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Media Release – For Immediate Distribution

InSphero human liver disease platform selected to test Cyclerion's sGC stimulator technology as potential therapeutic approach for NASH and fibrosis

3D InSight™ human liver models helped assess efficacy of praliciguat, a systemic small molecule sGC stimulator, in reducing hallmark symptoms of fatty liver disease.

Schlieren, Switzerland – August 27, 2019 InSphero today announced that in a recent study published in the *Proceedings of the National Academy of Sciences (PNAS)*, researchers at Cyclerion Therapeutics, a clinical stage biopharmaceutical company, used InSphero 3D InSight™ Human Liver Disease Microtissue models to evaluate praliciguat, a systemic small molecule stimulator of soluble guanylate cyclase (sGC), as a potential treatment for non-alcoholic steatohepatitis (NASH) and fibrotic liver disease. Study results support further investigation of sGC stimulation as a potential therapeutic approach for NASH and fibrosis, and validate the utility of 3D InSight™ human liver disease models for preclinical drug screening.

sGC is a complex of two proteins found in tissues throughout the body. It mediates nitric oxide signaling and the cyclic guanosine monophosphate (cGMP) pathway known to regulate diverse and critical biological functions, including inflammatory and fibrotic processes. The Cyclerion research team discovers and develops systemic and tissue-targeted sGC stimulators, intended to maximize the desired effects for the target disease, while minimizing side effects.

"The results published in this paper provide important validation of the sGC stimulator mechanism as a potential treatment for NASH and fibrotic liver disease. We expect to apply these learnings to our ongoing late-stage discovery program focused on a tissue-targeted sGC stimulator designed to maximize this pharmacology in the liver," said Cyclerion Chief Scientific Officer Mark Currie. "Our collaboration with InSphero provided further exciting insights into the effects of praliciguat on hepatic cells, and their 3D human liver microtissue models enabled us to better understand how these results may translate to clinical settings."

InSphero partners with pharmaceutical companies to provide comprehensive solutions and disease models for investigators engaged in non-alcoholic fatty liver disease (NAFLD) research and drug development. The 3D InSight™ Human Liver Disease Model used in this study includes a phenotypically relevant microtissue co-culture of primary human hepatocytes, Kupffer cells, hepatic stellate cells, and liver endothelial cells, with specially formulated media and inducers to stimulate inflammation and scarring of the liver (fibrosis). This 3D InSight™ Human Liver Disease Platform is ideal for high-throughput and longitudinal studies of NAFLD and NASH.

"Our research partnership with Cyclerion exemplifies how we support truly innovative pharmaceutical research with our versatile portfolio of scalable drug discovery and safety platforms. Our discovery platforms accelerate pharmaceutical R&D substantially, as we were able to show here," said InSphero CEO and Co-founder, Dr. Jan Lichtenberg.

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Additional Information

Read the *PNAS* paper, "sGC stimulator praliciquat suppresses stellate cell fibrotic transformation and inhibits fibrosis and inflammation in models of NASH": https://www.pnas.org/content/116/22/11057.full.

Learn more about Cyclerion and their sGC-stimulator-based therapeutics: https://www.cyclerion.com/.

Learn more about InSphero: www.insphero.com.

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About InSphero

InSphero is the pioneer of industrial-grade, 3D-cell-based assay solutions and scalable, scaffold-free microtissue technology. Through partnerships, InSphero supports pharmaceutical and biotechnology researchers in successful decision-making by recapitulating human physiology *in vitro*. Its robust and precisely engineered suite of 3D InSight™ human tissue platforms for liver toxicology, metabolic diseases, and immuno-oncology are used by major pharmaceutical companies worldwide to increase efficiency in drug discovery and safety testing. 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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