Immunitas Therapeutics Presents New Data for TLR9 Agonist Conjugate at the Society for Immunotherapy of Cancer 2023 Annual Meeting

In vitro proof-of-concept data shows effective delivery of CpG to endosomal TLR9 via anti CLEC2D antibody, resulting in sustained myeloid and B cell activation, enabling induction of stronger T cell responses

WALTHAM, Mass., November 3, 2023 – Immunitas Therapeutics ("Immunitas"), a clinical stage precision immunotherapy company committed to discovering and developing novel, differentiated therapeutics for patients with cancer, today presented the first proof-of-concept data on its second program, a myeloid and B cell modulating anti CLEC2D-Toll-like receptor 9 (TLR9) agonist conjugate, at the Society for Immunotherapy of Cancer's 38th Annual Meeting (SITC 2023), held November 1-5 in San Diego, California.

CLEC2D is a C-type lectin-like protein that is broadly expressed on a subset of immune cells and is naturally internalized by myeloid and B cells. Upon internalization, it can act as a vehicle to deliver histone/DNA complexes to endosomal TLR9, stimulating inflammatory responses. Harnessing this CLEC2D-mediated internalization offers a compelling immunotherapy approach of delivering CpG to TLR9 that can stimulate inflammatory responses with the potential to improve recruitment of functional T and NK cells into tumor tissues.

"The inability to induce adequate responses in tumors with poor T and NK cell infiltration has limited the clinical impact of existing immunotherapies. At Immunitas, we prioritize targeting novel biological pathways with first-in-class molecules that have potential to show monotherapy efficacy in early clinical development. This program leverages our specialized knowledge of the CD161-CLEC2D pathway, and we are excited to be progressing a therapeutic with demonstrated potential to address the challenge of poor T and NK cell infiltration and truly benefit patients who lack immunotherapy options," said Amanda Wagner, President and Chief Executive Officer of Immunitas Therapeutics. "We are pleased to have our team present this data demonstrating in vitro proof-of-concept for our anti-CLEC2D antibody conjugated to a CpG oligonucleotide."

The presented data showed that treatment with Immunitas' anti CLEC2D-TLR9 agonist immune stimulating antibody complex (ISAC) induced pro-inflammatory responses in THP1-TLR9 reporter cell lines and dramatically increased production of IFN-α, a critical cytokine for induction of anti-tumor T cells, in human plasmacytoid dendritic cells. Treatment of CLEC2D-expressing B cells with the ISAC molecule resulted in sustained B cell proliferation and upregulation of co-stimulatory molecules, enabling stronger induction of T cell immune responses.

The results further confirmed that CLEC2D is expressed on tumor-associated macrophages (TAMs)—macrophages that strongly contribute to the immunosuppression in tumor microenvironments and can also directly promote tumor cell growth. Treatment of TAMs with Immunitas' anti CLEC2D-TLR9 agonist ISAC reversed TAM-mediated suppression of T cell proliferation and activation, indicating that TLR9 agonism can reprogram TAMs towards an inflammatory state. Studies in human peripheral blood mononuclear cells (PBMCs) has demonstrated that treatment with the anti CLEC2D-TLR9 agonist ISAC did not trigger release of inflammatory cytokines, providing a preliminary indication of safety.

The presentation will be available on the Immunitas website following the meeting.

Presentation Details for SITC 2023

Title: Anti CLEC2D-TLR9 agonist conjugate binds to and internalizes CLEC2D on myeloid cells, plasmacytoid DCs and B cells leading to robust TLR pathway activation and inflammatory cytokine production

Abstract Number: 1131

Date/Time: Friday, November 3, 2023, 9:00am – 7:00pm PDT

About CLEC2D

CLEC2D is a C-type lectin-like protein broadly expressed on a subset of immune cells and tumor cells. It is also the ligand for CD161, target for Immunitas' lead investigational candidate, IMT-009. Additionally, CLEC2D naturally internalizes in TLR9 expressing myeloid and B cells. Building on this biology, Immunitas is developing a novel anti CLEC2D-TLR9 agonist immune stimulating antibody complex (ISAC) comprising a fully human anti-CLEC2D antibody conjugated to a CpG oligonucleotide. This CLEC2D-TLR9-ISAC molecule is capable of

triggering TLR9 pathway activation in myeloid cells, B cells, and plasmacytoid dendritic cells and enabling induction of sustained T cell immunity. Harnessing this biology offers a compelling immunotherapy approach that stimulates inflammatory responses that may improve recruitment of functional T and NK cells in tumors with otherwise poor T cell infiltration.

About Immunitas Therapeutics

Immunitas is a clinical stage precision immunotherapy company committed to discovering and developing novel, differentiated treatments for patients with cancer. A focus on human data, combined with fully integrated internal R&D capabilities and parallel discovery efforts, allows Immunitas to start with and stay closer to the most relevant and translatable biology for patients, accelerating the timeline from discovery to the clinic. The Immunitas discovery engine combines deep expertise in single-cell genomics with customized machine learning approaches to elucidate immune cell populations that are key actors in immuno-oncology. The company was founded by Longwood Fund with leading scientists from Dana-Farber, MGH, the Broad, and MIT. Since being founded in 2019, Immunitas has raised a total of $97 million in venture funding from a strong syndicate of investors including Agent Capital, Alexandria Venture Investments, Evotec, Leaps by Bayer, Longwood Fund, M Ventures, Medical Excellence Capital, and Novartis Venture Fund. To learn more, visit www.immunitastx.com.

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