

PRESS RELEASE

Results of Heidelberg Pharma's research cooperation with MD Anderson Cancer Center published in *Nature* journal

- **Subpopulation of colorectal cancers (CRC) is more vulnerable for therapy by ATACs because of a common genetic alteration**
- **Responsible for high subpopulation sensitivity is a hemizygous status of TP53 tumor suppressor gene and POLR2A gene, occurring in about 50% of CRC patients**
- **Patient stratification by gene status of TP53 or POLR2A could expand therapeutic window of ATACs significantly**

Munich, Germany, 23 April 2015 – WILEX AG (ISIN DE000A11QVV0 / WL6 / FSE) today announced that pioneering study results on the Antibody Targeted Amanitin Conjugates (ATACs) technology have been published in the peer-reviewed journal *Nature*, in a report by the Department of Cancer Biology, University of Texas MD Anderson Cancer Center and scientists of Heidelberg Pharma, a subsidiary of WILEX.

In preclinical studies, research groups from MD Anderson and Heidelberg Pharma demonstrated the extraordinary efficacy of ATAC therapeutics in the treatment of a colorectal cancer subpopulation with alterations in the status of the tumor suppressor gene TP53. The reason for these alterations is the co-deletion of one copy of TP53 and the neighbouring POLR2A gene, which codes for the ATAC-target RNA polymerase II. Such hemizygous gene status of TP53 and POLR2A leads to reduced expression of RNA polymerase II and thus the significantly higher sensitivity of cancer cells towards ATACs. In preclinical, *in vitro* and *in vivo*, studies ATACs exhibited an approximately ten times higher antitumoral activity on POLR2A hemizygous cancers compared to homozygous cancers. Initial data indicates similar gene status alterations in other tumors, making ATACs a promising therapeutic strategy for patients suffering from highly resistant malignancies. In a clinical setting the selection of patients based on TP53 or POLR2A gene status will allow the expansion of the therapeutic window of ATACs and ensure high efficacy while minimizing toxicity.

Professor Andreas Pahl, CSO of Heidelberg Pharma GmbH, commented: "The use of TP53 and POLR2A gene status as a biomarker for ATAC sensitivity could allow the stratification of patients most likely to benefit from treatment with ATACs. Patient selection with respect to payload sensitivity is a new approach in the field of antibody-drug conjugates (ADCs) and could help to circumvent the current limitations of this class of therapeutics."

Professor Xiongbing Lu, MD Anderson Cancer Center, said: "Today CRC patients with altered TP53 gene status have a non-favourable prognosis and only a few beneficial treatment options. With the discovery of POLR2A as a therapeutic target for p53 mutant tumors, ATACs could significantly improve the therapeutic outcome in such cancer populations."

The report abstract can be accessed at nature.com.

About Heidelberg Pharma's proprietary ATAC technology

Antibody-drug conjugates (ADCs) combine the high affinity and specificity of antibodies with the potential of small cytotoxic molecules for the treatment of cancer and inflammatory diseases. ATACs are ADCs based on highly potent amatoin payloads. Amatoxins are small bicyclic peptides naturally occurring in the Green Death Cap mushroom. Mode of action of amatoxins is the inhibition of mRNA transcription by binding to RNA polymerase II, a mechanism that is crucial for the survival of eukaryotic cells. Accordingly, ATACs exhibit comparable activity against proliferating and resting tumor cells. This proliferation independent activity differentiates ATACs from other ADCs, which preferentially target proliferating tumor cells. As an additional advantage ATACs could offer a substantial capability to overcome the resistance mechanisms that might limit the efficacy of other antibody drug conjugates.

About WILEX and Heidelberg Pharma

WILEX AG is a biopharmaceutical company which has a ready for partnering portfolio of antibody-based diagnostic and therapeutic Phase III product candidates for the detection and targeted treatment of clear cell renal cell carcinoma. Research and development focus on the operations of its subsidiary Heidelberg Pharma GmbH in Ladenburg, which primarily advances the development of the innovative platform technology for antibody drug conjugates (ADC technology) and provides pre-clinical drug discovery and development services. WILEX is listed at the Frankfurt Stock Exchange: ISIN DE000A11QVV0 / Symbol WL6. More information is available at www.wilex.com.

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