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

The draft EMA qualification opinion is available for public consultation until November 17, 2022

Secondary endpoint prognostic for allograft loss to catalyze development of novel therapies intended to improve long-term outcomes for kidney transplant recipients

TUCSON, Ariz., Oct. 13, 2022 — Critical Path Institute (C-Path) announced today that its Transplant Therapeutics Consortium (TTC) received a draft qualification opinion for the iBox Scoring System as a novel secondary efficacy endpoint for kidney transplant trials. This was achieved through the European Medicines Agency's (EMA) qualification of novel methodologies for drug development. After the draft qualification opinion undergoes the public consultation stage through Nov. 17, 2022, the iBox Scoring System will represent the first qualified endpoint for any transplant indication. This novel secondary endpoint supports the evaluation of novel immunosuppressive therapy (IST) applications with EMA.

As stated in the draft 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."

Although the current efficacy failure endpoint has typically shown the non-inferiority of IST regimens, the iBox Scoring System can be used to demonstrate the superiority of a new IST compared to the standard of care (SOC) at six months up to 24 months post-transplant in pivotal or exploratory drug therapeutic studies. "The ultimate goal is to improve the long-term outcomes in kidney transplant recipients, and this qualification is the first step to enhance development of innovative therapies in kidney transplant," said Kenneth Newell, M.D., co-leader for TTC's Efficacy and Endpoints Workgroup.

"Sponsors and investigators can assess and promote the potential advantages and superiority of novel ISTs when measured using the iBox Scoring System. Superiority to current SOC, thereby addressing an unmet need in kidney transplant, is one of the key criteria for Conditional Marketing Authorisation in the EU," said Ulf Meier-Kriesche, M.D., co-leader for TTC's Efficacy and Endpoints Workgroup.

The iBox Scoring System is a composite biomarker that utilizes multiple clinically relevant patient features to fully reflect the heterogeneity of graft failure, including measures of renal function (eGFR and proteinuria) and immunologic response to the graft (donor-specific antibody), with or without direct assessment of allograft health through histopathology (Banff lesion scores). "The collaboration with TTC has been instrumental in adapting the iBox Scoring System from a tool in patient-level decision-making to application as an efficacy endpoint in clinical trials," said Alexandre Loupy, M.D., Ph.D., head and founder of the Paris Transplant Group (INSERM) and professor of Nephrology and Epidemiology at the University of Paris Cité and Assistance Publique-Hôpitaux de Paris.

"In 2017, C-Path created TTC in partnership with the American Society of Transplantation (AST) and the American Society of Transplant Surgeons (ASTS) with a mission to accelerate the medical product development process for transplantation. The qualification of the iBox Scoring System has been TTC's primary initiative from inception," said C-Path's TTC Executive Director, Amanda Klein, Pharm.D. "This monumental achievement would not have been possible without the international transplant community's

ongoing collaboration, data sharing, expertise and dedication."

This regulatory draft 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, FDA, Hansa Biopharma, Immucor, Natera, National Institute 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 U.S. Food and Drug Administration (FDA), to whom the Qualification Plan has been submitted and is under review by the Agency.

The draft qualification opinion can be found on the EMA website. The draft EMA qualification opinion is now available for public consultation through November 17, 2022.

TTC
TRANSPLANT THERAPEUTICS CONSORTIUM

The 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).

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 U.S. Department of Health and Human Services (HHS) and is 54.2% funded by the FDA/HHS, totaling $13,239,950, and 45.8%

funded by non-government source(s), totaling $11,196,634. 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 EU. 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.

CSL Behring
Biotherapies for Life™

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.

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, KU Leuven welcomes almost 60,000 students from over 140 countries. Its 7,000 researchers are active in a comprehensive range of disciplines. KU 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.

Natera™ is a global leader in cell-free DNA testing, dedicated to oncology, women's health, and organ health. Our aim is to make personalized genetic testing and diagnostics part of the standard of care to protect health and enable earlier and more targeted interventions that help lead to longer, healthier lives. Natera's tests are validated by more than 100 peer-reviewed publications that demonstrate high accuracy. Natera operates ISO 13485-certified and CAP-accredited laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) in Austin, Texas and San Carlos, California. For more information, visit www.natera.com.

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.

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 wo'ld'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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