C-Path's Transplant Therapeutics Consortium Receives Acceptance of Letter of Intent for iBox Scoring System (Composite Biomarker Panel) as a Reasonably Likely Surrogate Endpoint

Biomarker aims to streamline the development of novel therapies intended to improve long-term outcomes for kidney transplant recipients.

TUCSON, Ariz., June 17, 2020 — Critical Path Institute (C-Path) announced today that its Transplant Therapeutics Consortium (TTC) has received a positive response to its Letter of Intent (LOI) from the U.S. Food and Drug Administration (FDA) detailing the decision to accept the Composite Biomarker Panel (iBox Scoring System) into the Center for Drug Evaluation and Research (CDER) Biomarker Qualification Program (BQP).

In its LOI, TTC provided information to support the qualification of the iBox Scoring System for its proposed context of use (COU) as a reasonably likely surrogate endpoint in clinical trials intended to evaluate immunosuppressive therapies (ISTs) for individuals living with a kidney transplant. Qualification as a surrogate or reasonably likely surrogate endpoint would allow drug sponsors to pursue accelerated approval, removing a significant barrier to kidney transplant drug development.

FDA indicated in its LOI Decision Letter that it supports the consortium's intent to pursue biomarker qualification and invited TTC to submit a Qualification Plan, the stage two submission that details how the consortium's will demonstrate the clinical and analytical validity of the Composite Biomarker Panel, for its intended COU. In its Decision Letter, FDA stated, "Based on our review of the LOI, we agree there is an unmet need, and the development of this composite scoring system to predict patient's long-term outcomes in clinical trials will facilitate the development of novel immunosuppressive therapies."

Long-term graft failure rates after kidney transplantation remain unacceptably high, despite improved short-term outcomes, with 10-year all-cause graft failure approaching 50% (Hart et al., 2019). Survival of the transplanted organ has been rated, by patients, as the most important outcome, including the overall survival of the patient (Howell et al., 2012). The iBox Scoring System, developed by the Paris Transplant Group, is the first tool of its kind to seek regulatory qualification for use in kidney transplant clinical trials. To date, no

biomarkers have been qualified for use as a surrogate or reasonably likely surrogate endpoint in any therapeutic area.

“This project is a meaningful example of what can be achieved by public-private-partnerships at the interface of translation science,” said TTC Executive Director Inish O’Doherty, Ph.D. Through collaboration and data sharing in the pre-competitive space, we are elevating the entire field of drug development in transplantation and working to improve the lives of those living with a kidney transplant.”

The iBox Scoring System is a risk prediction tool that combines measurements of kidney function, immunological status, and pathological assessment of kidney biopsy histology to predict the risk of graft-loss up to seven years after the time of risk assessment. The iBox Scoring System has been extensively validated for use in the treatment of individual patients in the clinical care setting. TTC, in close collaboration with the Paris Transplant Group, is seeking to translate this work into the regulatory setting for use in drug development programs. If qualified as a reasonably likely surrogate endpoint, the Composite Biomarker Panel (iBox Scoring System) will be publicly available and facilitate any drug sponsor seeking accelerated approval of novel agents, significantly reducing the time required to bring a new therapeutic agent to patients.

The iBox Scoring System will allow for greater application in drug development and lead to better therapies for patients,” said Alexandre Loupy, M.D., Ph.D., head of the National Institute of Medical Research (Inserm) U970. Loupy is a professor of Nephrology at Necker Hospital in Paris and a founder of the Paris Transplant Group. He has led the development of the iBox Scoring System over the past 10 years.

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, healthcare providers, academic researchers, and patient advocacy organizations are encouraged to work together to foster innovation in drug development through drug development tools that facilitate patient access to life-saving medications.

“Long-term transplant outcomes are still suboptimal, and people living with a kidney transplantation need novel anti-rejection medications with better long-term graft survival,” said Mark Stegall, M.D., Clinician Investigator, Department of Surgery, Mayo Clinic. “Improving long-term kidney graft survival would mean patients are less likely to need a second transplant during their lifetime and would allow them to lead longer and healthier lives. The positive response letter from FDA takes us one step closer to having new therapies that better the lives of transplant recipients.”

Ken Newell, M.D., Ph.D., past-president of AST and co-chair for TTC’s Endpoints and Efficacy Working Group said, “TTC has been instrumental in bringing together partners from industry, academia, and professional societies for this groundbreaking endeavor. This effort is a labor of love, and I’m honored to be part of this consortium and to be working with colleagues across the globe with a shared mission.”

