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**CRITICAL PATH INSTITUTE’S PREDICTIVE SAFETY TESTING CONSORTIUM (PSTC)
ANNOUNCES FIRST-EVER BIOMARKER QUALIFICATION DECISION BY THE
JAPANESE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY (PMDA)**

PSTC’s new kidney biomarkers accepted by PMDA as useful in assessing the safety of new drugs

Tucson, Arizona, June 21, 2010 –For the first time, new biomarker tests to detect drug-induced kidney injury have been accepted by the Japanese Pharmaceuticals and Medical Devices Agency (PMDA). Critical Path Institute’s (C-Path) Predictive Safety Testing Consortium (PSTC) submitted the data for seven urinary protein biomarkers (KIM-1, Albumin, Total Protein, β 2-microglobulin, Cystatin C, Clusterin and Trefoil Factor-3) to the PMDA in August 2009, and received the formal ruling at the end of May 2010 that they are considered as follows:

- These seven novel biomarkers can provide additional information for detection of drug-induced acute kidney injury in preclinical rat safety studies when used in addition to the current standard biomarkers serum creatinine and Blood Urea-Nitrogen (BUN). Six of the biomarkers (KIM-1, Albumin, Total Protein, β 2-microglobulin, Cystatin C, and Clusterin) also perform better than the current standard biomarkers.

- The use of these novel kidney biomarkers (in combination with the current standard biomarkers) in early clinical trials in Japan and other countries may be accepted on a case-by-case basis in order to gather further data that PMDA considers necessary to qualify their usefulness in monitoring drug-induced renal toxicity in man.

PMDA's announcement is the first-ever regulatory biomarker qualification decision for the agency under their new special consultation process on pharmacogenomics/biomarkers. The same qualification data set for the biomarkers was previously submitted by C-Path to the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), with a favorable decision announced in 2008 from both agencies. The seven kidney injury biomarkers are now considered qualified for voluntary use in nonclinical safety studies to support regulatory decision-making. These tests will result in greater confidence in the safety of drugs that enter human testing and are now being evaluated for use in humans to reduce risk of injury. For the full PMDA Report, click [here](#).

Dr. Uyama, the leader for PMDA Omics Project (POP), noted that the seven biomarkers are now qualified by all ICH regulatory agencies at the same level, which will significantly promote a use of these biomarkers in a global setting. "PMDA expects positive conduct of continuous non-clinical and clinical evaluations for further qualification of novel biomarkers in the future," he stated.

PSTC, a public-private partnership that includes sixteen global pharmaceutical companies, was launched by Critical Path Institute and announced publicly by Secretary of Health and Human Services, Michael Leavitt in March of 2006. Regulatory scientists from FDA and EMA, along with PSTC member* scientists, work to evaluate the performance of novel safety biomarkers.

"FDA, EMA and PMDA's commitment to evaluate safety biomarker data submissions from PSTC demonstrates global recognition of the importance of new pathways for advancing regulatory science. C-Path is honored to lead this partnership in which data and knowledge are openly shared to identify better tests of drug safety," said C-Path's Elizabeth Gribble Walker, PhD, Director of Predictive Safety Testing Consortium.

The kidney biomarker submission evaluated by the PMDA included data from PSTC member companies Novartis and Merck, as well as contributions from leading scientists at Harvard Medical School and FDA's research laboratories. The PMDA's opinion acknowledges the role of the new kidney biomarkers to improve safety in the development of new drugs. The biomarkers were found to have greater sensitivity

and specificity than BUN and serum creatinine when a large number of nephrotoxic and control compounds were tested.

PSTC member companies and the FDA confirm that since the qualification announcement by FDA and EMA in 2008, several sponsors have successfully used the new kidney biomarkers to support decisions to advance or terminate drug development programs.

This milestone represents a significant advance not just for PMDA and the pharmaceutical industry, but for public health in general, as new tools to enhance the safety evaluation of promising new medicines are now internationally endorsed for drug development use. Raymond Woosley, MD, PhD, President of Critical Path Institute, commended PMDA for joining FDA and EMA in recognizing the value of forging new pathways within the regulatory process for evaluating new testing methods. According to Dr. Woosley, “PSTC continues to pioneer collaborative efforts to advance new safety tests with continued commitment from its member companies – qualification processes have been initiated at FDA for PSTC-sponsored skeletal muscle and liver safety biomarkers as well.”

*Current members of Critical Path Institute’s PSTC are:

Abbott, Amgen Inc., AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals, Inc., Bristol-Myers Squibb Company, ClinXus, Daiichi Sankyo, Eli Lilly and Company, GlaxoSmithKline, Johnson&Johnson Pharmaceutical Research and Development LLC, Merck & Co., Inc., Mitsubishi Tanabe Pharmaceutical Corporation, Novartis Pharmaceutical Corporation, Pfizer, Inc., Roche, sanofi-aventis, U.S., Inc,. Scientists from FDA and EMA participate as observers.

About Critical Path Institute

Critical Path Institute (C-Path) is an independent, non-profit organization whose mission is to serve as the impartial facilitator of collaborative efforts among scientists from government, academia, patient advocacy organizations, and the private sector to support the U.S. Food and Drug Administration’s regulatory science initiatives. This involves creating faster, safer, and smarter pathways for innovative new drugs, diagnostics, and devices that will significantly improve public health. Established in 2005, C-Path is headquartered in Tucson, Arizona, with offices in Phoenix, Arizona, and Rockville, Maryland. Visit www.c-path.org for more information.

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