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HepaRegeniX Doses First Patient in Phase Ib Trial with Small Molecule Inhibitor HRX-215 to Promote Liver Regeneration

Tuebingen, Germany, June 10, 2025 – HepaRegeniX GmbH ("HepaRegeniX"), a clinical-stage company advancing novel therapies to treat acute and chronic liver disease, today announced that the first patient has been dosed in their Phase Ib clinical trial of its lead candidate HRX-215. The trial is evaluating the safety and efficacy of HRX-215, an orally available small-molecule inhibitor of MKK4, in patients undergoing partial liver resection due to liver metastases deriving from colorectal cancer. HXR-215 is designed to treat advanced-stage liver disease by increasing the regenerative capacity of hepatocytes. An initial data readout is planned for the second half of 2025.

"We aim to address a critical unmet need in patients with advanced liver disease who are often considered inoperable due to the limited regenerative capacity of the remaining liver after partial resection," said **Linda Greenbaum, Chief Medical Officer at HepaRegeniX**. "HRX-215 may offer a new therapeutic option by promoting hepatocyte regeneration, thereby increasing the safety and feasibility of liver resections in patients who have insufficient predicted postoperative liver mass and/or reduced liver function associated with fatty liver (steatosis) or liver scarring (fibrosis)."

"Dosing the first patient in this trial marks an important milestone for HepaRegeniX as we advance HRX-215 into the next stage of clinical development," said **Elias Papatheodorou, Chief Executive Officer at HepaRegeniX**. "Together with our recently completed €21.5 million Series C financing round, we are well-positioned to advance HRX-215 through clinical development and ultimately improve outcomes for patients facing limited treatment options."

The randomized, double-blinded Phase Ib/IIa trial (NCT06638502), conducted in the United States, will evaluate the safety and efficacy of HRX-215 in 85 patients with liver metastases originating from colorectal cancer. Participants will be divided into three cohorts: (1) active treatment arm for patients requiring minor liver resection (30%), (2) active treatment arm including patients requiring major liver resection (50 – 72%), and (3) active treatment and a placebo comparator arms for patients requiring major liver resection.

The study builds on preclinical and clinical data published in Cell in March 2024, which demonstrated the potential of HRX-215 to significantly boost liver regeneration and prevent post-hepatectomy liver failure (PHLF) in animal models and which demonstrated acceptable safety

profile and pharmacokinetics in a Phase I trial in healthy participants. The compound showed favorable safety and tolerability, with no drug-related adverse events observed.

About HRX-215 and Liver Regeneration
Patients with late-stage liver disease often have limited therapeutic options beyond surgical intervention. Successful liver resection depends on the ability of the remaining liver, known as the future liver remnant (FLR), to sustain essential functions and regenerate. When the FLR is insufficient in volume or function, the risk of post-operative liver failure increases significantly, rendering many patients ineligible for potentially curative surgery.

HRX-215 is an orally available small molecule inhibitor of mitogen-activated protein kinase kinase 4 (MKK4), a key regulator of liver regeneration. By selectively inhibiting MKK4, HRX-215 has been shown in preclinical models to stabilize and protect hepatocytes, while accelerating and enhancing regenerative processes, even in compromised or diseased livers. This therapeutic approach has the potential to expand surgical eligibility to patients requiring extended liver resection who would otherwise be deemed inoperable, offering a new path to potentially lifesaving treatment.

About HepaRegeniX GmbH
HepaRegeniX is advancing therapies to treat acute and chronic liver diseases based on the groundbreaking discoveries of a novel cellular target and small molecules that enable the liver to regenerate rapidly. We do so by harnessing the liver's inherent regenerative power not only in healthy but also in diseased livers. The company's lead candidate, HRX-215, an orally available small molecule currently in a Phase Ib/IIa trial, selectively inhibits Mitogen-Activated Protein (MAP) Kinase Kinase 4 (MKK4), a master regulator of liver regeneration. Building on demonstrated safety in clinical trials, HepaRegeniX is progressing HRX-215 to prevent post-hepatectomy liver failure, facilitate transplantation of smaller living donor liver grafts, and treat severe alcohol-associated hepatitis. Beyond liver diseases, the company is also developing HRX-233 to target kinase inhibitor treatment resistance in KRAS-driven tumors.

HepaRegeniX is backed by experienced life science investors, including Vesalius Biocapital IV, Novo Holdings A/S, Boehringer Ingelheim Venture Fund (BIVF), Coparion, High-Tech Gründerfonds, Ascenion GmbH and Wellington Partners.

Visit our website at www.heparegenix.com to learn more about the company.

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