Data from ImmunoGenesis' Lead Programs Presented in Six Posters at Society for Immunotherapy of Cancer (SITC) Conference

HOUSTON, TX, November 15, 2021 – ImmunoGenesis, a clinical-stage biotechnology company developing science-driven immune therapies, announced today that preclinical data from its lead development programs were presented in six scientific posters at the Society for Immunotherapy of Cancer 36th Annual Meeting (SITC 2021), which was held November 10-14, 2021, in Washington, DC. The preclinical results presented advance the development of ImmunoGenesis' immunotherapy programs.

"We are very pleased to have data from our programs presented at SITC," said James Barlow, ImmunoGenesis President and CEO. "These strong study findings support our development programs focused on creating therapies that target cold cancers—including pancreatic cancers—refractory to currently available immunotherapy. We look forward to further building upon these successful results with the advancement of our drug candidates as we look to enter clinical trials next year."

Posters Related to IMGS-001: PD-L1/PD-L2 Dual-Specific Antibody with Effector Function

Human PD-L2 triggers a unique T cell inhibitory program through PD-1 engagement distinct from that of PD-L1

Using a T cell line with an NFAT reporter, this study validated that human PD-L2, unlike murine PD-L2, generates a purely co-inhibitory signal in human T cells, albeit with a reduced inhibitory potential relative to PD-L1. Further, preliminary data in a syngeneic murine model of EL4 showed that antibody dependent cellular cytotoxicity capable PD-L2 blocking antibodies are therapeutically superior to PD-L1 or PD-L2 blockade alone. The study was the first demonstration of T cell immunoregulatory functions of PD-L2, which are distinct from those of PD-L1, and demonstrate that the more tumor-selective expression pattern of PD-L2 relative to PD-L1 provides a therapeutic advantage to effector-function capable PD-L2 antibodies.

Dual-specific antibodies blocking both PD-L1 and PD-L2 engagement of PD-1 restore anti-tumor immunity

This study investigated the capacity of monoclonal antibodies capable of bivalent binding to both PD-L1 and PD-L2 to restore the function of PD-1-suppressed T cells *in vitro*. The study also evaluated whether enhancing the cytotoxic effector function of these bispecific antibodies might further enhance their efficacy through the depletion of tumor cells and supportive stroma. Results indicated that these bispecific antibodies restore the function of PD-1-suppressed T cells with equivalent efficiency to pembrolizumab. ADCC-capable PD-Ligand bispecific antibodies suppress the growth of U2940 lymphoma in immunodeficient mice more efficiently than Rituximab, and in a syngeneic model of PD-L1/PD-L2 double positive colon carcinoma, these antibodies demonstrate superiority to PD-1 blocking antibodies to limit tumor growth and increase survival. This study showed that ADCC-capable PD-Ligand bispecific antibodies display higher therapeutic potential than existing anti-PD-1 antibodies and represent a new class of PD-1 pathway therapeutics with significant potential for the treatment of a variety of human cancers.

Posters Related to IMGS-501: STING Immune Stimulating Antibody Conjugate (STING-ISAC)

High-potency synthetic STING agonists rewire the myeloid stroma in the tumor microenvironment to amplify immune checkpoint blockade efficacy in refractory pancreatic ductal adenocarcinoma

This study profiled myeloid-derived suppressor cell (MDSC) and M2 macrophage function following stimulation with cyclic dinucleotides (CDNs) of ascending potency using RNA sequencing and protein arrays to uncover molecular and cellular mechanisms by which stimulator of interferon genes (STING) agonists reprogram the suppressive myeloid stroma to drive proinflammatory conversion of tumor myeloid stroma to sensitize tumors to immune checkpoint blockade. For the first time, this study concluded that synthetic CDN STING agonists affect MDSC and M2 macrophage repolarization, in part through altering metabolism and c-Myc signaling. Lastly, the study demonstrated the potential for high-potency STING agonists to overcome resistance to checkpoint blockade in an aggressive orthotopic tumor model of pancreatic ductal adenocarcinoma.

Intratumoral delivery of high potency STING agonists modulates the immunosuppressive myeloid compartment and induces curative responses in checkpoint-refractory glioblastoma models

This study utilized the synthetic cyclic di-nucleotide STING agonists IACS-8803 (8803) and ML-RR-S2-CDA (MLRR) to assess survival and tumor immune infiltrate functional reprogramming in two orthotopic transplantable human and murine glioblastoma tumor models, U87 and the recently developed QPP8 ($QKi^{-/-}$ $Pten^{-/-}$ $P53^{-/-}$). The study concluded that STING agonists prolong survival in human and murine orthotopic models of glioblastoma. This prolonged survival is associated with a decrease in immunosuppressive M2 functional markers in human tumor infiltrating myeloid populations. Additionally, M2-polarized microglia demonstrated a reduction in M2 functional markers and upregulation of proinflammatory M1 markers following treatment with STING agonists. Together these results indicate that delivery of STING agonists can induce proinflammatory repolarization of the glioblastoma myeloid stroma, including both infiltrating myeloid populations and brain-resident microglia, to drive prolonged survival in refractory models of glioblastoma.

