C-Path's Transplant Therapeutics Consortium Receives EMA Qualification Opinion for iBox Scoring System

The iBox Scoring System is available for use in kidney transplant clinical trials as a novel secondary endpoint prognostic for allograft loss.

TUCSON, Ariz., Dec. 20, 2022 — Critical Path Institute (C-Path) announced today that its Transplant Therapeutics Consortium (TTC) received a qualification opinion for the iBox Scoring System as a secondary efficacy endpoint in clinical trials investigating novel immunosuppressive medicines in kidney transplant patients. This regulatory milestone was achieved through the European Medicines Agency's (EMA) qualification of novel methodologies for drug development and is the first qualified endpoint for any transplant indication. With this successful qualification, the transplant community is one step closer to having new therapies that better the lives of transplant recipients.

As stated in the qualification opinion, "The CHMP encourages the use of the iBox scoring system as a secondary endpoint in future trials of kidney transplantation and further development of the scoring system targeting a potential future qualification as a surrogate endpoint."

Long-term graft survival is an important unmet need for kidney transplantation recipients, and new ISTs are needed to improve kidney transplant outcomes. The iBox Scoring System can now be used to evaluate the efficacy of novel treatments intended to improve long-term allograft survival. Specifically, the iBox Scoring System can now be used to demonstrate the superiority of a novel therapy to the standard of care from six to 24 months post-transplant in pivotal or exploratory drug therapeutic studies.

"Improving long-term renal allograft survival remains a major unmet need and developing new immunosuppression treatments requires new approaches to clinical trials," said Mark Stegall, M.D., Clinician Investigator, Department of Surgery, Mayo Clinic Rochester. "Improving graft survival likely would have a positive impact not only on the individual patient (reduced mortality due to graft failure and reduced need for a second transplant) but also increase the number of kidneys available for other transplant candidates."

To assist sponsors in designing clinical trials using the iBox Scoring System as an endpoint, TTC developed a sample size calculator using iBOX scores. With this tool, sponsors can apply various inclusion/exclusion criteria and other specifications to better understand how group differences in iBOX parameters translate to a difference in iBOX scores. "This sample size calculator is publicly available HERE to benefit the kidney transplant community and improve future clinical trial efficiency," said C-Path's TTC Executive Director, Amanda Klein, Pharm.D.

In 2017, C-Path started TTC in partnership with the American Society of Transplantation (AST) and the American Society of Transplant Surgeons (ASTS) aimed at accelerating the medical product development process for transplantation. "This EMA qualification opinion is a result of many years of extensive work and extraordinary collaboration and would not have been possible without the international transplant community's ongoing collaboration, data sharing, expertise and dedication," said Shandie Covington, AST Executive Director. "We are grateful to our many collaborators for their continued support. We look forward to the impact this qualified endpoint will make in developing novel therapies focused on long-term graft survival in kidney transplantation," said Maggie Kebler-Bullock, ASTS Executive Director.

This regulatory qualification achievement was accomplished by employing the resources of the TTC members and engaging with EMA throughout the qualification process. TTC is supported through funding and input from the American Society of Transplantation, American Society of Transplant Surgeons, argenx, Bristol Myers Squibb, CareDx, CSL Behring, Eledon Pharmaceuticals, the European Society for Organ Transplantation, the U.S. Food and Drug Administration (FDA), Hansa Biopharma, Immucor, National Institutes of Health, Novartis, Sanofi, Takeda, Talaris Therapeutics, Thermo Fisher Scientific, The Transplantation Society, Transplant Genomics and Veloxis Pharmaceuticals.

TTC is also working on its next regulatory milestone: the regulatory endorsement of the iBox Scoring System as a reasonably likely surrogate endpoint by the FDA, to whom the Qualification Plan has been submitted and is under review.

As part of the 21st Century Cures Act, passed into law in December 2016, public-private partnerships consisting of government entities, including FDA, the biopharmaceutical industry, health care providers, academic researchers and patient advocacy organizations, have been encouraged to work together to foster innovation in the development of new therapies by qualifying new drug development tools that can accelerate the process of making new therapies available to patients. Any groups that would like to join in this effort, or have information or data that may contribute to further advances, can contact Amanda Klein (aklein@c-path.org).

The qualification opinion can be found on the EMA website, or on the TTC website here.

TTC
TRANSPLANT THERAPEUTICS CONSORTIUM

Transplant Therapeutics Consortium (TTC) was launched in April 2017 and co-founded by the American Society of Transplantation (AST) and the American Society of Transplant Surgeons (ASTS). TTC brings together pharmaceutical companies, diagnostic companies, academic and nonprofit partners working toward a common goal of moving the field forward toward drug development solutions in transplantation. TTC is managed and supported by the Critical Path Institute (C-Path).
For more information, visit c-path.org/ttc.

