheresis (ECP) platform in Australia, announced today that both the Medical Services Advisory Committee (MSAC) and the Pharmaceutical Benefits Advisory Committee (PBAC) recently recommended that UVADEX® (methoxsalen) for extracorporeal administration with the THERAKOS® CELLEX® Photopheresis System be listed on the Pharmaceutical Benefits Scheme (PBS) in Australia for the treatment of steroid dependent, intolerant or resistant chronic graft versus host disease (cGvHD) in adults.

In this two-part evaluation, the PBAC supported the cost-effectiveness of UVADEX, the pharmaceutical component of the treatment system; and the MSAC accepted the claim of superiority for safety and non-inferiority for efficacy between ECP with UVADEX and comparators. The role of both committees is to advise the Australian Minister for Health to help inform Australian Government decisions about public funding.[1] The full assessment report related to the MSAC recommendation can be found in the published public summary document. The PBAC recommendation, found here, states:

The PBAC recommended the Section 100 (Highly Specialised Drugs Program – Public and Private Hospital) Authority Required (STREAMLINED) listing for methoxsalen, delivered as part of an integrated, closed system ECP service for the treatment of patients with steroid dependent, steroid intolerant or steroid refractory cGVHD. The PBAC was satisfied that ECP involving methoxsalen provides, for some patients, a significant improvement in efficacy over current standard of care. The PBAC noted that MSAC accepted that ECP had likely superior clinical effectiveness and non-inferior safety compared with current standard of care. Further, the PBAC noted that MSAC advised that ECP plus methoxsalen has acceptable cost-effectiveness in the treatment of cGVHD compared with current standard of care for the proposed patient population.

UVADEX is indicated for extracorporeal administration with the THERAKOS CELLEX Photopheresis System for the treatment of steroid-refractory and steroid-intolerant cGVHD in adults following allogeneic hematopoietic stem cell transplantation; and for palliative treatment of the skin manifestations of cutaneous T-cell lymphoma that is unresponsive to other forms of treatment.

“Treatment for patients with cGvHD who do not respond to steroids has long been a challenge, and as a pharmaceutical company focused on improving outcomes for underserved patients with severe and critical conditions, we strive to provide treatment options that address unmet medical needs,” said **Maro Williams, Ph.D., Country Medical Director, International Medical**

Affairs at Mallinckrodt. “The positive reimbursement recommendation is an important step to help ensure that UVADEX with the THERAKOS ECP system is broadly available to patients who may benefit from this treatment.”

In July 2020, UVADEX also received recommendations from both the MSAC and the PBAC to be listed on the PBS in Australia for the treatment of cutaneous T-cell lymphoma in adults.

“The PBAC assessment supports THERAKOS ECP with UVADEX as a cost-effective option for the treatment of patients with cGvHD in Australia, compared to other standard-of-care therapies,” said **Xavier Dubois, General Manager Australia and New Zealand, Terumo Blood and Cell Technologies**. “This important milestone underscores the value of this treatment option for patients who are unresponsive to other forms of treatment.”

About Chronic Graft Versus Host Disease (cGvHD)
Graft versus host-disease is a common complication of hematopoietic stem cell transplantation resulting in significant morbidity and mortality.[2] It can be classified as acute or chronic based on the clinical presentation and the time of occurrence after the transplantation. Signs and symptoms of cGvHD nearly always occur within the first year post transplantation, but can occasionally happen several years later.[3] In cGvHD, the skin is the most frequently affected organ with manifestations of itchy rash, hyper or hypopigmentation and changes in texture. However, the disease can affect multiple sites, which may have a major impact upon a patient's quality of life.[3,4] Chronic GvHD can lead to debilitating consequences, such as joint contractures, loss of sight, end-stage lung disease, or mortality resulting from profound chronic immune suppression leading to recurrent or life-threatening infections.[2]

Minimum Product Information: UVADEX® (methoxsalen) Concentrated Injection for extracorporeal circulation via photopheresis (ECP)

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

Indications in Australia: UVADEX (methoxsalen) is indicated for extracorporeal administration with the THERAKOS CELLEX Photopheresis System for the:

- treatment of steroid-refractory and steroid-intolerant chronic graft versus host disease (cGVHD) in adults following allogeneic HSC transplantation.
- palliative treatment of the skin manifestations of cutaneous T-cell lymphoma (CTCL) that is unresponsive to other forms of treatment.