Posters Related to Evofosfamide Hypoxia-Reversal Agent in Combination with Checkpoint Inhibitors

Disrupted oxygen supply and tumor hyper-oxygen consumption contribute independently to prostate cancer immune privilege

This study investigated the capacity of two mitochondrial complex I inhibitors to reduce tumor oxidative metabolism, diminish myeloid suppressive capacity, and improve anti-tumor T cell immunity, alone and in combination with evofosfamide and checkpoint blockade to sensitize unresponsive tumors to immunotherapy. This study found that while evofosfamide or inhibition of oxidative metabolism alone did not significantly impact tumor regression, dual combination and triple combination with checkpoint blockade led to a significant reduction in tumor burden. Conclusions indicate that tumor hypoxia and associated immune suppressive programming can be reduced through both local tissue remodeling and limitation of tumor oxygen metabolism. Complex I inhibition selectively inhibits tumor and myeloid cell function, while sparing T cells. This provides opportunities to craft synergistic immuno-metabolic therapies with the potential to treat cold tumor patients refractory to current FDA approved immunotherapeutics.

Hypoxia reduction in tandem with anti-angiogenic therapy remodels the PDAC microenvironment and potentiates CD40 agonist therapy

In this study, evofosfamide (TH-302, IMGS-101) and a vascular endothelial growth factor receptor-2 (VEGFR-2) blocking antibody were used to treat several syngeneic murine models, including orthotopic pancreatic cancer and a transplantable model of prostate cancer. The researchers concluded that evofosfamide and DC101 utilize unique yet complementary mechanisms to improve the survival of mice challenged with pancreatic or prostate tumors. This combination relieves hypoxic stress and simultaneously reinvigorates T cell function and reduces macrophage mediated immunosuppression. In this setting, CD40 agonist therapy provides an additive benefit in prolonging mouse survival. Put together, these data indicate that targeted reduction of hypoxia with anti-angiogenic therapy remodels the tumor microenvironment and enhances immunotherapy responses in PDAC.

About IMGS-001 PD-L1/PD-L2

ImmunoGenesis' lead program is IMGS-001, a PD-L1/PD-L2 dual-specific inhibitor with an engineered cytotoxic effector function. As the first molecule to target PD-L2 in addition to PD-L1, IMGS-001 has the potential to shut down the entire PD-1 pathway, potentially providing superior blockade compared to other PD-1 or PD-L1 inhibitors. The built-in engineered effector function allows IMGS-001 to kill immunosuppressive cells that express PD-L1 and/or PD-L2. Preclinical data showed that IMGS-001 offered five times the response rate in cold tumors than currently available immunotherapies. Additionally, IMGS-001 can provide a foundation for add-on therapies.

About IMGS-501 STING-ISAC

STING-ISAC builds on ImmunoGenesis' novel platform PD-L1/PD-L2 inhibitor by conjugating a STING agonist to the antibody, combining an optimal PD-1 pathway blockade with a powerful immune agonist. ImmunoGenesis is developing this agent to effectively and systemically transport the intravenously delivered STING agonist to all tumor sites and targets within the tumor microenvironment. This therapeutic advance pushes through an important barrier seen with traditional STING agonists, which consistently produce an effect only at the site of the intratumoral injection. ImmunoGenesis' STING-ISAC, delivered intravenously, could precisely target where it is most effective across tumor sites.

About Evofosfamide

ImmunoGenesis has extended its program to include the hypoxia-reversal agent evofosfamide. Hypoxia predicts poor outcomes in patients across tumor types, as it suppresses T-cell

immunity in the tumor microenvironment. Evofosfamide reduces hypoxia by a tissue-remodeling process that includes replacement of disrupted tumor vasculature with fully functional new vessels, allowing for restoration of T-cell infiltration into previously hypoxic zones. Prior Phase 1 data of evofosfamide in combination with ipilimumab resulted in an overall response rate of 17% and a disease control rate of 83% across four dose levels in 21 heavily pre-treated patients with advanced cancer. While not the primary target, this hypoxia-reversal agent sensitizes tumors for checkpoint inhibition and is on target to be in clinic in combination with immune checkpoint blockades in 2022.

About ImmunoGenesis, Inc.

ImmunoGenesis is a clinical stage immuno-oncology biopharmaceutical company re-envisioning "cold" tumor treatment. Representing more than half of all cancers, cold tumors lack activated T cells or have other immune resistance mechanisms, and current immunotherapies have shown limited to no efficacy. ImmunoGenesis' immune therapies are based in the pathology of these cold tumors, transforming them into hot tumors by targeting key mechanisms of immune resistance. The company expects to initiate clinical trials of its lead programs in 2022. For more information about the company, visit www.immunogenesis.com.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this press release are forward-looking statements. These forward-looking statements may be identified by terms such as "will," "could," "believe," "plan," "expect," "target," "continue," "to," and similar terms or expressions or the negative thereof. Examples of such statements include, but are not limited to, statements regarding the development and/or effectiveness of evofosfamide and the ability of evofosfamide to achieve the desired results whether as a monotherapy or in combination with other therapies. We may not actually achieve the plans, carry out the intentions or meet the expectations or objectives disclosed in the forward-looking statements. You should not place undue reliance on these forward-looking statements. These statements are subject to risks and uncertainties which could cause actual results and performance to differ materially from those discussed in the forward-looking statements. The forward-looking statements contained in this press release speak only as of the date of this press release and are based on management's assumptions and estimates as of such date. We disclaim any intent or obligation to update these forward-looking statements to reflect events or circumstances that exist after the date on which they were made.

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