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DUKE UNIVERSITY's CENTER FOR HUMAN GENOME VARIATION AND THE INTERNATIONAL SERIOUS ADVERSE EVENT CONSORTIUM TO PARTNER ON RESEARCH INTO THE GENETICS OF CLOZAPINE INDUCED AGRANULOCYTOSIS

Duke to lead effort to better understand the role of rare genetic variation in Clozapine-induced Agranulocytosis (CIA) using whole genome sequencing

Chicago (January 27, 2010) – The International Serious Adverse Events Consortium (SAEC) announced today it will collaborate with Duke University's Center for Human Genome Variation (http://www.genomics.duke.edu/centers/pg2/) to research the genetics of Clozapine-induced agranulocytosis (CIA), with the goal of identifying potential rare genetic variants predictive of this serious drug induced adverse event. The SAEC is a novel, non-profit international research consortium, formed by the global pharmaceutical industry, to better understand the role of genetics in drug safety. Duke University's Center for Human Genome Variation, under the leadership of David Goldstein, PhD and Professor of Molecular Genetics & Microbiology, applies state-of-the-art genomic science to help understand how human genetic variation influences disease and drug response. Dr. Anna Need, of Duke's Department of Psychiatry will jointly manage the collaborative research.

Clozapine is an atypical antipsychotic agent used extensively in the treatment of schizophrenia patients. An important factor limiting its use is the risk of potentially fatal agranulocytosis, estimated in less than 2 percent of treated patients. Agranulocytosis is the failure of the bone marrow to produce enough white blood cells (neutrophils) resulting in a significantly reduced immune response. Clozapine is made available through a special FDA sanctioned special surveillance system (Clozapine Patient Management System). Under this program, patients must have a weekly white-cell count to receive their supply of the drug.

Last fall, the SAEC received as a gift, the research materials and data relating to the CIA cohort to be used in the collaboration from PGx Health (http://www.pgxhealth.com/), a division of Clinical Data, Inc. These data corroborated the already published evidence for genetic associations in HLA region (Chromosome 6) consistent with a proposed immunological mechanism as an important causal factor associated with CIA. The Duke-SAEC plans to expand on these data by conducted more extensive studies of CIA using state-of-the-art whole genome sequencing techniques.

"Our genetic research on both drug-induced liver injury and serious skin rashes points to a strong role of the immune system in contributing to these adverse responses." said Arthur L. Holden, Chairman of the SAEC. "By researching the genetics of drug induced CIA, we hope to further our understanding into the genetics of immunologically mediated adverse drug responses. Our collaboration with Duke University's Center for Human Genome Variation represents our first pilot to use whole genome sequencing technology to better understand the role of rare genetic variation in such events."

"For many patients Clozapine is the most effective drug available, but its use is constrained by the possibility of this serious adverse event requiring intrusive monitoring programs." said David Goldstein, PhD, Professor of Molecular Genetics & Microbiology at Duke University. "We hope that understanding the genetics of CIA will not only reduce its occurrence, but also allow wider use of Clozapine."

Founded in the fall of 2007, the SAEC is a private, global partnership of leading pharmaceutical companies, the U.S. Food and Drug Administration and academic institutions from around the world to identify and confirm genetic markers that may help predict which patients are at risk for drug-related serious adverse events. Through identifying and ultimately validating genetic markers associated with

SAEs, the Consortium hopes to reduce the patient and economic costs caused by drug-related SAEs. The SAEC also hopes to improve the flow of safe and effective medical therapies by better addressing idiosyncratic safety risks of new drugs before they reach the market. The SAEC provides free access to its study data and results to all qualified researchers.

About the International SAEC
The International Serious Adverse Event Consortium (SAEC, www.saeconsortium.org) is a 501(c) 3 organization dedicated to identifying and validating DNA variants useful in predicting the risk of drug-related serious adverse events. The Consortium brings together the pharmaceutical industry, regulatory authorities, and academic centers to address clinical and scientific issues associated with drug-related serious adverse events.

SAEC members include representatives from the pharmaceutical industries, the scientific community, and the Wellcome Trust.

- Pharmaceutical industry partners are involved in all aspects of the Consortium launch, providing ongoing consultation on the development and structure of the Consortium's scientific model, contributing cohort data, and underwriting costs of the SAEC's studies. SAEC members include: Abbott, Amgen, Daiichi Sankyo, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Pfizer, Roche, Sanofi-Aventis, and Takeda.

- The FDA provides consultation on the direction of the SAEC, the design and conduct of SAEC studies, and support of the release of resulting research data.

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