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InSphero and Pharmaceutical Companies Form Pre-Competitive Consortium to Advance Development of *In Vitro* Tools to Screen and Predict Drug-Induced Liver Injury (DILI)

DILI is of significant concern to the pharmaceutical industry and regulatory authorities due to limitations of existing preclinical animal models

Founding members include Pfizer, Sanofi, Merck, and Genentech

Schlieren, Switzerland – June 16, 2021 InSphero AG, the pioneer of 3D cell-based assay technology today officially launched a pre-competitive consortium that brings together representatives from pharmaceutical companies engaged and invested in the development of cross-species drug testing and validation strategies for rapid, reliable drug-testing of drug-induced liver injury (DILI) and translation to humans.

The consortium will evaluate methods for recapitulating DILI-specific effects observed in animal models and patients using *in vitro* human and animal liver spheroid models and a DILI compound library.

“DILI is recognized as a significant cause of drug candidates being terminated during development or drugs being withdrawn from the market,” said Armin Wolf, Ph.D., Professor of Toxicology and Chief Scientific Officer at InSphero and former pharmaceutical industry executive. “Preclinical safety assessment of drug candidates typically relies on animal testing. Unfortunately, this does not always reliably translate to humans. This shortcoming likely contributes to the prevalence of DILI reported in late-stage drug development. We intend to use 3D liver microtissues from animals and humans to evaluate DILI mechanisms leading to observed *in vivo* effects. Our goal is to help bridge the gap between human and animal *in vivo* and *in vitro* responses for a wide range of compounds and therapeutics.”

Each participating pharma member will provide a set of DILI compounds for 3D *in vitro* mechanistic investigations conducted by InSphero. These compounds may have failed or are from halted drug programs having a well-documented preclinical DILI-specific *in vivo* profiles and history in the most common regulatory animal models. For confidentiality reasons, the chemical structure and therapeutic target of test compounds will be blinded and not revealed in any consortium publications.

“The ability to accurately evaluate DILI potential *in vitro* across multiple species can be very useful to understand the human relevance of liver signals from *in vivo* preclinical studies” said Piyush Bajaj, Ph.D. senior principal scientist at Sanofi.

InSphero will employ a cross species DILI validation strategy to compare the documented *in vivo* response to the *in vitro* response in 3D liver microtissues derived from the corresponding preclinical animal models. Each type of drug-induced liver pathology will be investigated *in vitro* by the specific underlying DILI mechanism or biomarker. The validation criterion will be recapitulation of the documented *in vivo* DILI effect by mechanism in the relevant *in vitro* liver microtissue.

“Development of a reliable, *in vitro* hepatic platform capable of accurately translating the DILI risk of drug candidates across preclinical species and humans would help improve our ability to predict hepatic safety,” said Jonathan P. Jackson, Ph.D., senior principal scientist, Pfizer. This sentiment was emphasized by fellow consortium member Phil Hewitt, Ph.D. global head of early investigative toxicology at Merck Healthcare KGaA who noted “Having a validated liver model for all relevant preclinical test species would greatly improve our ability to both predict DILI and retrospectively assess potential clinical mechanisms.”

Another important aspect of developing robust and predictable *in vitro* models for safety assessment is the potential to reduce the use of animals for this purpose. “From a practical standpoint, the most important factor to enable utilization of these new models effectively is having enough foundational high-quality data available to understand the appropriate context of use,” said Leah Norona, Ph.D., scientist at Genentech, Inc. “This consortium will take the critical first steps towards that goal.”

For more information about the Consortium, please visit: X-Species Consortium | InSphero

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About InSphero

InSphero is the pioneer of industrial-grade, 3D-cell-based assay solutions and scaffold-free 3D organ-on-a-chip technology. Through partnerships, InSphero supports pharmaceutical and biotechnology researchers in successful decision-making by accurately rebuilding the human physiology *in vitro*. Its robust and precisely engineered suite of 3D InSight™ human tissue platforms are used by major pharmaceutical companies worldwide to increase efficiency in drug discovery and safety testing. The company specializes in liver toxicology, metabolic diseases (e.g., T1 & T2 diabetes and NAFLD & NASH liver disease), and oncology (with a focus on immuno-oncology and PDX models). The scalable Akura™ technology underlying the company’s 3D InSight™ Discovery and Safety Platforms includes 96 and 384-well plate formats and the Akura™ Flow organ-on-a-chip system to drive efficient innovation throughout all phases of drug development.

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