CRITICAL PATH INSTITUTE

Critical Path Institute (C-Path) is an independent, nonprofit organization established in 2005 as a public and private partnership. C-Path's mission is to catalyze the development of new approaches that advance medical innovation and regulatory science, accelerating the path to a healthier world. An international leader in forming collaborations, C-Path has established numerous global consortia that currently include more than 1,600 scientists from government and regulatory agencies, academia, patient organizations, disease foundations, and hundreds of pharmaceutical and biotech companies. C-Path U.S. is headquartered in Tucson, Arizona, C-Path in Europe is headquartered in Amsterdam, Netherlands and C-Path Ltd. Operates from Dublin, Ireland with additional staff in multiple other locations. For more information, visit c-path.org.

Critical Path Institute is supported by the Food and Drug Administration (FDA) of the Department of Health and Human Services (HHS) and is 55% funded by the FDA/HHS, totaling $17,612,250, and 45% funded by non-government source(s), totaling $14,203,111. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, FDA/HHS or the U.S. Government.

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argenx is a global immunology company committed to improving the lives of people suffering from severe autoimmune diseases. Partnering with leading academic researchers through its Immunology Innovation Program (IIP), argenx aims to translate immunology breakthroughs into a world-class portfolio of novel antibody-based medicines. Argenx developed and is commercializing the first-and-only approved neonatal Fc receptor (FcRn) blocker in the U.S., Japan and the E.U. The Company is evaluating efgartigimod in multiple serious autoimmune diseases and advancing several earlier stage experimental medicines within its therapeutic franchises. For more information, visit www.argenx.com and follow us on LinkedIn, Twitter, and Instagram.

Founded in 1982, the **American Society of Transplantation (AST)** is a non-profit, 501(c)3 organization dedicated to advancing the field of transplantation and improving patient care by promoting research, education, advocacy, organ donation, and service to the community through a lens of equity and inclusion. The society is the largest transplant organization in North America (consisting of more than 4,200 professional members), representing a majority of the nation's medical professionals engaged in the field of transplantation. AST members are sought out as transplant experts and advocates. Other transplant organizations, policy makers, regulatory agencies, payors, academic institutions, and the general public look to the AST for guidance, research, and resources related to transplantation.

To learn more, visit: www.myast.org.

Follow us: Twitter @AST_info and Facebook.

The **American Society of Transplant Surgeons (ASTS)** was founded in 1974; today it is comprised of over 2000 solid organ transplant surgeons, physicians, scientists, pharmacists, advanced transplant providers and allied health professionals dedicated to advancing surgical care in transplantation. The ASTS is the leadership organization of the surgeons, physicians and scientists who have pioneered and continue to advance the frontiers of life-sustaining organ transplantation. The ASTS has taken the field from experimental trials to highly developed treatment modalities that increasingly offer a growing number of men, women and children a new chance at an ever longer and healthier life. ASTS advances the art and science of transplant surgery through patient care, research, education, and advocacy. To learn more, visit ASTS.org.

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CareDx, Inc., headquartered in Brisbane, California, is a leading precision medicine solutions company focused on the discovery, development, and commercialization of clinically differentiated, high-value healthcare solutions for transplant patients and caregivers. CareDx offers testing services, products, and digital healthcare solutions along the pre- and post-transplant patient journey and is the leading provider of genomics-based information for transplant patients. For more information, please visit:?www.CareDx.com.

CHARITÉ
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Charité is one of the largest university hospitals in Europe. Charité proudly lays claim to more than half of all German Nobel Prize winners in Physiology or Medicine, including Emil von Behring, Robert Koch, and Paul Ehrlich. Charité is internationally renowned for its excellence in teaching and training. Charité – Universitätsmedizin Berlin represents a single medical faculty, which serves both Humboldt Universität zu Berlin and Freie Universität Berlin. Having marked its 300-year anniversary in 2010, Charité is now one of

the largest employers in Berlin, employing 17,600 staff (or 20,900 if including its subsidiaries), and with a total annual turnover of €2.3 billion (including external funding and investment grants). Charité kidney transplant center is the largest Transplant program in Germany.

