Nektar Announces Publication in Nature Communications of Results from Phase 1b Studies of Rezpegaldesleukin in Two Inflammatory Skin Diseases

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- Data from multiple Phase 1b studies in inflammatory skin conditions demonstrate durable dose-dependent improvements in physician-assessed disease activity and patient-reported outcomes -

- Biomarker analyses demonstrate plurality of Treg-mediated pathways with potential effect on tissue resident memory T cell populations resulting in sustained efficacy seen in the antigen challenged mouse model and in clinical trials -

SAN FRANCISCO, Oct. 29, 2024 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR), today announced the publication of peer-reviewed data from two Phase 1b studies in *Nature Communications* highlighting the efficacy, safety, and tolerability of rezpegaldesleukin in patients with atopic dermatitis (AD) and psoriasis (PsO).

Rezpegaldesleukin is a first-in-class interleukin-2 receptor (IL-2R) agonist that enhances the activity of regulatory T cells (Tregs) with promising dose-dependent clinical activity across multiple physician-assessed and patient-reported endpoints for AD and PsO.

Results from the Phase 1b studies showed that rezpegaldesleukin safely and dose-dependently increased Tregs and rapidly improved measurable exploratory disease outcomes that are largely durable for at least 36 weeks after ceasing treatment.

"These promising findings clinically validate, for the first time, the Treg hypothesis – that restoring Treg function through a central pathway of IL-2R-driven Treg rescue can have disease remittive potential across a variety of chronic inflammatory skin diseases," said Jonathan Silverberg, M.D., Ph.D., Professor of Dermatology at George Washington University School of Medicine and lead study author. "Newer evidence suggests that diseases like atopic dermatitis are not exclusively Th2-mediated. These results show that rezpegaldesleukin can act on multiple disease-driving pathways and is uniquely poised to address a diversity of immunopathologies."

"The exciting clinical cross-indication efficacy here is buttressed by serum biomarker analysis demonstrating that rezpegaldesleukin can modulate multiple immunoregulatory pathways to provide rapid onset and duration of efficacy" said Jonathan Zalevsky, Ph.D., Chief Research & Development Officer at Nektar. "These findings further validate our therapeutic approach of using a Treg stimulator to dampen inflammatory responses and simultaneously restore immune balance in patients with chronic inflammatory skin diseases. We look forward to reporting topline data next year from our two Phase 2b rezpegaldesleukin studies in atopic dermatitis and alopecia areata."

Key findings are summarized below:

- Rezpegaldesleukin was evaluated in two randomized, double-blind, placebo-controlled Phase 1b trials in patients with moderate-to-severe atopic dermatitis (AD) (NCT04081350) or chronic plaque psoriasis (PsO) (NCT04119557)
- Rezpegaldesleukin is safe and well-tolerated and demonstrates consistent pharmacokinetics in participants receiving subcutaneous doses of 10 to 12 µg/kg or 24 µg/kg once every 2 weeks for 12 weeks, meeting the primary and secondary objectives of each study
- AD patients receiving high dose rezpegaldesleukin demonstrate an 83% improvement in EASI score after 12 weeks of treatment EASI improvement of ≥ 75% (EASI-75) and vIGA-AD responses are maintained for 36 weeks after treatment discontinuation in 71% and 80% of week 12 responders, respectively
- The clinical improvements are accompanied by sustained increases in CD25bright Tregs
- Serum proteomic biomarkers demonstrated rezpegaldesleukin's ability to engage multiple immunoregulatory mechanisms to facilitate immune homeostasis, which may indicate a potential mechanism of attenuating Th1, Th2, and Th17 responses by restoring the balance of Tregs.
- Results validate the role of IL-2-induced Treg proliferation and activation in the AD treatment paradigm, and support the advancement of rezpegaldesleukin in the Phase 2b study in AD.
- The delayed-type hypersensitivity (DTH) mouse model and the profound reduction in serum IL-15 levels in atopic dermatitis patients treated with rezpegaldesleukin provides mechanistic insight for the durable efficacy that persists for months following treatment

The full citation of this article can be accessed at: https://rdcu.be/dX8lr.

About Rezpegaldesleukin

Autoimmune and inflammatory diseases cause the immune system to mistakenly attack and damage healthy cells in a person's body. A failure of the body's self-tolerance mechanisms enables the formation of the pathogenic T lymphocytes that conduct this attack. Rezpegaldesleukin is a potential first-in-class resolution therapeutic that may address this underlying immune system imbalance in people with many autoimmune and inflammatory conditions. It targets the interleukin-2 receptor complex in the body

in order to stimulate proliferation of powerful inhibitory immune cells known as regulatory T cells. By activating these cells, rezpegaldesleukin may act to bring the immune system back into balance.

Rezpegaldesleukin is being developed as a self-administered injection for a number of autoimmune and inflammatory diseases. It is wholly-owned by Nektar Therapeutics.

About Nektar Therapeutics

Nektar Therapeutics is a clinical-stage biotechnology company focused on developing treatments that address the underlying immunological dysfunction in autoimmune and chronic inflammatory diseases. Nektar's lead product candidate, rezpegaldesleukin (REZPEG, or NKTR-358), is a novel, first-in-class regulatory T cell stimulator being evaluated in two Phase 2b clinical trials, one in atopic dermatitis and one in alopecia areata. Our pipeline also includes a preclinical candidate NKTR-0165, which is a bivalent tumor necrosis factor receptor type II agonist antibody. Nektar, together with various partners, is also evaluating NKTR-255, an investigational IL-15 receptor agonist designed to boost the immune system's natural ability to fight cancer, in several ongoing clinical trials. Nektar is headquartered in San Francisco, California. For further information, visit www.nektar.com and follow us on LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "will," "can," "expect," "develop," "potential," "advance," "anticipate," and similar references to future periods. Examples of forward-looking statements include, among others, statements regarding the therapeutic potential of, and future development plans for rezpegaldesleukin. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results to differ materially from those indicated in the forward-looking statements include, among others: (i) our statements regarding the therapeutic potential of rezpegaldesleukin are based on preclinical and clinical findings and observations and are subject to change as research and development continue; (ii) rezpegaldesleukin is an investigational agent and continued research and development for this drug candidate is subject to substantial risks, including negative safety and efficacy findings in future clinical studies (notwithstanding positive findings in earlier preclinical and clinical studies); (iii) rezpegaldesleukin is in clinical development and the risk of failure is high and can unexpectedly occur at any stage prior to regulatory approval; (iv) the timing of the commencement or end of clinical trials and the availability of clinical data may be delayed or unsuccessful due to challenges caused by regulatory delays, slower than anticipated patient enrollment, manufacturing challenges, changing standards of care, evolving regulatory requirements, clinical trial design, clinical outcomes, competitive factors, or delay or failure in ultimately obtaining regulatory approval in one or more important markets; (v) patents may not issue from our patent applications for our drug candidates, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required; and (vi) certain other important risks and uncertainties set forth in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 9, 2024. Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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