OncoImmune, Inc.
www.oncoimmune.com

Immunotherapy drug development powered by deep biology insights

Guided by long-term scientific research and in-depth biology insights, OncoImmune develops novel immune-modulators targeting innate checkpoint mechanisms involving CD24–Siglec10 signaling as well as potential best-in-class anti-CTLA-4 antibody therapy that can separate its therapeutic effect from toxicity. The company is looking for partners to drive clinical development and commercialization.

Clinical-stage biopharmaceutical company OncoImmune develops first-in-class and best-in-class cancer therapeutics and is pioneering new pathways with the goal of developing safer and more efficient immunotherapies than those on the market.

OncoImmune has a rich pipeline of immunotherapy products that are moving through clinical and preclinical testing, and the company is looking for strategic partners and investors to support further programs from preclinical stages through to late-stage clinical development.

Improving GVL while reducing GVHD

OncoImmune's lead product is CD24Fc, a first-in-class recombinant fusion protein in development for the prophylactic treatment of graft-versus-host disease (GVHD) that preserves or enhances the graft-versus-leukemia (GVL) effect in patients with leukemia undergoing hematopoietic stem cell transplantation (HSCT).

In 2009, OncoImmune's founders identified a signal transducer molecule, CD24, which suppresses inflammation by binding to a pattern recognition receptor called Siglec10. They further determined that CD24 also binds to several danger-associated molecular patterns (DAMPs), helping reduce the host response to these factors. Preclinical studies demonstrated that CD24Fc reduces GVHD by binding both DAMPs and Siglec10, reducing the overall inflammatory response.

After completing a phase 1 clinical trial for safety in healthy volunteers, OncoImmune has recently completed a phase 2 trial to evaluate the addition of CD24Fc to standard of care acute GVHD prophylaxis in leukemia patients undergoing HSCT. Preliminary clinical evidence from the study suggests that CD24Fc greatly improves outcomes in patients with leukemia by improving GVHD-free survival, overall survival and relapse-free survival, and reduces conditioning toxicity. The company has received orphan drug designation for CD24Fc in the US and Europe, and is planning to prove clinical efficacy of CD24Fc in HCT in a pivotal phase 3 clinical trial. Meanwhile, OncoImmune is expanding oncology indications of CD24Fc, including toxicity associated with chemotherapy, radiotherapy and immunotherapy.

Anti-CTLA-4 antibodies: version 2.0

The approval in 2011 by the US Food and Drug Administration of the first cytotoxic T lymphocyte protein 4 (CTLA-4) antagonistic antibody, Bristol-Myers Squibb's ipilimumab, for the treatment of melanoma, ushered in the concept of treating cancer by blocking immune tolerance checkpoints to fight tumors.

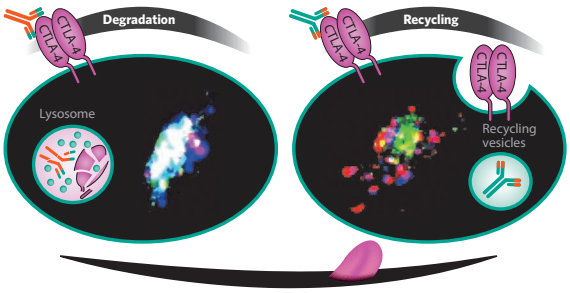

Fig. 1 | Separating therapeutic effect from toxicity for anti-CTLA-4 antibody. pH-sensitive anti-cytotoxic T lymphocyte protein 4 (CTLA-4) antibodies preserve the CTLA-4 immune checkpoint and allow more effective regulatory T cell elimination within the tumor microenvironment, while pH-insensitive antibodies cause degradation of CTLA-4 and subsequent loss of the protective function of CTLA-4 against autoimmune diseases.

Under normal conditions, immune checkpoints such as CTLA-4 help keep the immune system under control to pre-empt autoimmunity and other negative effects of a highly activated immune system. Inactivation of CTLA-4 function by the anti-CTLA-4 antibodies in the clinic can cause high rates of immunotherapy-related adverse events (irAEs). These events could be attributed to the destruction of the CTLA-4 immune checkpoint molecule (**Fig. 1**).

OncoImmune cofounders Yang Liu and Pan Zheng tackled this problem by determining that the irAE mechanisms of CTLA-4-targeting antibodies could be isolated from the drugs' cancer immunotherapeutic effect (CITE). Their work established that irAE and CITE are mediated by distinct mechanisms and could be uncoupled by screening for and engineering antibodies with a strong CITE but minimal irAE.

ONC-392 is OncoImmune's lead antibody in this program. ONC-392 targets CTLA-4 in a way that selectively eliminates tumor-infiltrating regulatory T cells without affecting peripheral T cell activation by a mechanism illustrated in **Fig. 1**. Compared with commercial and other clinical-stage anti-CTLA-4 antibodies, ONC-392 had a more robust CITE and dramatically reduced irAE in preclinical studies. OncoImmune plans to file an investigational new drug (IND) application for ONC-392 and begin a phase 1 clinical trial in the second half of 2019.

ONC-781: novel cancer target

OncoImmune is also searching for new therapeutic targets. The company's most advanced program in this area is ONC-781, a monoclonal antibody (mAb) against a previously undescribed glycosylation-regulated epitope that is highly expressed on cancer cells. Critical to the therapeutic potential of this proprietary target is that in normal tissues, the epitope is masked by *O*-glycosylation, eliminating the risk of nontumor binding by the mAb and any related side effects.

ONC-781 binds to all major types of cancer tissue, in particular some hard-to-treat cancers of the central nervous system, lung cancer, ovarian cancer and hepatocellular carcinoma. The company has generated a humanized, affinity-matured version of ONC-781 to develop bispecific antibodies and chimeric antigen receptor T cells and test for an optimal therapeutic strategy, and has started the process of prioritizing a cancer indication or indications for clinical development.

Partnering at all stages

OncoImmune has a robust pipeline, deep biology insights into CD24–Siglec and CTLA-4 signaling, and a very flexible approach to partnering. It is looking for strategic partners and/or investors for the late-stage clinical development and commercialization of CD24Fc and to move other assets into the clinic. According to Yang Liu, OncoImmune's founder, president and CSO, "by preserving immune tolerance mechanisms of the cancer patients while focusing immune destructive force on cancer cells, safer and more effective cancer immunotherapies may emerge from the horizon."

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