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Leveraging the full power of T cells to fight solid tumors

Trans-Atlantic biopharmaceutical company, Immatics, is poised to unlock and deliver innovative T cell-based therapies to cancer patients by harnessing two proprietary technology platforms for its own pipeline, and for collaborations with world-leading partners.

Immatics is a clinical-stage biopharmaceutical company at the forefront of the discovery and development of T cell–based immunotherapies to treat cancer. Its mission is to open new therapeutic avenues for cancer patients with high medical need, with a focus on solid tumors. Founded in Tübingen, Germany in 2000, the Nasdaq-listed company has developed two proprietary technology platforms feeding a pipeline of seven wholly-owned Adoptive Cell Therapy (ACT) and TCR Bispecific product candidates, of which three ACT candidates are in clinical trials. Immatics is also developing 10 programs in partnership with major industry players, including Bristol Myers Squibb, Amgen, Genmab, and GlaxoSmithKline.

The company's technology platforms combine the discovery of novel cancer targets through XPRESIDENT with the development of the right T cell receptors (TCRs) through XCEPTOR, for its ACT and TCR Bispecifics programs.

"Immatics has identified and characterized a trove of novel intracellular targets presented on tumors to develop its cancer immunotherapies," said Carsten Reinhardt, Immatics' Chief Development Officer. "We aim to leverage our drug discovery advantage for our own proprietary pipeline, as well as for our collaborations with world-leading partners."

Immatics' targeted approach to fight solid tumors includes two therapeutic modalities: Adoptive Cell Therapies (ACT) and TCR Bispecifics. In a first wave to tackle solid cancers, Immatics recently presented early signs of anti-tumor activity for its clinical ACT programs. In parallel, the company is also at the forefront of advancing its TCR Bispecifics programs.

Advancing off-the-shelf solutions

Immatics' TCR Bispecifics molecules, called TCERs (T Cell Engaging Receptors), have the potential to treat tumors at all stages of disease and could therefore address a broad patient population.

TCERs are engineered, antibody-like molecules that leverage the body's immune system by redirecting and activating T cells towards cancer cells expressing specific tumor targets. The design of these novel biologics potentially allows any T cell in the body to become activated and attack the tumor, regardless of their intrinsic specificity.

TCER molecules consist of two binding regions that can empower T cells to selectively kill cancer cells. The first region—the TCR domain—specifically binds to a target that is presented on the tumor cell surface by human leukocyte antigens (HLAs). Once the TCER molecule is bound to the tumor cell, T cells are recruited to the tumor utilizing its second region—the T cell recruiter domain—that enables binding to a T cell surface antigen, resulting in the activation of these T cells against the tumor. Affinities of both regions are optimized in relation to each other, with the goal of producing efficient anti-tumor efficacy minimizing systemic side effects (Fig. 1).

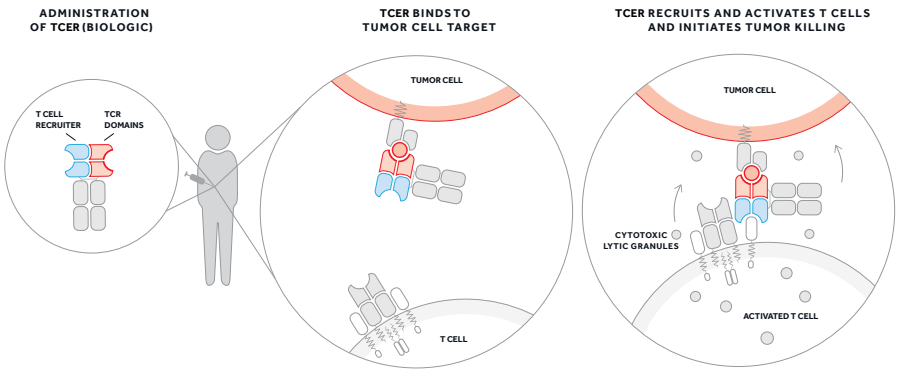

Fig. 1 | Immatics' TCR Bispecifics molecules. Schematic describing the mechanism of action of Immatics' TCR Bispecifics molecule recruiting and activating T cells to fight cancer cells.

The TCER molecules are designed to exhibit a long functional half-life in the patient's bloodstream to achieve clinical activity without the need for daily or continuous intravenous application. The goal of these modular biologics is to enable the efficient exchange of binding regions, and providing cost-effective manufacturing and immediate off-the-shelf availability for patient treatment.

> "Immatics' targeted approach to fight solid tumors includes two therapeutic modalities: Adoptive Cell Therapies and TCR Bispecifics

Unlocking immunotherapies across indications

Immatics is generating a pipeline of TCER molecules with currently two product candidates, called IMA401 and IMA402, in advanced preclinical development. Both compounds have been well characterized in preclinical safety and efficacy studies, showing a favorable safety profile and significant tumor growth inhibition in vitro and in vivo, including complete remissions in different tumor cell lines and patient-derived (PDX) mouse models.

The lead product candidate, IMA401, targets the cancer testis antigens MAGEA4 and/or A8 (melanoma-associated antigen A4 and/or A8), which are expressed at significant levels on tumors present in the lung, head and neck, bladder, and esophagus of cancer patients. IMA402 targets PRAME (preferential antigen in melanoma), which is highly prevalent and homogenously expressed in a multitude of cancer indications, including melanoma, breast, uterine, and ovarian cancer.

The first-in-human clinical trial with IMA401 is planned to start recruitment in the first half of 2022 while IMA402 is currently undergoing GMP process development activities. Within the next five years, Immatics aims to change the treatment paradigms of patients with different solid cancers by a targeted application of its ACT or TCR Bispecifics.

"With the excellent profile seen with our first TCER preclinical program and having reached preclinical proof-of-concept with our second TCER program, we are well on our way to the clinic," Reinhardt said. "We are excited about the potential of delivering the power of T cells to patients in need, and continuing to harness our TCER biologics to advance the next wave in cancer immunotherapy."

CONTACT
Anja Heuer
Director Corporate Communications
Immatics Biotechnologies GmbH
Munich, Germany
Tel: +49 89 540415 606
Email: anja.heuer@immatics.com