



## TILT Biotherapeutics

tiltbio.com

# Next-generation armed oncolytic immunotherapies

**Aiding the immune response in the fight against cancer, TILT Biotherapeutics is developing armed oncolytic viruses that replicate in cancer cells making them more discoverable by T cells and other immunotherapies.**

Effective treatments are sorely needed for solid tumors, which make up more than 90% of cancers. TILT Biotherapeutics, a clinical-stage biopharma company, is developing a solution.

TILT was founded on the unique discovery from clinical observations that oncolytic adenoviruses potently engage T cell responses in cancer patients. Successfully translating this discovery, the company's therapeutic approach revolves around the use of armed oncolytic adenoviruses that replicate only in cancer cells and, when they do so, modify the tumor microenvironment, restoring the ability of the immune system to eliminate aberrant cells.

"We are not targeting specific tumor cells, but instead the out-of-control growth that makes cancer cancer," explained TILT's founder and CEO Akseli Hemminki. "Our oncolytic viruses better enable T cells to search out and destroy cancer cells of all tumor types, as the immune system inherently adapts to fight potential hazards."

In addition to direct lytic effects through viral replication, the presence of a virus in the tumor activates pathogen-associated molecular pattern receptors. These signals are intensified by cytokines, significantly increasing the recruitment and activation of T cells. Once released from ruptured tumor cells, the viruses can travel through the blood system to tumors elsewhere in the body.

"Not only does this approach synergistically improve the efficacy of other T cell-based immunotherapies, it also enables these treatments in solid tumors that otherwise would not respond to available immunotherapies—a significant unmet medical need and market opportunity," said Hemminki.

### Promising pipeline

Adenoviruses, which have been used safely in clinical trials involving thousands of participants, have several class advantages over other viruses with oncolytic potential. In addition to their natural interaction with T cells—a predominant part of the immune system in clearing potential threats—they can be manufactured at high-titer as homogeneous drug batches, are more stable than RNA viruses, and are easy to store. Moreover, TILT's oncolytic viruses encoding a variety of cytokines can be delivered either directly to tumors or intravenously, and have applicability across a wide range of cancer indications. TILT is building a pipeline of innovative cancer immunotherapies tailored to trigger different immune mechanisms, to treat a variety of solid tumors, including melanoma, head and neck cancer, and cancers of the ovary, lung and pancreas.

The company's lead candidate, TILT-123, is an adenovirus armed with two human T cell-stimulating



cytokines: tumor necrosis factor-alpha (TNF $\alpha$ ), which recruits T cells into the tumor and also has its own anti-tumor effects; and interleukin-2 (IL-2), which is important for retaining high T cell activity at the tumor. Producing TNF $\alpha$  and IL-2 locally in the tumor should also obviate the need for high-dose prechemotherapy and postconditioning IL-2 (currently required in other promising immunotherapeutic regimens).

In various in vivo preclinical cancer models, TILT-123 has demonstrated a 100% survival rate, shown it can transduce tumors, and is able to heat up immunologically cold tumors. "Our armed adenovirus is uniquely designed to make silent tumors visible to the immune system, enabling T cell therapies and checkpoint inhibitors to work," said Akseli Hemminki.

Two ongoing phase 1 clinical trials, one studying TILT-123 as monotherapy and one studying TILT-123 as monotherapy and as combination with tumor infiltrating lymphocyte therapy, are approaching completion of the dose escalation. Interim clinical data from these studies show TILT's approach to be safe and highly tumor specific, and support further development of the candidate. Phase 1 clinical trials in the USA and Finland have been approved for testing TILT-123 in combination with immune checkpoint inhibitors for treating ovarian cancer and cancers of the head and neck. The company also has a pipeline of preclinical candidates in a range of solid tumors, including pancreatic, breast and sarcoma.

### Present and future partnering

TILT's approach has been validated through several partnerships, including collaborations with Merck KGaA and Pfizer (Merck-Pfizer Alliance)

to investigate TILT-123 in combination with the checkpoint inhibitor Bavencio (avelumab); with Merck & Co., Inc. to explore the combination of TILT-123 with the checkpoint inhibitor Keytruda (pembrolizumab); and with Biotheus Inc. for the development of TILT-123 in Greater China.

TILT is looking for global partners for later-stage development and commercialization of its candidates. It is open to collaborations with pharmaceutical companies keen to enhance the therapeutic efficacy of chimeric antigen receptor T cells (CAR-T) and other cancer immunotherapies, and/or those interested in commercializing TILT's pipeline.

"Our best-in-class oncolytic adenoviruses, armed with T cell-modulating molecules, are engineered to be potent, targeted and safe," said Hemminki. "By significantly boosting the body's ability to fight cancer and considerably enhancing T cell therapy of solid tumors, we are set to benefit the majority of patients who do not currently receive long-term positive effects from available immunotherapy drugs."

#### CONTACT

TILT Biotherapeutics  
Helsinki, Finland

Victor Cervera-Carrascón  
Head of Immunology  
Email: victor@tiltbio.com

Aino Kalervo  
Chief Business Officer  
Email: aino@tiltbio.com