Nektar Therapeutics Announces Multiple Presentations for Rezpegaldesleukin at EADV 2024

September 25, 2024

- New proteomic analyses show that rezpegaldesleukin increases the protein levels of immune-regulating pathways while reducing specific serum proteins known to be elevated in patients with atopic dermatitis -

SAN FRANCISCO, Sept. 25, 2024 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced several presentations for rezpegaldesleukin (REZPEG) at the 2024 European Academy of Dermatology and Venereology (EADV) Congress. In addition to two trial-in-progress posters, new proteomic analyses were presented that showcases a unique serum proteomic profile in patients with atopic dermatitis (AD).

"As an agonist, REZPEG has a differentiated mechanism of action which is demonstrated by its unique proteomic profile presented today at EADV 2024," said Jonathan Zalevsky, Ph.D., Senior Vice President and Chief Research & Development Officer at Nektar. "The data show that REZPEG induces important immunoregulatory pathways, such as IL-10, a key anti-inflammatory cytokine. In addition, REZPEG reduced specific cytokines and chemokines which are known to be elevated in patients with atopic dermatitis and other atopy diseases, including IL-15, CCL22, CX3CL1, and IL-19. These data provide a greater mechanistic understanding of how treatment with REZPEG led to dose-dependent efficacy in the Phase 1b study over the 12-week treatment period, including its rapid onset of action, and it also provides insight into pathways that could result in the sustained efficacy that was observed in that study even after treatment was removed."

REZPEG is a novel first-in-class regulatory T (Treg) cell stimulator designed to address the imbalance in the immune system underlying autoimmune disorders and chronic inflammatory conditions. REZPEG works by targeting the IL-2 receptor complex and preferentially stimulating the proliferation of Treg cells without stimulating cytotoxic CD8+ T and CD4+ T cells, which drive autoimmune disease, to restore immune balance. REZPEG is currently being evaluated in two Phase 2b studies, one in moderate-to-severe AD and one in severe to very severe alopecia areata (AA). Nektar expects topline data from the AD study in the first half of 2025 and topline data from the AA study in the middle of 2025.

"In recent years, significant progress has been made in the treatment of atopic dermatitis. However, some patients still do not respond to the available biologics and small molecules. Therefore, there is a strong need for molecules with different mechanisms of action, particularly those that are immunoregulatory rather than immunosuppressive," said Spyridon Gkalpakiotis, M.D., Ph.D., MBA, a principal investigator on the Phase 2b study of rezpegaldesleukin in atopic dermatitis and Professor in the Department of Dermatovenerology 3FM CU and UHKV at the University Hospital Královské Vinohrady, Prague, Czech Republic. "My colleagues and I are excited to be a part of a study that can potentially offer the hope of durable effects and long-term remission which could change the paradigm of how we treat patients with atopic dermatitis."

The poster presentations are available for download at www.nektar.com/science/scientific-posters-and-presentations.

Key details and takeaways from the presentations are as follows:

Abstract 5560/ePoster P0662: "Serum proteomic biomarker analysis of the interleukin-2 receptor pathway agonist rezpegaldesleukin in patients with atopic dermatitis", Yu, *et al*.

- Patients with moderate-to-severe AD received 12 or 24 µg/kg REZPEG or placebo once every two weeks for 12 weeks. The Olink proteomics platform was used to measure the levels of soluble serum proteins from patients at baseline and throughout the induction period.
- REZPEG modulated Treg pathways and those involving lymphocyte immune homeostasis, MHC expression and regulation, ectodomain shedding of cell surface receptors, as well as cellular migration and adhesion processes.
- As an IL-2 receptor pathway agonist, REZPEG demonstrated a unique serum proteomic profile in AD patients, reducing the expression of serum proteins known to be elevated in patients with AD and demonstrated an effect on the expression levels of known targets for current AD therapy.

Abstract 4505/ePoster P0600 (Trial in Progress): "A Phase 2b, Randomized, Double-Blinded, Parallel-Group, Placebo-Controlled, International, Multicenter, Study to Evaluate the Efficacy and Safety of Rezpegaldesleukin in Adults with Moderate-to-Severe Atopic Dermatitis", Gkalpakiotis, *et al*.

- The Phase 2b trial is enrolling biologic and JAK-inhibitor naïve adults with moderate-to-severe AD. The primary outcome is reduction in Eczema Area and Severity Index (EASI) score from baseline at the end of the treatment induction phase. Secondary and exploratory endpoints include reduction in Investigator's Global Assessment (IGA) AD score, affected total body surface area (BSA) improvement, as well as safety and tolerability.

Abstract 2459/ePoster P2080 (Trial in Progress): "A Phase 2b Study Evaluating the Efficacy and Safety of Single Agent

Rezpegaldesleukin, an Interleukin-2 Receptor (IL-2R) Pathway Agonist, in the Treatment of Severe to Very Severe Alopecia Areata", Reich, *et al*.

- The Phase 2b trial is enrolling JAK-inhibitor naïve patients with severe to very severe alopecia areata. The primary endpoint is percent change from baseline in Severity Alopecia Tool (SALT) score at the end of the treatment period. Secondary and exploratory endpoints include percent change from baseline in SALT score at other assessed timepoints, safety and tolerability, as well as various patient reported outcomes.

About REZPEG

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. REZPEG 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, REZPEG may act to bring the immune system back into balance.

REZPEG 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 (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," "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 are investigational agents and continued research and development for these drug candidates 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 health epidemics, including the COVID-19 pandemic, 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) we may not achieve the expected cost savings we expect from our 2022 corporate restructuring and reorganization plan or our 2023 cost restructuring plan and we may undertake additional restructuring and cost-saving activities in the future, (vi) 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 (vii) 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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