Contraindications: History of idiosyncratic or hypersensitivity reaction to methoxsalen, psoralen compounds or any excipients of UVADEX; co-existing melanoma, basal cell or squamous cell skin carcinoma; lactation; aphakia. ECP procedure contra-indications: Photosensitive disease; inability to tolerate extracorporeal volume loss; WBC count > 25,000 mm^3; previous splenectomy; coagulation disorders. **Special warnings and precautions:** Only physicians who have special competence in the diagnosis and treatment of cGVHD and CTCL who have special training and experience with the THERAKOS CELLEX Photopheresis System should use UVADEX. Psoralen and ultraviolet radiation therapy should be under constant supervision of such a physician. Because of the possibilities of ocular damage, the patient should be fully informed by the physician of the risks inherent in this therapy. UVADEX

should only be used *ex vivo* and administered directly into the photoactivation bag. Visually inspect for haemolysis. In the event of unscheduled damage to the blood during the photopheresis procedure (e.g. >43ºC alarm sounding), the fractionated blood should only be reinfused into the patient if haemolysis has not occurred. Both Men and women being treated with UVADEX should take adequate contraceptive precautions both during and after completion of photopheresis treatment. Exposure to large doses of UVA causes cataracts in animals, an effect enhanced by the administration of oral methoxsalen. As the concentration of methoxsalen in the human lens is proportional to the serum level, the concentration will be substantially lower following ex vivo methoxsalen treatment (with UVADEX) compared to that seen following oral administration. Nonetheless, if the lens is exposed to UVA during the time methoxsalen is present in the lens, photochemical action may lead to an irreversible binding of methoxsalen to protein and DNA components of the lens. For this reason the patient's eyes should be protected from UVA light by wearing wrap-around, UVA-opaque sunglasses during the treatment cycle and during the following 24 hours. Following oral administration of psoralen, where serum concentrations may exceed 200 ng/mL, exposure to sunlight or ultraviolet radiation (even through window glass) may result in serious burns and, in the long-term, "premature aging" of the skin. Oral psoralens may increase the risk of skin cancer. Extracorporeal use of UVADEX is associated with much lower systemic exposure than from oral methoxsalen. The phototoxicity of UVADEX has not been characterised; as a precaution, patients should avoid exposure to sunlight during the 24 hours following photopheresis treatment. Thromboembolic events, such as pulmonary embolism and deep vein thrombosis, have been reported with UVADEX administration through photopheresis systems for treatment of patients with graft versus host disease. This product contains 4.1% w/v ethanol and each 1 mL of UVADEX contains 40.55 mg of ethanol. Caution is advised in patients with liver disease, alcoholism, epilepsy, brain injury or disease. No specific information is available for use in renal or hepatic impairment and there is no evidence for dose adjustment in the elderly. Since hepatic biotransformation is necessary for urinary excretion, this may lead to prolonged photosensitivity requiring continued precautions against exposure to sunlight beyond 24 hours following photopheresis treatment. The potential benefits of photopheresis treatment should be weighed against any possible risk before embarking on the procedure. The safety and efficacy of UVADEX have not been established in children. **Use in pregnancy**: Category D. **Use in Lactation**: UVADEX is contra-indicated. **Interactions with other medicines:** Effects on P450 system metabolism may affect clearance / activation of other drugs (caffeine, paracetamol) or may extend the methoxsalen half-life leading to prolonged photosensitivity in patients. Methoxsalen binding to albumin may be displaced by dicoumarol, warfarin, promethazine and tolbutamide with potential for enhanced photosensitivity. Caution when treating with concomitant photosensitising agents. **Adverse effects:** In the clinical trials, published information and postmarketing surveillance of UVADEX/ECP, adverse events were usually mild and transient and in most cases, related to the underlying pathology*. Very common*: diarrhoea, anaemia, nausea, headache, hypertension, sinusitis, upper respiratory tract infection, fatigue, pain in extremity, pyrexia, cough, dyspnoea, cushingoid, dry eye, photophobia, toothache, anorexia. *Common*: depression, lacrimation increased, abdominal pain, hypokalaemia, paraesthesia oral, pharyngolaryngeal pain, tachycardia, conjunctivitis, eye pain, visual acuity reduced, dysphagia, chills, mucosal inflammation, nasopharyngitis, contusion, blood pressure diastolic decreased, haemoglobin decreased, hyperglycaemia, hypocalcaemia, neuropathy peripheral, tremor, rash, hypotension. Additional adverse effects seen in clinical trials include vomiting, infections. Adverse events related to the ECP/CELLEX procedure – thromboembolism and severe allergic reactions, vascular access complication, vasovagal spasm, hickman catheter infection/thrombosis, headache, hypercoagulability, haemolysis. Additional adverse events identified post-marketing:

