Nektar Therapeutics Announces Phase 2 Topline Data for Rezpegaldesleukin in Patients with Systemic Lupus Erythematosus

February 23, 2023

Improvement in SLEDAI-2K score observed as compared to placebo, although study did not meet primary endpoint

Clinically meaningful improvements observed as compared to placebo across secondary endpoints including BICLA and LLDAS at the mid-dose level in the study

Nektar and Lilly are discussing next steps for trials planned in other indications

SAN FRANCISCO, Feb. 23, 2023 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced topline data from a Phase 2 randomized, double-blind, placebo-controlled study of rezpegaldesleukin (also known as LY3471851 or REZPEG) in adults with moderately-to-severely active systemic lupus erythematosus (SLE) despite receiving standard-of-care treatment such as corticosteroids, anti-malarials, and non-biological immunosuppressants. REZPEG is an investigational, potential first-in-class selective regulatory T-cell inducing IL-2 conjugate designed to treat select autoimmune diseases.

The Phase 2 ISLAND study (NCT04433585) enrolled 291 adults with moderate-to-severe SLE. The study consisted of three arms evaluating rezpegaldesleukin administered subcutaneously at different doses (low-dose of 300mcg Q2W, mid-dose of 900mcg Q2W, high-dose of 1800mcg Q2W) compared to placebo. The primary endpoint of the study was a 4-point reduction in the SLEDAI-2K score in pre-defined study populations. Although the mid-dose level demonstrated a numeric improvement in SLEDAI-2K score as compared to placebo (with a placebo-adjusted response of 8.8% for the modified intent-to-treat (mITT) population [p=0.309] and 13.9% for the per protocol population [p=0.06]), the primary endpoint was not met. The placebo-adjusted responses for the low- and high-doses were less than those of the mid-dose for both populations.

The mid-dose level in the study also demonstrated consistent and potentially clinically meaningful improvements for the majority of secondary clinical endpoints in patients treated with REZPEG compared with placebo, including the endpoints of British Isles Lupus Assessment Group (BILAG)-Based Composite Lupus Assessment (BICLA) response (with a placebo-adjusted response of 16.4% for the mITT BICLA-evaluable population and 19.1% for the per protocol BICLA-evaluable population) and Lupus Low Disease Activity State (LLDAS) (with a placebo-adjusted response of 12.2% for the mITT population and 15.1% for the per protocol population). The placebo-adjusted responses for BICLA and LLDAS for the low and high doses were less than those of the mid-dose for both populations.

Biomarker data demonstrated REZPEG led to dose-dependent proliferation of T regulatory cells, which was consistent with prior studies.

Lilly has notified Nektar that they do not intend to advance REZPEG to Phase 3 development for SLE. Nektar and Lilly plan to work together to determine next steps for the planned Phase 2b study in atopic dermatitis.

"We believe that these study results seen in the ISLAND study show that rezpegaldesleukin had a positive impact on disease activity in patients with moderately-to-severely active systemic lupus erythematosus," said Brian L. Kotzin, M.D., Chief Medical Officer of Nektar. "These data also further support rezpegaldesleukin's ability to expand regulatory T cells and the potential for this T regulatory cell stimulator to be used as a novel approach in the field of autoimmune disease."

Key details and takeaways for the primary endpoint and secondary clinical endpoints for the mid-dose level in the study are as follows:

- 8.8% of patients (placebo-adjusted, [p = 0.309]) achieved a reduction of ≥4 points in SLEDAI-2K score at week 24 in the mITT population; 13.9% of patients (placebo-adjusted, [p = 0.06]) achieved a reduction of ≥4 points in the SLEDAI-2K score at week 24 in the per protocol population.
- 8.8% of patients (placebo-adjusted) achieved a Systemic Lupus Erythematosus Responder Index 4 (SRI-4) response at week 24 in the mITT population; 13.9% of patients (placebo-adjusted) achieved an SRI-4 response at week 24 in the per protocol population.
- 16.4% of patients (placebo-adjusted) achieved a BICLA response at week 24 in the mITT BICLA-evaluable population; 19.1% of patients (placebo adjusted) achieved a BICLA response at week 24 in the per protocol BICLA-evaluable population.
- 12.2% of patients (placebo-adjusted) achieved a LLDAS response at week 24 in the mITT population; 15.1% of patients (placebo adjusted) achieved a LLDAS response at week 24 in the per protocol population.

