HepaRegeniX initiates a preclinical collaboration with the Netherlands Cancer Institute to explore the potential of its 2nd MKK4 inhibitor HRX-0233 for use in cancer combination therapy

- HRX-0233 is a new MKK4 inhibitor and the 2nd drug candidate from the company´s small molecule-based drug discovery platform
- HRX-0223 is being investigated for the treatment of tumors with mutated KRAS gene, a common oncogenic driver in combination with other treatments
- KRAS mutations are associated with poor prognosis

Tubingen (Germany), October 20, 2021 – HepaRegeniX GmbH, a clinical stage company developing novel therapies for the treatment of acute and chronic liver diseases, announced today a collaboration with the Netherlands Cancer Institute (NKI) to investigate HepaRegeniX' new drug candidate HRX-0233 in preclinical *in vivo* models with Kirsten rat sarcoma virus (KRAS) mutant tumors. Under the partnership, NKI will conduct the preclinical research to find the most promising combinations of the small molecule inhibitor of **M**itogen-Activated Protein (MAP) **K**inase **K**inase **4** (MKK4) with other inhibitors of the MAP kinase pathway. Preliminary data obtained by Prof. Bernards' group at the NKI have shown promising results in cell culture experiments.[1]

"It is exciting to see our second MKK4 inhibitor candidate now entering the late preclinical development phase with the aim to learn more about the additional therapeutic potential of our new drug candidate HRX-0233 for patients with KRAS gene mutated cancers," said **Dr. Wolfgang Albrecht, Managing Director of HepaRegeniX.** "Prof. Bernards and his group at the NKI are experts in cancer research, especially when it comes to uncovering synthetic lethal drug combinations, where the specific gene mutation and a drug efficiently kill the cancer cells."

"HepaRegeniX has successfully discovered and developed drug candidates for the novel molecular target MKK4. Its inhibitor HRX-0233 shows promising initial results in synergy with other kinase-inhibitors in KRAS mutant tumors *in vitro*," added **Prof. René Bernards, Researcher of NKI and principal investigator at the Oncode Institute**. "We are looking forward to the outcome and see a high value for this new small molecule in fighting KRAS mutant tumors."

The mutation of the KRAS gene is present in 90 % of pancreatic, 40 % of lung, and 50 % of colorectal cancers and one of the most common oncogenic drivers. KRAS mutant tumors have a very poor response to current therapies[2].

References

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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-0215 recently entered clinical development. 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 Tubingen, Germany. Investors in HepaRegeniX include the Boehringer Ingelheim Venture Fund (BIVF), Novo Holdings A/S, Coparion, High-Tech Gruenderfonds and Ascenion GmbH.

About the Netherlands Cancer Institute, Amsterdam – www.nki.nl
The Netherlands Cancer Institute, founded in 1913, is among the world's best comprehensive cancer centers, combining world-class fundamental, translational, and clinical research with dedicated patient care. Our initiatives to promote excellent translational research have been recognized by the European Academy of Cancer Sciences, when they designated us 'Comprehensive Cancer Center of Excellence in Translational Research.

About the Oncode Institute, Utrecht
Oncode Institute unites more than 900 excellent fundamental cancer researchers in the Netherlands. Our mission is to stimulate innovations in the diagnosis and treatment of cancer. The ultimate goal is to help patients survive, improve the quality of life for those affected and contribute to a more affordable healthcare system. Oncode Institute translates fundamental insights into the biology of cancer into new diagnostics, new drugs and innovative treatments. Oncode's three strategic pillars to improve patient outcomes are Excellent Science, Collaboration and Valorization. Oncode is funded by The Dutch Cancer Society, together with the Ministries of Economic Affairs & Climate, Education Culture & Science and Health, Welfare & Sport, and Health~Holland, with a total amount of €120 million until 2022.