GEMoaB Monoclonals GmbH
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GEMoaB: next-generation immunotherapies for hard-to-treat cancers

GEMoaB's three proprietary technology platforms have produced a deep pipeline of immunotherapy assets, three of which are currently being investigated in clinical studies, providing the basis for future growth.

Despite great progress in cancer therapy over the past two decades, more effective treatments for late-stage cancers and other hard-to-treat tumor types are urgently required. GEMoaB, a privately owned clinical-stage biopharmaceutical company based in Dresden, Germany, is working to fill that gap with next-generation immunotherapies to treat patients with currently unmet needs in cancer and beyond.

GEMoaB was formed in 2011 and today has a deep pipeline of next-generation immunotherapies, three of which are being trialled in a range of cancer indications, and a significant number of preclinical candidates for solid tumors and hematological malignancies. GEMoaB's immunotherapies are built around three proprietary platforms: two based on chimeric antigen receptor T cells (CAR-T cells) named UniCAR and RevCAR, and another employing GEMoaB's Affinity-Tailored Adaptors for T cells (ATACs), all of which offer significant advantages over existing immunotherapies.

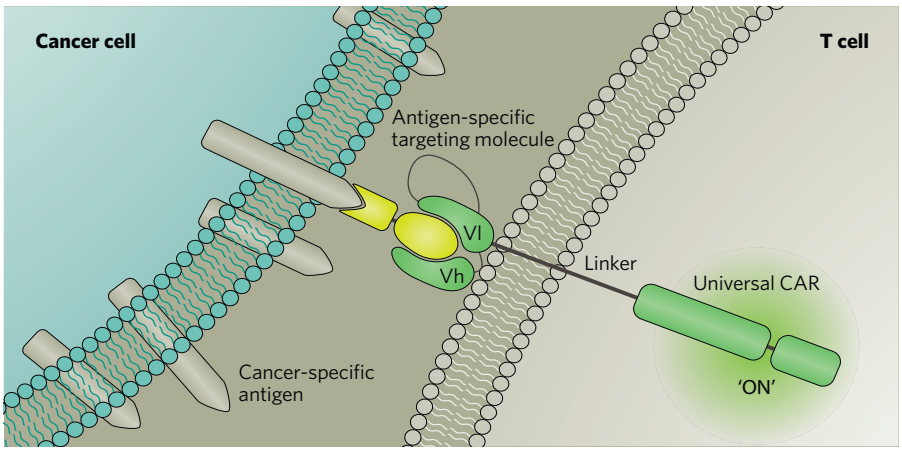

Fig. 1 | The UniCAR platform. The rapidly switchable UniCAR system consists of two components: a genetically modified CAR-T cell with a universal chimeric antigen receptor (Universal CAR) and a soluble adaptor termed the targeting molecule (TM).

Dual-controlled UniCAR

UniCAR is a universal CAR-T platform that can be rapidly turned on and off with a switch consisting of two components. The first is a genetically modified T cell with a chimeric antigen receptor that by itself does not recognize tumor antigens and is therefore not directly activated by them. The second component is a targeting module (TM), a soluble adaptor that comprises a motif recognized by the UniCAR's receptor and a highly flexible antigen-binding moiety directed against a cancer antigen (Fig. 1).

TMs efficiently penetrate and accumulate in bone marrow and solid tumor tissue. When TMs simultaneously bind to the UniCAR receptor and the target antigen on a cancer cell, the UniCAR effector T cells become activated and expanded, and then lyse the cancer cells. Crucially, TMs have a short half-life and are rapidly internalized, so UniCAR cells rapidly revert to an 'off' state in less than 4 hours, which avoids acute and long-term toxicity usually associated with continuous activation of CAR-T cells. In addition, preclinical data suggest that lysis of cancer cells by UniCAR cells occurs at lower doses of TM than the induction of cytokine release, which is responsible for typical CAR-T-related side effects. By achieving effective killing of cancer cells without excessive release of potentially toxic cytokines, UniCAR offers an improved therapeutic window for clinical applications.

UniCAR-T-CD123, GEMoaB's lead asset based on the UniCAR platform, is directed against the CD123 antigen and is being developed for the treatment of relapsed/refractory acute myeloid leukemia (rrAML) and acute lymphocytic leukemia (rrALL). UniCAR-T-CD123 is currently being investigated in a phase 1a dose-finding study, with initial clinical results expected by the second half of 2020. GEMoaB is also developing UniCAR-T-PSMA, which targets prostate-specific membrane antigen (PSMA) for the treatment of castration-resistant prostate cancer (CRPC) and other PSMA-expressing solid tumors. A phase 1a trial of UniCAR-T-PSMA in CRPC and other solid tumors is planned to begin enrollment in the second half of 2020.

RevCAR, GEMoaB's second cellular immunotherapy platform, is similar to UniCAR in featuring a rapid switch system, but with a different design. Whereas the UniCAR receptor consists of a single-chain variable fragment (scFV) domain that binds to a TM, RevCAR employs a CAR with an inert peptide attached. RevCAR TMs consist of a highly flexible antigen-binding moiety linked to a scFv domain that binds to the inert peptide attached to the CAR of the RevCAR effector T cell. After proof-of-concept, GEMoaB expects to develop RevCAR in future oncology and non-oncology indications.

Progress and partnering

GEMoaB's ATACs are fully humanized antibodies that combine a domain with high affinity for tumor antigens with a domain that binds with lower affinity to the CD3 antigen on effector T cells. In preclinical models, ATACs, with their low-affinity CD3 binding, were shown to activate effector cells without T cell auto-activation, promising a best-in-class safety profile. Two ATAC assets are now in clinical trials: GEM333, which binds to the CD33 cancer antigen, is in a phase 1a study for the treatment of CD33-positive rrAML; and GEM3PSCA, which binds to the prostate stem cell antigen (PSCA), is being tested in a phase 1a study for a range of PSCA-expressing metastatic solid cancer indications. Both GEM333 and GEM3PSCA are being developed under a global partnership agreement with Bristol Myers Squibb.

GEMoaB welcomes discussions with potential investors about further advancing and accelerating the company's clinical development programs and pipeline based on proof-of-concept data from the phase 1a trial of UniCAR-T-CD123. In addition, GEMoaB is seeking new partnerships with companies with a presence in the USA or Asia and access to relevant oncology clinical infrastructure to collaborate on the clinical development of GEMoaB's assets, as well as research companies with the expertise to help to further expand the optionality of GEMoaB's technology platforms.

CONTACT
Michael Pehl, Chief Executive Officer
GEMoaB Monoclonals GmbH
Dresden, Germany
Tel: +49 351 4466 45030
Email: m.pehl@gemoab.com