

VRG Therapeutics announces successful in vivo efficacy results of their CAR-T project targeting glioblastoma

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Therapeutics Plc. announces successful in vivo efficacy results of their CAR-T project with patented chlorotoxin analogue targeting glioblastoma, encouraging further development.

VRG Therapeutics (VRG Tx), a biotechnology R&D company focused on miniprotein pharmaceuticals and cellular & gene therapy (CGT) products has announced that their proprietary chlorotoxin (CTX) analogue, CTXA8, applied as a targeting molecule in chimeric antigen receptor T (CAR-T) cells, shows efficacy in an in vivo heterotopic glioblastoma murine model. CTXA8 has been developed leveraging VRG Tx's AI-powered

miniprotein platform. The promising preclinical results give a solid background to speed up the allogenic gamma-delta CAR-T ($\gamma\delta$ CAR-T) program. The company is committed to proceed with the project towards clinical development and is looking for a co-development partner with expertise in CAR-T preclinical and clinical development.

CAR-T therapy targeting brain tumors: CAR-T cells are modified white blood cells expressing a chimeric antigen receptor (CAR) against a specific tumor antigen that holds the potential of identification and elimination of cancer cells. The extraordinary therapeutic effect experienced with CAR-T cell therapies targeting hematological malignancies have drawn interest in developing similar products for solid tumors, including brain tumors. High overexpression of MMP2 protein on tumor cells is a recently utilized new target in CAR-T therapy in glioblastoma. The expected increased safety and efficacy of CTXA8-based CAR-T therapy can be explained by the enhanced affinity and selectivity of CTXA8 versus original CTX towards MMP2 overexpressing



tumors, such as glioblastoma.

VRG Tx's animal in vivo proof of concept (PoC) study: VRG Tx established a heterotopic xenograft mice model to demonstrate the effectiveness and safety of its CTXA8-targeting CAR-T cell therapy that is designed to treat patients with glioblastoma multiforme (a common type of brain tumor). The mouse model closely mirrors the clinical trial that is currently ongoing with CAR-T cells targeting the original CTX (NCT04214392, City of Hope Medical Center).

CTXA8-CAR-T cells showed effective tumor growth inhibition compared to non-specific T cell controls at three different dose levels. The highest dose of administered CTXA8-CAR-T resulted in over 60% inhibition of tumor growth including two individuals with complete tumor remission. The animals did not show any signs of toxicity or body weight loss during the study indicating promising safety features.

VRG Tx's allogenic CAR-T therapy targeting brain tumors: VRG Tx is currently looking for a co-development partner experienced in allogenic CAR-T development, to step into preclinical phase with its proprietary CTXA8 analogue applied in allogenic cell therapy applications. Based on the same MoA, in vitro results of VRG Tx's CTXA8- $\gamma\delta$ CAR-T cells show efficacy and high durability against glioblastoma multiforme cells.

About VRG Tx's Miniprotein platform utilizing ISEP and WISDOM technologies: VRG Tx's proprietary miniprotein technology leverages artificial intelligence (AI) and pioneers in protein engineering to create CGT and peptide-based applications. The Wetlab-verified In Silico Design of Miniproteins (WISDOM) and Individual Sequence Enrichment Pattern (ISEP) technologies build on the evolutionary conserved structures of natural peptides and applies both in silico and in vitro high throughput screenings. Combining AI-powered interaction modelling with NGS-based advanced analytics, VRG Tx designs novel therapeutic candidates with unprecedented selectivity and affinity in an extremely fast discovery process. Miniproteins combine the benefits of small molecules and biologics.

About VRG Tx: VRG Therapeutics is an original biopharmaceutical research and development company located in Budapest, Hungary. VRG Tx's vision is to leverage its unique miniprotein ISEP and WISDOM technologies to create cure for diseases through targets and mechanisms of action that are beyond the reach of conventional biopharma approaches. For more information, please visit www.vrgtherapeutics.com.

Zalán Péterfi, PhD - Managing Director

VRG Therapeutics Plc.

zalan.peterfi@vrgtherapeutics.com

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