Most adverse events reported were mild or moderate in severity. A dose dependent increase was observed in adverse events reported. The most common adverse events included fever, injection site reaction, fatigue, pain and arthralgia. The frequency of infections and infestations across placebo and all dose levels of REZPEG was similar. The treatment discontinuation rate across

the groups was 12% for placebo, 24% for low-dose, 19% for mid-dose and 40% for high-dose. At the high dose, discontinuations were due primarily to a higher rate of adverse events for this dose level in these patients with moderate-to-severe active lupus.

The prespecified study populations identified from the protocol are as follows: mITT population defined as all patients who were randomized and received at least one dose of study medication. The per protocol population was defined as all randomized patients who did not commit an Important Protocol Deviation (IPD) that could potentially compromise efficacy results. Eligibility for the BICLA evaluable populations were determined by a patient with a baseline of one BILAG A and/or two BILAG B criteria.

Nektar entered a strategic collaboration with Lilly in 2017 to develop and potentially commercialize REZPEG (formerly known as NKTR-358). The Phase 2 program for REZPEG includes the recently completed Phase 2 study in lupus, a planned Phase 2 study in atopic dermatitis, and another Phase 2 study in a yet-to-be-announced autoimmune indication outlined in the collaboration agreement.

Nektar to Host Conference Call at 2:00 PM Pacific Standard Time/5:00 PM Eastern Standard Time

Nektar Therapeutics will host an analyst and investor conference call today with Nektar executives, which will include a more detailed presentation of these data. The call will be held today, Thursday, February 23, 2023, at 2:00 p.m. Pacific Standard Time (PST).

The press release, slides and live audio-only webcast of the conference call can be accessed through a link that is posted on the Home Page and Investors section of the Nektar website: http://ir.nektar.com/. The web broadcast and the slides for the conference call will be available for replay through March 27, 2023.

To access the audio conference call, please follow this pre-registration link at Nektar Analyst and Investor Call Registration. All registrants will receive dial-in information and a PIN allowing access the live call.

About Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE), the most common type of lupus, is an autoimmune disease in which the immune system attacks its own tissues, causing widespread inflammation and tissue damage in the affected organs. It can affect the joints, skin, brain, lungs, kidneys, and blood vessels. The seriousness of SLE can range from mild to life-threatening. The causes of SLE are unknown, but are believed to be linked to environmental, genetic, and hormonal factors.[1]

About Rezpegaldesleukin (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 an investigational, potential first-in-class T regulatory cell stimulator that may address this underlying immune system imbalance in people with many autoimmune and inflammatory conditions. It is designed to target 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.

About Nektar Therapeutics

Nektar Therapeutics is a biopharmaceutical company with a robust, wholly owned R&D pipeline of investigational medicines in oncology and immunology as well as a portfolio of approved partnered medicines. Nektar is headquartered in San Francisco, California, with additional operations in Huntsville, Alabama. Further information about the company and its drug development programs and capabilities may be found online at http://www.nektar.com.

Nektar Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "may," "demonstrate," "potential," "designed," "plan" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the therapeutic potential of, and future development plans for rezpegaldesleukin, the prospects and plans for our collaborations with other companies, and the timing of the initiation of clinical studies and the data readouts for our drug candidates. 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 reported to us by our partner Lilly, and observations and are subject to change as research and development continue; (ii) rezpegaldesleukin is an investigational agent and continued research and development for these drug candidates is subject to substantial risks, including negative safety and efficacy findings in ongoing clinical studies (notwithstanding positive findings in earlier preclinical and clinical studies); (iii) rezpegaldesleukin is in various stages of 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 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 previous corporate restructuring and reorganization, as well as from any new restructuring and reorganization, (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 November 4, 2022. 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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1. Centers for Disease Control and Prevention. (2022, July 5). Systemic lupus erythematosus (SLE). Centers for Disease Control and Prevention. Retrieved January 2023, https://www.cdc.gov/lupus/facts/detailed.html

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