New Clinical Data Presented from Phase 1b Study of NKTR-358, a Novel T Regulatory Cell Stimulator, at 2020 American College of Rheumatology (ACR) Congress

November 4, 2020

SAN FRANCISCO, Nov. 4, 2020 /PRNewswire/ -- Nektar Therapeutics (NASDAQ:NKTR) announced the presentation of additional clinical data from the Phase 1b study evaluating multiple ascending doses of NKTR-358, a first-in-class T regulatory cell stimulator, currently in development for the treatment of a range of autoimmune disorders, including systemic lupus erythematosus (SLE).

Initial data presented earlier this year at the European Congress of Rheumatology (EULAR) 2020 showed that NKTR-358 was safe and well tolerated in patients with mild-to-moderate SLE and led to a marked and selective, dose-dependent expansion of regulatory T cells (Tregs) that was maintained over multiple administrations. The ACR 2020 presentation includes additional clinical and pharmacodynamic data from this Phase 1b study including key biomarkers of Treg function and assessment of disease characteristics in mild to moderate SLE patients.

"In our data presented at ACR 2020, we were excited to see that NKTR-358 demonstrated a dose-dependent reduction in CLASI-A composite clinical scores in patients with mild-to-moderate SLE after only 3 treatment cycles. Complementing these clinical results, we also observed dose-dependent biomarker changes associated with Treg activation including increases in Treg functional markers, changes in DNA methylation of the *FoxP3* locus, and increased expression of Treg functional genes," said Jonathan Zalevsky, Ph.D., Chief Research & Development Officer at Nektar. "These results support further investigation of NKTR-358 in patients with auto-immune disorders and inflammatory diseases, including the Phase 2 study underway in lupus patients being conducted by our partner Eli Lilly & Co."

The randomized, double-blind, multiple-ascending dose Phase 1b data from the study being presented at 2020 ACR evaluated safety, pharmacokinetics (PK) and pharmacodynamics (PD) in a total of 48 SLE patients across 4 separate ascending dose cohorts who received subcutaneous Q2W doses of NKTR-358 (n=9 per cohort) or placebo (n=3 per cohort). Subjects were treated for a total of six weeks.

Key conclusions from today's data presentation at ACR 2020 include:

- NKTR-358 was safe and well tolerated with a similar safety profile for single and repeat doses in patients with mild-to-moderate SLE as was observed in healthy volunteers from a prior Phase 1 study
- A selective, dose-dependent expansion of $CD25^{bright}$ Tregs was observed, which was maintained through multiple NKTR-358 administrations
- Treg induction was further supported by a correlation between the number of Tregs and the extent of demethylated *FoxP3*
- Increases in Treg activation markers (CD25, Helios, and CTLA-4) and genes associated with Treg regulation were observed with NKTR-358
- Low-level increases in NK cell numbers occurred in most patients at the highest NKTR-358 dose; the $CD56^{bright}$ NK cell population was more sensitive than the $CD56^{dim}$
- A dose-dependent reduction in CLASI-A[1] score was seen with NKTR-358 treatment, which supports further exploration in patients with moderate-to-severe SLE
- No observed changes in SLEDAI or joint scores were noted due to the short treatment duration in this study

A Phase 2 trial of NKTR-358 in patients with SLE (NCT04433585) as well as two separate Phase 1b studies in patients with atopic dermatitis (NCT04081350) and psoriasis (NCT04119557) are currently recruiting.

Nektar will host a call today for analysts and investors to review the data presented at ACR 2020. Details of the call are as follows:

Date and Time: Wednesday, November 4, 2020 at 4:15 p.m. Eastern Standard Time

Dial- in: (877) 881-2183 (toll-free) or (970) 315-0453 (access code 7083115)

Investors and analysts can view slides and listen to the live audio webcast of the presentation at https://edge.media-server.com/mmc/p/yppmbgt9. The event will also be available for replay for two weeks on the company's website, www.nektar.com.

About NKTR-358 (LY3471851)

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. NKTR-358 is a potential first-in-class therapeutic that may address an underlying immune system imbalance in people with many autoimmune conditions. It targets the interleukin (IL-2) receptor complex in the body in order to stimulate proliferation of inhibitory immune cells known as regulatory T cells. By activating these cells, NKTR-358 may act to bring the immune system back into balance. Nektar entered into a strategic collaboration with Lilly in 2017 to develop and commercialize NKTR-358.

NKTR-358 is being developed by Lilly as a self-administered injection for a number of autoimmune and inflammatory diseases. A Phase 2 study of NKTR-358 is underway in adults with systemic lupus erythematosus (ISLAND-SLE) (NCT04433585). The investigational therapy is also currently being evaluated in two separate Phase 1b studies in patients with atopic dermatitis (NCT04081350) and psoriasis (NCT04119557).

About Nektar

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 and Hyderabad, India. Further information about the company and its drug development programs and capabilities may be found online at http://www.nektar.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "may," "can," "develop," "will," and similar references to future periods. Examples of forward-looking statements include, among others, statements we make concerning the therapeutic potential of NKTR-358, and future development plans for this drug candidate. 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) the extent and duration of the impact of the COVID-19 pandemic on our business, regulatory efforts, research and development, clinical trials (including those being led by us and our partner), and corporate development activities will depend on future developments that are highly uncertain and cannot be accurately predicted, such as the ultimate duration of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements in the U.S. and in other countries, as well as the effectiveness of actions taken globally to contain and treat the disease; (ii) NKTR-358 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 ongoing clinical studies (notwithstanding positive findings in earlier preclinical and clinical studies); (iii) the timing of the commencement or end of clinical trials and the availability of clinical data may be delayed or unsuccessful due to regulatory delays, decisions and policies of our partner, 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; (iv) 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 (v) 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 8, 2020. 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.

1. CLASI-A: cutaneous lupus erythematosus disease area and severity index - activity

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View original content:http://www.prnewswire.com/news-releases/new-clinical-data-presented-from-phase-1b-study-of-nktr-358-a-novel-t-regulatory-cell-stimulator-at-2020-american-college-of-rheumatology-acr-congress-301166421.html

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