About the Organizations:

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 dozens of pharmaceutical and biotech companies. C-Path US is headquartered in Tucson, Arizona and C-Path, Ltd. EU is headquartered in Dublin, Ireland, with additional staff in multiple other locations. For more information, visit www.c-path.org and c-path.eu.



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. The society is the largest transplant organization in North America (consisting of more than 4,000 professional members) and is recognized as the premier society for 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 www.facebook.com/AmericanSocietyofTransplantation



The **American Society of Transplant Surgeons** represents approximately 1,900 professionals dedicated to excellence in transplantation surgery. ASTS advances the art and science of transplant surgery through patient care, research, education, and advocacy. To learn more, visit ASTS.org.



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 communication, continuing education of its membership 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 6500 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 nine Sections specializing in various areas of transplantation: cell and regenerative medicine, Vascularized Composite Allotransplantation (VCA), pancreas and islet transplant, pediatric, organ donation and procurement, intestinal rehabilitation and transplant, xenotransplantation, pediatric liver transplantation, and transplant infectious disease. TTS also partners with 35 national and regional transplant societies to bring the science and clinical practice of transplantation around the world.

Bristol Myers Squibb™

Bristol Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube, Facebook and Instagram. Celgene and Juno Therapeutics are wholly owned subsidiaries of Bristol-Myers Squibb Company. In certain countries outside the U.S., due to local laws, Celgene and Juno Therapeutics are referred to as, Celgene, a Bristol Myers Squibb company and Juno Therapeutics, a Bristol Myers Squibb company.

CareDx®
Your Partner in Transplant Care

CareDx, Inc., headquartered in South San Francisco, 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 is a global biotherapeutics leader driven by its promise to save lives. Focused on serving patients' needs by using the latest technologies, we develop and deliver innovative therapies that are used to treat coagulation disorders, primary immune deficiencies, hereditary angioedema, respiratory disease, and neurological disorders. The company's products are also used in cardiac surgery, burn treatment and to prevent hemolytic disease of the newborn.

CSL Behring operates one of the world's largest plasma collection networks, CSL Plasma. The parent company, CSL Limited (ASX:CSL;USOTC:CSLLY), headquartered in Melbourne, Australia, employs more than 25,000 people, and delivers its life-saving therapies to people in more than 70 countries. For inspiring stories about the promise of biotechnology, visit Vita CSLBehring.com/vita and follow us on Twitter.com/CSLBehring.

Hansa Biopharma is leveraging its proprietary enzyme technology platform to develop immunomodulatory treatments for enabling transplantations and rare immunoglobulin G (IgG)-mediated autoimmune conditions, transplant rejection and cancer.

The Company's lead product candidate, imlifidase, is an antibody cleaving enzyme being developed to enable kidney transplantation in highly sensitized patients and may be further developed for use in other organ and tissue transplantation as well as acute autoimmune indications. Imlifidase is currently under review for a potential marketing authorization by the European Medicines Agency (EMA).

Hansa's research and development program is advancing the Company's enzyme technology to develop the next generation of IgG-cleaving enzymes with potentially lower immunogenicity, suitable for repeat dosing in relapsing autoimmune diseases and oncology. Hansa Biopharma is based in Lund, Sweden and also has operations in other European countries and in the U.S.

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. 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 is nationally centralized to HUS.

HUS is the biggest 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 293 kidney transplantations and 39 pancreas transplantations performed in 2019.

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 109,000 people of more than 145 nationalities work at Novartis around the world. Find out more at https://www.novartis.com .

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.
Sanofi, Empowering Life.

Transplant Genomics, Inc. (“TGI”) 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 and within the Eurofins family, TGI is commercializing a suite of tests enabling diagnoses and prediction of transplant recipient immune status. Our flagship product is TruGraf, the only blood test approved by CMS for surveillance and to rule out “silent” subclinical acute rejection in kidney transplant recipients with stable graft function. Test services are offered through TGI’s CLIA laboratory in Fremont, CA. TGI was acquired by Eurofins in 2019.

Veloxis Pharmaceuticals A/S, an Asahi Kasei company, is a commercial-stage specialty pharmaceutical company committed to improving the lives of transplant patients. Veloxis Pharmaceuticals A/S operates in the U.S. through Veloxis Pharmaceuticals, Inc., a wholly owned subsidiary headquartered in Cary, North Carolina, USA. Veloxis is focused on the direct commercialization of immunosuppression medications in the US, expansion of partnerships for markets around the world, and acquisition of assets utilized in transplant patients and by adjacent medical specialties. For further information, please visit www.veloxis.com.

Contact:

Kissy Black
C-Path
615.310.1894
kblack@c-path.org