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UNIQUE PUBLIC/PRIVATE PARTNERSHIP EXPANDS RESEARCH TO IDENTIFY PREDICTIVE GENETIC MARKERS FOR DRUG-INDUCED SERIOUS ADVERSE EVENTS

– International Serious Adverse Events Consortium enters Stage II of landmark research effort to study the genetics of rare adverse reactions to existing medications –

Chicago, IL (September 30, 2010) – The non-profit International Serious Adverse Events Consortium (iSAEC) announced today the launch of the second stage of its landmark effort to research the genetic underpinnings of drug-induced serious adverse events (SAEs). Stage II of the research effort, building on Stage I findings, will further explore gene variants that may predict an individual's risk of developing immunologic-related adverse reactions to specific drugs or classes of drugs.

Formed in late 2007, the iSAEC includes members from the pharmaceutical industry and the Wellcome Trust, working in collaboration with the U.S. Food and Drug Administration (FDA). Pharmaceutical partners supporting Stage II include Abbott, Amgen, AstraZeneca, Daiichi Sankyo, GlaxoSmithKline, Merck, Novartis, Pfizer and Takeda. iSAEC provides researchers with open access to its data through a controlled-access database. Twelve months after genotyping studies are complete, data is released without any patent or intellectual property constraints, allowing for further use and study by interested researchers.

"Understanding the genetic underpinnings of major drug-related adverse events such as drug-induced liver injury remains one of our top priorities at FDA," said Janet Woodcock, M.D., Director for FDA's Center for Drug Evaluation and Research. "We are encouraged by iSAEC's progress and applaud their leadership in this area. They are providing invaluable information to the medical and scientific community to predict and prevent serious drug risks in patients."

Building on Stage I Findings

The consortium recently completed Stage I of its research activities, focused on pilot genome-wide association studies of drug-induced liver injury (DILI) and serious skin rash (SSR). The iSAEC supported researchers identified important genetic underpinnings for certain drug-induced SAEs. In addition, they revealed that some genetic variants associated with risk of developing immune-system mediated adverse events – including skin rashes, acute hypersensitivity reactions and DILI – confer this risk for multiple drugs.

"Our Stage I research has significantly advanced our understanding of the potential genetic causes of SAEs and, like many studies of this nature, reveal the genetic complexity of these events," said Michael Dunn, PhD., Head of the Wellcome Trust Molecular and Physiological Sciences Department. "The finding that some genetic variants confer risk for multiple drugs tells us that it may be possible to develop well-characterized maps that identify specific genes that could put patients at risk for a number of drug-specific adverse events. These results have energized our interest in exploring the genome to gain a better understanding of rare, serious adverse events and lay the foundation for our Stage 2 Research effort."

iSAEC researchers believe that a spectrum of drug-induced immunologic reactions may be influenced by common genetic factors. Stage II will explore this hypothesis through a focused expansion of current SSR and DILI cohorts. The consortium also will initiate an international acute hypersensitivity reaction research network. These efforts will focus on achieving a more integrated biological understanding of the genetics associated with immunologic-based drug-induced SAEs.

"Our ideal outcome would be to generate a set of predictive markers for drug-induced SAEs, across a number of drugs/drug classes. The launch of our Stage II research represents an important step towards this goal," said Arthur Holden, chairman of iSAEC. "The consortium is funded entirely through private contributions by our member pharmaceutical companies and the Wellcome Trust. It is advancing our understanding of the genetic causes of SAEs using an innovative collaborative research model which is producing results that no single organization could accomplish on its own. Increasingly, biomedical research will require similar large-scale, collaborative efforts."

New Partners Join Stage II

In Stage II, iSAEC's collaborators have expanded to include leaders in electronic medical records and health maintenance organizations as well as expanded partnerships with academic research collaborators:

- HMO Research Network (HMORN): iSAEC is collaborating with the HMO Research Network to improve the safe use of drugs by exploring why the genetic makeup of some individuals makes them more likely to experience SAEs. The HMORN is the nation's premier resource for population-based health care outcomes research.
- The University of Liverpool (Liverpool): iSAEC will collaborate with Liverpool to research the genetics of acute hypersensitivity reactions, through the creation of the International Hypersensitivity Consortium (ITCH). Liverpool will serve as the global coordinating center for ITCH.
- Newcastle University (Newcastle): iSAEC will collaborate with Newcastle to research the genetics of DILI through the creation of the International DILI Consortium (IDILIC). Newcastle will serve as the global coordinating center for IDILIC.
- Cerner Corporation: the iSAEC will use *Cerner Discovere™*, their web-based research platform, to gather data for studies that focus on liver injury, serious skin rash, and other hypersensitivity reactions.

About Drug-Induced SAEs

Drug-induced SAEs are an important cause of morbidity, resulting in hospitalizations, avoidable healthcare utilization and costs and, in some cases, death. Beyond the human costs, drug-induced SAEs observed during the development of new therapies can halt the study of what might have otherwise been a promising new treatment. If genetic

factors are determined to contribute to these events, those at risk could be identified and exposure to the adverse event avoided.

About the iSAEC

The International Serious Adverse Event Consortium (iSAEC) is a 501(c) 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. iSAEC partners are providing financial support, in-kind donations, and participation in data collection to the Stage II research. The iSAEC is the only privately-funded partnership currently dedicated to studying SAE genomics.

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