



Alpine Immune Sciences Announces Preclinical Data from ALPN-101 Program Demonstrating Efficacy in Humanized Model of Graft Versus Host Disease

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— Data Presented at 59th American Society of Hematology Annual Meeting & Exposition —

SEATTLE, December 9, 2017 – Alpine Immune Sciences, Inc. (NASDAQ:ALPN), a leading immunotherapy company focused on developing treatments for autoimmune/inflammatory diseases and cancer, today announced results from a preclinical study of the company's ALPN -101 program in a humanized model of graft vs. host disease (GvHD). Results showed Alpine's ICOSL vIgD-Fc fusion proteins demonstrated therapeutic efficacy, including suppressing an allogeneic immune response in vitro, improving survival, and reducing GvHD disease activity. The data were presented in a poster session, titled "Experimental Transplantation: Basic Biology, Pre-Clinical Models: Poster I" (poster #1892) during the 59th American Society of Hematology (ASH) Annual Meeting & Exposition in Atlanta.

"These preclinical data showing activity with novel ICOS/CD28 dual antagonists from our vIgD platform in a humanized model of GvHD are encouraging because of the ongoing unmet medical need in GvHD," said Stanford Peng, M.D., Ph.D., Executive Vice President of Research and Development and Chief Medical Officer of Alpine. "These preclinical findings suggest our platform can generate novel immuno-oncology molecules with potential broad clinical therapeutic utility."

GvHD, a complication that can occur after stem cell or bone marrow transplants, has a major impact on survival following transplantation. Transplant-related mortality is as high as 92 percent in grade IV acute GvHD. Approximately 30 to 50 percent of bone marrow transplant patients will develop clinically significant GvHD – or 2,500 to 4,200 patients per year in the United States.

Background on Alpine's ICOSL vIgD-Fc Fusion Proteins

The immunoglobulin superfamily (IgSF) is a large, diverse family of proteins expressed on immune cells collectively playing a critical role in immune regulation. Well-known IgSF proteins include PD-1, PD-L1, CTLA-4, CD28, CD80/CD86 (B7-1/2), inducible T cell costimulator (ICOS), and TIGIT. Most therapeutic strategies targeting this family of proteins for the treatment of cancers and autoimmune/inflammatory diseases have employed monoclonal antibodies binding to a single target.

Alpine's vIgD platform, in contrast, transforms natural IgSF proteins into multifunctional protein domains. CD28 and ICOS are expressed on T cells, interacting with CD80/CD86 and ICOS ligand (ICOSL), respectively, and play critical roles in T cell activation. Alpine's ICOSL vIgD-Fc bind and inhibit both ICOS and CD28 co-stimulatory pathways.

Preclinical Study Design and Results

The preclinical study presented at ASH 2017 evaluated the function of Alpine's ICOSL vIgD-Fcs both in vitro and in a humanized mouse model of GvHD. Belatacept, an immunosuppressive T cell co-stimulation blocker approved by the U.S. Food and Drug Administration (FDA) to prevent kidney transplant rejection, was used as a comparator.

Results showed Alpine's ICOSL-vIgD-Fc:

- Demonstrated superior efficacy to belatacept in vitro in inhibiting T cell proliferation (CD4 and CD8 T cells) and cytokine production, including interferon gamma and tumor necrosis factor alpha, two key cytokines induced in a GvHD response
- Significantly protected against GvHD at levels comparable to or better than belatacept in the humanized model
- Significantly prolonged survival and greatly reduced GvHD disease activity in the humanized model as assessed by a disease activity score and weight loss compared with saline and wild-type ICOSL-Fc

About Alpine Immune Sciences, Inc.

Alpine Immune Sciences, Inc. is focused on developing novel protein-based immunotherapies using its proprietary variant Ig Domain (vIgD) platform technology. The vIgD platform is designed to interact with multiple targets including many present in the immune synapse. Alpine's vIgDs are developed using a process known as directed evolution, which produces proteins capable of either enhancing or diminishing an immune response and thereby may potentially apply therapeutically to cancer, autoimmune and inflammatory diseases. Alpine has also developed Transmembrane Immunomodulatory Protein (TIP) technology, based on the vIgD platform, to potentially enhance engineered cellular therapies. For more information, visit www.alpineimmunesciences.com.

Forward-Looking Statements

This release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These forward-looking statements are not based on historical fact, and include statements regarding Alpine's platform technology, potential therapies and the potential efficacy of such therapies. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "expect," "plan," "intend," and other similar expressions among others. These forward-looking statements are based on current assumptions that involve risks, uncertainties and other factors that may cause actual results, events or developments to be materially different from

those expressed or implied by such forward-looking statements. These risks and uncertainties, many of which are beyond our control, include, but are not limited to: Alpine's discovery-stage and pre-clinical programs may not advance into the clinic or result in approved products on a timely or cost-effective basis or at all; Alpine may not achieve additional milestone payments pursuant to its collaborations; the impact of competition; adverse conditions in the general domestic and global economic markets; as well as the other risks identified in Alpine's filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and Alpine undertakes no obligation to update forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements.

"Transmembrane Immunomodulatory Protein," "TIP," "Variant Ig Domain," "vIgD", and the Alpine logo are registered trademarks or trademarks of Alpine Immune Sciences, Inc. in various jurisdictions.

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