



NEWS RELEASE

Alpine Immune Sciences Presents New Translational Data on Povetacicept at the European Lupus Meeting 2024

3/21/2024

-- Povetacicept demonstrates greater reductions in disease activity in a mouse model of lupus compared to WT TACI-Ig or B cell depletion --

-- Povetacicept exhibits greater distribution to disease-related end organs compared with WT TACI-Ig --

-- A phase 2 study in SLE (DENALI) is in preparation for initiation in 2H 2024 --

SEATTLE--(BUSINESS WIRE)-- **Alpine Immune Sciences, Inc.** (NASDAQ: ALPN), a leading clinical-stage immunotherapy company focused on developing innovative treatments for autoimmune and inflammatory diseases, announced today that the Company presented new translational data for povetacicept (ALPN-303) at the SLEuro 14th European Lupus Meeting in Bruges, Belgium, March 19-22, 2024.

Presentation Highlights Include:

- BAFF- and APRIL-related genes are increased in myeloid and B cells in systemic lupus erythematosus (SLE) patients compared to healthy adults.
- Povetacicept significantly reduces multiple disease parameters in the NZB/W mouse model of lupus, more effectively than WT TACI-Ig or B cell depletion.
- Povetacicept exhibits greater distribution to multiple tissues – 19-fold higher in the kidney and 3-4-fold higher in the lung, skin, and brain – in normal mice, compared to WT TACI-Ig, potentially related to advantageous differences in molecular weight, target affinity and/or isoelectric point.



"We have long known that povetacept possesses unique molecular attributes that were conferred by our discovery platform's directed evolution process," remarked Stanford Peng, MD, PhD, President and Head of Research and Development at Alpine. "At least one of these attributes is its ability to distribute to disease-relevant tissues to a greater extent than wild-type TACIs, which may explain its superiority in multiple preclinical or translational disease models. These findings are particularly intriguing considering that these organs are of particular relevance to our lead indications, systemic lupus erythematosus and IgA nephropathy. These findings further support our intent to initiate both a pivotal trial in IgA nephropathy, RAINIER, as well as a phase 2 study in SLE, DENALI, later this year."

Table 1: Greater Tissue Distribution vs. WT TACI-Ig

Tissue	% Positive (Mean ± SE)		Fold Difference (Povetacept/Telitacept)
	Povetacept	Telitacept	
Kidney	1.9 ± 0.2	0.1 ± 0.0	19.0
Lung	0.49 ± 0.13	0.13 ± 0.05	3.8
Skin	2.7 ± 0.4	0.8 ± 0.2	3.4
Brain	0.10 ± 0.03	0.03 ± 0.01	3.3

Table 2: Molecular Attributes

Attribute	Povetacept	Telitacept
MW (kDa) ¹	62.6	75.3-75.4 ²
pI ¹	6.5-7.0	7.1-8.4
K _D , BAFF	59 pM	491 pM
K _D , APRIL	1 pM	CNBD

¹ Theoretical, calculated by ExPASy (web.expasy.org/compute_pi/), Prot pI (Protpi.ch/Calculator/Protein Tool), or at Alpine based on Anal. Biochem ² 179:319 (1989).
² MW reported as 80.24 kDa in J Clin Pharmacol 56:948 (2016)

SLEuro 14th European Lupus Meeting Poster Presentation Details

Date: Thursday, March 21, 2024

Poster Title: The Enhanced Dual BAFF/APRIL Inhibitor Povetacept (TACI vTD-Fc; ALPN-303) More Potently Reduces Disease Activity in Murine Lupus Compared to CD20 Depletion and WT TACI-Ig, Associated with Greater

End-Organ Distribution

Poster Number: Tour 2, P104

About Povetacicept (ALPN-303)

Povetacicept (ALPN-303) is a dual antagonist of the BAFF (B cell activating factor) and APRIL (a proliferation inducing ligand) cytokines, which play key roles in pathogenesis of multiple autoimmune diseases via their roles in the activation, differentiation and/or survival of B cells, particularly antibody-secreting cells, as well as T cells and innate immune cells. Based upon an engineered TACI (transmembrane activator and CAML interactor) domain, povetacicept has exhibited greater potency in preclinical studies versus other inhibitors of BAFF and/or APRIL alone and B cell depletion. Povetacicept is in development for multiple autoimmune diseases, including IgA nephropathy and other autoimmune kidney diseases, systemic lupus erythematosus, and autoimmune cytopenias.

About Alpine Immune Sciences

Alpine Immune Sciences is committed to leading a new wave of immune therapeutics. With world-class research and development capabilities, a highly productive scientific platform, and a proven management team, Alpine is seeking to create first- or best-in-class multifunctional immunotherapies via unique protein engineering technologies to improve patients' lives. Alpine has entered into strategic collaborations with leading global biopharmaceutical companies and has a diverse pipeline of clinical and preclinical candidates in development. For more information, visit www.alpineimmunesciences.com. Follow @AlpineImmuneSci on **X** and **LinkedIn**.

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 our platform technology and potential therapies; the timing of and results from clinical trials and preclinical development activities; clinical and regulatory objectives and the timing thereof; expectations regarding the sufficiency of cash, including cash equivalents and restricted cash, and investments to fund our planned operations into 2026; our ability to achieve additional milestones in our collaborations and proprietary programs; the progress and potential of our development programs; future development plans and clinical and regulatory milestones and objectives, including the timing and achievement thereof; the efficacy of our clinical trial designs; anticipated enrollment in our clinical trials and the timing thereof; expectations regarding the anticipated reporting of data from our ongoing and planned clinical trials and potential publication of future clinical data; our ability to potentially advance povetacicept directly into a pivotal trial in the second half of 2024 as well as a phase 2 study in systemic lupus erythematosus,

pending engagement with and approval of the Food and Drug Administration; and the potential efficacy, safety profile, addressable market, regulatory success and commercial or therapeutic potential of our product candidates. 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: clinical trials may not demonstrate safety and efficacy of any of our product candidates; our ongoing discovery and preclinical efforts may not yield additional product candidates; our discovery stage and preclinical programs may not advance into the clinic or result in approved products; any of our product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; we may not achieve additional milestones in our proprietary or partnered programs; the impact of competition; adverse conditions in the general domestic and global economic markets; we may be unable to advance povetacicept directly into a pivotal trial or a phase 2 study in systemic lupus erythematosus in the second half of 2024; the impact of pandemics, or other related health crises on our business, research and clinical development plans and timelines and results of operations, including the impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf; as well as the other risks identified in our filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and we undertake no obligation to update forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements.

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