CSL Behring is a global biotherapeutics leader driven by our promise to save lives. Focused on serving patients' needs by using the latest technologies, we discover, develop and deliver innovative therapies for people living with conditions in the immunology, hematology, cardiovascular and metabolic, respiratory, and transplant therapeutic areas. We use three strategic scientific platforms of plasma fractionation, recombinant protein technology, and cell and gene therapy to support continued innovation and continually refine ways in which products can address unmet medical needs and help patients lead full lives.

CSL Behring operates one of the world's largest plasma collection networks, CSL Plasma. Our parent company, CSL Limited, headquartered in Melbourne, Australia, employs more than 25,000 people, and delivers its lifesaving therapies to people in more than 100 countries.

Eledon Pharmaceuticals is a clinical stage biotechnology company using its expertise in targeting the CD40 Ligand (CD40L, also called CD154) pathway to develop potential treatments for persons requiring an organ or cell-based transplant, living with autoimmune disease, or living with ALS. The company's lead compound in development is tegoprubart, an anti-CD40L antibody with high affinity for CD40 Ligand, a well-validated biological target with broad therapeutic potential. Eledon is headquartered in Irvine, Calif. For more information, please visit the company's website at www.eledon.com. Follow Eledon Pharmaceuticals on social media: LinkedIn; Twitter.

The **European Society for Organ Transplantation (ESOT)** was founded 40 years ago and is dedicated to the pursuit of excellence in organ transplantation. Facilitating a wealth of international clinical trials and research collaborations over the years, ESOT remains committed to its primary aim of improving patient

outcomes in transplantation. With a community of over 8,000 members from around the world, ESOT is an influential international organisation and the facilitator of the biennial congress which hosts approximately 3,500 experts who come to meet to explore and discuss the latest scientific research. ESOT attracts the foremost transplantation experts to work in its committees and sections, and has an impressive track record in supporting research, supporting extensive education, and promoting changes in European policy.

Hansa Biopharma is a pioneering commercial-stage biopharmaceutical company on a mission to develop and commercialize innovative, lifesaving, and life-altering treatments for patients with rare immunological conditions. Hansa has developed a first-in-class immunoglobulin G (IgG) antibody cleaving enzyme therapy, which has been shown to enable kidney transplantation in highly sensitized patients. Hansa has a rich and expanding research and development program, based on the Company's proprietary IgG-cleaving enzyme technology platform, to address serious unmet medical needs in transplantation, autoimmune diseases, gene therapy, and cancer. Hansa Biopharma is based in Lund, Sweden, and has operations in Europe and the U.S. The Company is listed on Nasdaq Stockholm under the ticker HNSA. Find out more at https://hansabiopharma.com.

At **HUS Helsinki University Hospital** about 680 000 patients receive medical care annually. We have almost 27,000 professionals working for the best of all patients, and we are responsible for providing specialized health care for the residents of our 24 member municipalities. In addition, the treatment of many rare and severe diseases in Finland, such as solid-organ transplantations, is nationally centralized to HUS.

HUS is the biggest public health care provider and the second largest employer in Finland. Our expertise is internationally recognized and accredited. As a university hospital, we continuously develop and evaluate our treatment methods and activities.

HUS Abdominal Center, Transplantation and Liver Surgery, is currently one of the largest kidney and pancreas transplant programs in Northern Europe, with a total of 268 kidney transplantations and 31 pancreas transplantations performed in 2021."

Founded in 1982, **Immucor** is a global leader in transfusion and transplantation diagnostics that facilitate patient-donor compatibility. We strive to create a world where anyone, anywhere in need of transfusion or transplantation gets the right blood or transplant that is safe, accessible and affordable. With the right match, we can transform a life together. To learn more, visit https://www.immucor.com or our social media channels: LinkedIn, Twitter, Facebook, Instagram, and YouTube.

KU Leuven is Europe's most innovative university (Reuters) and ranks 42nd in the Times Higher Education World University Rankings. As Belgium's largest university, K.U. Leuven welcomes almost 60,000 students from over 140 countries. Its 7,000 researchers are active in a comprehensive range of disciplines. K.U. Leuven is a founding member of the League of European Research Universities (LERU) and has a strong European and international orientation. University Hospitals Leuven, its network of research hospitals, provides high-quality healthcare and develops new therapeutic and diagnostic insights with an emphasis on translational research.

The **University of Manitoba** is the province's only research-intensive university, educating the majority of professionals in Manitoba. The U of M is a trailblazer in many areas of learning, research and discovery, well-placed to encourage debate and discussion around the understanding of health, human rights, climate change and Indigenous studies. The U of M is home of the Truth and Reconciliation Commission of Canada.

Mayo Clinic is the first and largest integrated group practice in the world. Doctors from every medical specialty work together to care for patients. The entire staff at Mayo Clinic is joined by the philosophy “the needs of the patient come first.”

