HepaRegeniX publishes data for its first-in-class MKK4 inhibitor HRX-215 for the treatment of acute and chronic liver diseases in Cell

- Clinical and pre-clinical data generated from collaborations between the Tuebingen University Hospital, researchers from the Mayo Clinic in Rochester (USA) and HepaRegeniX
- HRX-215 proved to be safe and well tolerated in healthy volunteers, pre-clinical data showed increased regeneration of liver cells
- HRX-215 to be further developed to usher in a new era in oncological liver surgery and liver transplantation

Tuebingen (Germany), March 14, 2024 – HepaRegeniX GmbH, a clinical stage company developing novel regenerative therapies for the treatment of acute and chronic liver diseases, today published clinical and preclinical results on its first-in-class MKK4 inhibitor HRX-215 in the prestigious journal **Cell**. The manuscript, available online here (DOI: 10.1016/j.cell.2024.02.023), describes strongly enhanced liver regeneration and prevention of liver failure by HRX-215 in preclinical model systems and a first-in-human trial showing safety and tolerability. HRX-215 is a small molecule inhibitor of **M**itogen-Activated Protein (MAP) **K**inase **K**inase **4** (MKK4).

"The positive results in terms of safety and tolerability confirm our intention to soon offer a drug that has the potential to revolutionize the treatment of severe liver diseases. The data pave the way for further Phase II studies evaluating the efficacy of HRX-215 in humans," emphasizes **Dr. Wolfgang Albrecht, COO of HepaRegeniX**.

In patients with liver metastases from colorectal cancer, which affect about 1 million people per year worldwide, or with primary liver tumors, complete resection of the liver tumors is the only curative therapeutic approach. However, when the remaining liver volume would be below a certain threshold, patients are at high risk of developing post-hepatectomy liver failure (PHLF), an often lethal complication limiting the surgical treatment of liver cancers. HRX-215 holds promise to make more extensive liver resections possible by safely preventing PHLF.

“HRX-215 would not only be an urgently needed treatment option in the surgical removal of liver tumors, but would also be able to help overcome the major problem of organ shortage in the field of liver transplantation," **Prof. Lars Zender, Medical Director at the University Hospital Tuebingen** points out the possible applications. Living donor transplants from the smaller left part of a healthy donor's liver would be a solution, as removal poses little health risk for healthy donors. However, this part of the liver is often too small to take over the function of the liver that was removed from the recipient. "Due to the rapid enhancement of liver regeneration mediated by HRX-215, we assume that HRX-215 treatment would enable the safe transplantation of small left liver lobes in normal size adults," Prof. Zender continues.

Before HRX-215 was tested in healthy volunteers in a Phase I study, it was thoroughly investigated in animal models. In particular, Tuebingen collaborated with Prof. Dr. Scott L. Nyberg at the Mayo Clinic in Rochester (USA), an internationally renowned expert in the field of transplantation and regenerative medicine. His team was able to show that

treatment with HRX-215 can boost liver regeneration after partial liver removal (hepatectomy) while intact livers are not affected by the drug candidate. Further, HRX-215 was also able to protect hepatocytes from cell death in a model for acute liver injury.

In the consecutive first in human trial, conducted by HepaRegeniX, HRX-215 was well tolerated at all doses with no drug-related adverse events being observed.

"We are very excited about the results from this collaborative effort that have now resulted in a publication in Cell. I would like to congratulate the three teams for even making the cover of this leading scientific journal. MKK4 inhibition has proven to be an ideal mechanism of action for inducing liver regeneration because it depends on the activation of stress pathways and has an excellent safety profile even after long-term treatment without the risk of tumorigenesis. Our successfully completed Phase I trial further underlines the enormous potential this drug candidate has for treating acute and chronic liver damage in patients," concludes **Elias Papatheodorou, Chairman of HepaRegeniX' Board of Directors**.

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About HepaRegeniX GmbH – www.heparegenix.com
Since 2017, HepaRegeniX has successfully discovered and developed several drug candidates for the treatment of acute and chronic liver diseases based on a novel proprietary molecular target **M**itogen-Activated Protein (MAP) **K**inase **K**inase **4** (MKK4). The first MKK4 inhibitor HRX-215 recently completed Phase 1 clinical testing. MKK4 is a key regulator of liver regeneration and suppression of MKK4 unlocks the regenerative capacity of hepatocytes even in severely diseased livers. This new and unique therapeutic concept was discovered by Prof. Lars Zender and his research group at the University Hospital Tuebingen, Germany. Investors in HepaRegeniX include the Boehringer Ingelheim Venture Fund (BIVF), Novo Holdings A/S, Coparion, High-Tech Gruenderfonds and Ascenion GmbH.