

## **HepaRegeniX achieves further milestone related to proof of safety and efficacy for MKK4 inhibition in an advanced chronic liver disease model**

New preclinical data indicate beneficial therapeutic effects in non-alcoholic steatohepatitis (NASH)-associated liver carcinomas

**Tubingen (Germany), December 3, 2020** – HepaRegeniX GmbH, a preclinical stage company developing novel therapies for the treatment of acute and chronic liver diseases, announced today that treatment with selective Mitogen-Activated Protein (MAP) Kinase Kinase 4 (MKK4) inhibitors over a three month period reduced hepatic steatosis and liver damage in a murine model of nonalcoholic steatohepatitis (NASH)-associated hepatocellular carcinoma (HCC). MKK4 inhibition was not only safe and well tolerated but even showed marked growth suppression of NASH-associated hepatocellular carcinoma.

These new findings not only confirm previous results related to the overall safety of MKK4 inhibition,<sup>1</sup> but also imply a potential therapeutic efficacy of MKK4 inhibitors in NASH-associated HCC. NASH is a main etiological risk factor for HCC with the incidence of NASH-associated HCC expected to further increase globally.<sup>2,3</sup> To date, no effective drug therapy is available for NASH-associated HCCs as they seem, unlike HCCs of other etiology, not amenable to treatment with immune checkpoint blocking antibodies.<sup>4,5</sup>

Dr. Michael Lutz, CEO of HepaRegeniX said, “We are very pleased to have accomplished another milestone in the preclinical validation of MKK4 as a promising target for the treatment of a broad range of both acute and chronic liver diseases. In combination with the encouraging safety profile in the model of severe liver disease such positive findings, if translated into the clinic, may improve the prognosis of patients who currently have very few therapeutic options.”

Prof. Dr. Lars Zender, Founder and Board member of HepaRegeniX as well as Professor and Chairman of Medical Oncology & Pneumology at the University Hospital Tubingen added, “We are very excited to see that small molecule-based MKK4 inhibitors not only reduce NASH-associated liver damage, which represents a major risk factor for HCC development, but at the same time suppress growth of NASH-driven HCC. Successful translation of MKK4 inhibition into the clinic holds a great promise to improve the prognosis of patients with NASH and NASH associated HCC.”

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**About HepaRegeniX GmbH [www.heparegenix.com](http://www.heparegenix.com)**

Since 2017, HepaRegeniX has successfully discovered and developed several preclinical drug candidates for the treatment of acute and chronic liver diseases based on a novel proprietary molecular target Mitogen-Activated Protein (MAP) Kinase Kinase 4 (MKK4). 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 for the treatment of liver diseases 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.

**References**

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- <sup>1</sup> Wüstefeld T et al., Cell 2013; 153(2):389-401; DOI: <https://doi.org/10.1016/j.cell.2013.03.026>
  - <sup>2</sup> Negro F, Liver International 2019; 40(S1):73-76; DOI: <https://doi.org/10.1111/liv.14362>
  - <sup>3</sup> Fingas CD et al., CLD 2016; 8(5):119-122; DOI: <https://doi.org/10.1002/cld.585>
  - <sup>4</sup> Yau T et al. Ann Oncol 2019; 30:mdz394.029 DOI: <https://doi.org/10.1093/annonc/mdz394.029>
  - <sup>5</sup> Finn RS et al., N Engl J Med 2020; 382:1894-1905; DOI: <https://doi.org/10.1056/nejmoa1915745>