Transplant teams in Arizona, Florida and Minnesota apply novel techniques to improve care for their patients. These collaborations produce outcomes that set Mayo’s transplant programs in high standing with national norms and reinforce their worldwide reputation for quality and excellence. See more information at www.mayoclinic.org/transplant.

Novartis is reimagining medicine to improve and extend people’s lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com .

The **Paris Transplant Group (PTG)** is a French INSERM research team founded in 2008. The PTG is developing a personalized approach for transplant medicine that integrates multidimensional information derived from standard of care (clinical and biological data, histology and immunology) together with novel information coming from cutting edge technologies in immunology, molecular biology, genetics and biomarkers. It also leads multiple clinical trials and focuses on providing endpoints for clinical trials with insights in therapy and patient clinical management. The team includes several departments in kidney, heart, lung and liver transplantation worldwide with many different experts including clinicians, surgeons, pathologists, immunologists, epidemiologists, statisticians, mathematicians.

Sanofi. We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people's lives. Our team, across some 100 countries, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.

Takeda is a patient-focused, global biopharmaceutical company. We continue to seek new possibilities in transplantation, including potential treatment options to help address the unmet medical needs of transplant recipients with cytomegalovirus (CMV) infection. More information can be found on www.clinicaltrials.takeda.com.

Talaris Therapeutics, Inc. is a late-clinical stage cell therapy company developing therapies with the potential to transform the standard of care in solid organ transplantation and severe immune and blood disorders. Talaris maintains corporate offices in Boston, MA, its cell processing facility in Louisville, KY, and additional research operations in Houston, TX.

Thermo Fisher Scientific Inc. is the world leader in serving science, with annual revenue of approximately $40 billion. Our Mission is to enable our customers to make the world healthier, cleaner and safer. Whether our customers are accelerating life sciences research, solving complex analytical challenges, increasing productivity in their laboratories, improving patient health through diagnostics or the development and manufacture of life-changing therapies, we are here to support them. Our global team delivers an unrivaled combination of innovative technologies, purchasing convenience and pharmaceutical services through our industry-leading brands, including Thermo Scientific, Applied Biosystems, Invitrogen, Fisher Scientific, Unity Lab Services, Patheon and PPD. For more information, please visit www.thermofisher.com.

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Transplant Genomics is a personalized diagnostics company committed to improving organ transplant outcomes worldwide through innovative tests that detect early signs of graft injury, differentiate among actionable causes, and enable the optimization of therapy. Working alongside the transplant community, Transplant Genomics is commercializing a suite of tests enabling diagnoses and prediction of transplant recipient immune status. Our flagship product is OmniGraf, a non-invasive dual-biomarker combination test that offers the earliest and most accurate detection of rejection for transplant recipients – empowering clinicians to offer patients the best possible opportunity for successful long-term outcomes. Transplant Genomics became part of the Eurofins family of companies in 2019. Learn more about Eurofins Transplant Genomics at http://www.transplantgenomics.com.

Established in 1966, **The Transplantation Society** serves as the principal international forum for the advancement and development of both the science and clinical practice of transplantation throughout the world. Its mandate is fulfilled through scientific advancement and communication, continuing education and guidance on the ethical practice of transplantation. The Transplantation Society is a Non-Governmental Organization (NGO) in official relations with the World Health Organization, and is composed of over 6,000 professionals including but not limited to, physicians, surgeons, scientists and allied health professionals in 105 countries. TTS is one of two parent organizations of the Declaration of Istanbul, the other being the International Society of Nephrology. In addition, TTS has ten Sections specializing in various areas of transplantation: cell transplant and regenerative medicine, vascularized composite allotransplantation, pancreas and islet transplant, pediatric, organ donation and procurement, intestinal rehabilitation and transplant, xenotransplantation, pediatric liver transplantation, uterus and transplant infectious disease. TTS is a founding and sponsoring organization of the Declaration of Istanbul Custodian Group (DICG) formed to combat organ trafficking, transplant tourism, and transplant commercialism and to encourage adoption of effective and ethical transplantation practices around the world. TTS also partners with 35 national and

regional transplant societies to advance the science and clinical practice of transplantation around the world.

Veloxis Pharmaceuticals, Inc., an Asahi Kasei company, is a fully integrated specialty pharmaceutical company committed to improving the lives of transplant patients. Headquartered in Cary, N.C., USA, Veloxis is focused on the global development and commercialization of medications utilized by transplant patients and by patients with serious related diseases. For further information, please visit www.veloxis.com.

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