anaphylactic reaction, allergic reaction, dysgeusia, exacerbation of congestive heart failure, sepsis, endocarditis, vomiting and photosensitivity reactions. **Dosage and Administration**: Chronic Graft versus Host Disease: Three ECP treatments in the first week then two ECP treatments per week for at least 12 weeks, or as clinically indicated. Cutaneous T-cell Lymphoma: ECP treatment on two successive days each month for six months. Patients who show an increase in skin scores after eight treatment sessions may have their treatment schedule increased to two successive days every two weeks for the next three months. Refer to full Product Information and THERAKOS CELLEX Operator's Manual for information regarding administration.

Store below 25°C. Date of first approval: 16 September 2019. Date of revision: 19 November 2020.

Indications and Prescribing Information for UVADEX vary globally. Please refer to the individual country product label for complete information.

Before prescribing UVADEX, please refer to the full Product Information also available by calling +61 2 9429 3606.

ABOUT THERAKOS
Mallinckrodt is the world's only provider of approved, fully integrated systems for administering immunomodulatory therapy through ECP. Its Therakos ECP platforms, including the latest generation THERAKOS® CELLEX® Photopheresis System, are used by academic medical centres, hospitals, and treatment centres in nearly 40 countries and have delivered more than 1 million treatments globally. For more information, please visit www.therakos.eu.

Terumo Blood and Cell Technologies is the exclusive distributor of the Therakos ECP platform in Australia, as well as Latin America and select countries in Europe. To learn more about Terumo Blood and Cell Technologies, visit www.terumobct.com.

UVADEX (methoxsalen) and THERAKOS CELLEX Photopheresis Systems are separately approved in a number of global markets. Please refer to your local approved labelling for UVADEX and the Operator's Manual for CELLEX for more information on approved uses for specific indications.

Before administering therapy using the THERAKOS CELLEX Photopheresis System, please refer to the Operator's Manual available at +61 2 9429 3606.

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.

About Terumo Blood and Cell Technologies
Terumo Blood and Cell Technologies is a medical technology company. Our products, software and services enable customers to collect and prepare blood and cells to help treat challenging diseases and conditions. Our employees around the world believe in the potential of blood and cells to do even more for patients than they do today.

Terumo Blood and Cell Technologies' customers include blood centers, hospitals, therapeutic apheresis clinics, cell collection and processing organizations, researchers and private medical practices. Our customers are based in over 130 countries across the globe. We have 750+ granted patents, with an additional 150 pending.

We have global headquarters in Lakewood, Colo., U.S.A., along with five regional headquarters, six manufacturing sites and six innovation and development centers across the globe. Terumo Blood and Cell Technologies is a subsidiary of Terumo Corporation (TSE: 4543), a global leader in medical technology. TERUMOBCT.COM

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS
This release includes forward-looking statements concerning the use of UVADEX with the THERAKOS CELLEX Photopheresis System including potential benefits associated with its use. 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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