PRESS RELEASE

Heidelberg Pharma and Indiana University Publish Results on HER2-ATAC for Targeted Immunotherapy of Triple Negative Breast Cancer in *Science Translational Medicine*

- Extraordinary efficacy of a HER2-targeting Trastuzumab-ATAC in the treatment of Triple-Negative Breast Cancer (TNBC) with low HER2 expression and hemizygous deletion of chromosome 17p in preclinical models
- Induction of immunogenic cell death by an HER2-ATAC - Synergistic and increased efficacy in combination with checkpoint inhibitors

Ladenburg, Germany, 11 February 2021 – Heidelberg Pharma AG (FSE: HPHA) today announced that new study results on the Antibody Targeted Amanitin Conjugate (ATAC) technology have been published in the journal *Science Translational Medicine*, in a joint report by a research group at the School of Medicine, Indiana University, Indianapolis, IN, USA, and scientists of Heidelberg Pharma.

Trastuzumab-ATAC, which consists of the antibody Trastuzumab targeting HER2 and the toxin Amanitin, demonstrated extraordinary efficacy in the treatment of certain Triple-Negative Breast Cancers (TNBCs). HER2 is a surface protein that is overexpressed by breast cancer cells. TNBC cells do express HER2, albeit at a low level (HER2-low) that is not sufficient for treatment with Trastuzumab antibody or Kadcyla. In addition, about half of TNBC patients harbor the so-called 17p deletion, a mutation that allows cancer cells to bypass a special mechanism of cell protection, but also renders them especially sensitive to Amanitin.[1] TNBC patients with 17p-deleted tumors show a poorer response to standard therapies and have a significantly worse prognosis.

In the preclinical study, Trastuzumab-ATAC exhibited superior efficacy in treating HER2-low TNBC with a 17p deletion. Further, Trastuzumab-ATAC induced an immunogenic cell death of the tumor cells, a type of cell death that elicits an immune response. As a consequence, when combined with immune checkpoint blockade therapy in preclinical HER2-low breast cancer models mimicking TNBC, the efficacy of the Trastuzumab-ATAC treatment was greatly increased.

Andreas Pahl, Chief Scientific Officer at Heidelberg Pharma, commented: "We are delighted with the publication of these extraordinary data in the *Science Translational Medicine* journal. The Trastuzumab-ATAC is a novel treatment strategy in TNBC, an indication with high medical need. These patients do not benefit from currently available anti-hormonal or trastuzumab-based therapies because the tumors lack estrogen or progesterone receptors and also show very low expression of the HER2 protein, which is insufficient for approved HER2-targeting drugs. The synergies of our ATAC technology in combination with checkpoint inhibitors further highlights the potential of ATACs in the treatment of solid tumors."

The report abstract can be accessed at Science Translational Medicine.

[1] https://www.nature.com/articles/nature14418

About Heidelberg Pharma's proprietary ATAC technology

Antibody Drug Conjugates (ADCs) combine the high affinity and specificity of antibodies with the potency of cytotoxic small molecules for the treatment of cancer. Antibody Targeted Amanitin Conjugates (ATACs) are ADCs whose active ingredient is made up of Amanitin molecules. Amanitins are small bicyclic peptides naturally occurring in the death cap mushroom. They inhibit mRNA transcription by binding to RNA polymerase II, a mechanism that is crucial for the survival of eukaryotic cells. In preclinical testing, ATACs have been shown to be highly efficacious, overcoming frequently encountered resistance mechanisms and combating even quiescent tumor cells.

About Heidelberg Pharma

Heidelberg Pharma is an oncology company and the first company to develop the toxin Amanitin into cancer therapies using its proprietary Antibody Targeted Amanitin Conjugate (ATAC) technology and to advance the biological mode of action of the toxin as a novel therapeutic principle. This proprietary technology platform is being applied to develop the Company's proprietary therapeutic ATACs as well as in third-party collaborations to create a variety of ATAC candidates. The proprietary lead candidate HDP-101 is a BCMA ATAC for multiple myeloma.

Heidelberg Pharma AG has entered into partnerships to further develop and commercialize its clinical assets upamostat (formerly MESUPRON®) and TLX250-CDx (formerly REDECTANE®). Heidelberg Pharma AG is listed on the Frankfurt Stock Exchange: ISIN DE000A11QVV0 / WKN A11QVV / Symbol HPHA. More information is available at www.heidelberg-pharma.com.

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