Nektar Therapeutics Presents Data from First-in-Human Phase 1a Study on Novel T Regulatory Cell Stimulator, NKTR-358 at 2019 Annual Meeting of the American College of Rheumatology

November 10, 2019

SAN FRANCISCO, Nov. 10, 2019 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) today announced updated results from the first-in-human Phase 1a study of NKTR-358, a novel T regulatory (Treg) cell stimulator in development for the treatment of autoimmune and other chronic inflammatory conditions.

The data, which were presented at the 2019 Annual Meeting of the American College of Rheumatology in Atlanta, show that treatment with NKTR-358 led to a marked and selective dose-dependent expansion in the numbers and proliferative capacity of FoxP3+CD25^{bright} Treg cells, and a measurable activation of Treg cells. These data are a continuation of initial results reported at 2019 Annual European Congress of Rheumatology (EULAR) in June 2019.

NKTR-358 is designed to treat autoimmune and inflammatory conditions by correcting the immune system imbalance that results from reduced numbers and impaired function of immune-regulating Treg cells. NKTR-358 works by targeting the interleukin-2 receptor complex to stimulate the proliferation and activation of Treg cells. NKTR-358 was discovered by Nektar and is being co-developed and commercialized in partnership with Eli Lilly and Company.

"We're pleased to report that final results from our first-in-human Phase 1a study continue to support the positive safety and tolerability profile of NKTR-358, while reinforcing its selective and measurable impact on the numbers, expansion and activation of regulatory T cells or Tregs," said Brian Kotzin, M.D., Senior Vice President, Clinical Development and NKTR-358 Program Lead at Nektar Therapeutics. "Autoimmune and inflammatory diseases are marked by an imbalance in the body's self-tolerance and self-regulatory immune pathways, and the ability of NKTR-358 to expand functional Tregs could help restore normal balance. The results support further studies into the potential of NKTR-358 as a treatment for several types of immune-mediated disorders."

The data were presented today in a poster titled *"Selective induction of functional regulatory T-cells in healthy volunteers by NKTR-358, a novel IL-2 conjugate Treg stimulator, in development for the treatment of autoimmune diseases"*, by Dr. Christie Fanton of Nektar Therapeutics during the T Cell Biology & Targets in Autoimmune & Inflammatory Disease poster session being held from 9:00 a.m. to 11:00 a.m. Eastern Standard Time.

The double-blind, single-ascending dose Phase 1a study evaluated 100 healthy volunteers who received subcutaneous doses of NKTR-358 ranging from 0.3 to 28.0 µg/kg and were followed for 50 days after dosing.

Key highlights from today's data presentation include:

- NKTR-358 was safe and well tolerated in this first-in-human study consistent with prior reported results.
  - No anti-drug antibodies were detected.
- Final data show dose-proportional pharmacokinetics, with maximal concentrations reached in 5-7 days and prolonged exposure with an estimated half-life of 8-11 days.
- New data confirm that single-ascending doses of NKTR-358 led to marked dose-dependent and sustained increases in the absolute numbers, percentages and proliferation of circulating FoxP3+CD25^{bright} Treg cells. In addition,
  - At the highest dose tested of NKTR-358, 28.0 µg/kg, the mean percentage of Ki67+ CD25^{bright} Tregs was 6-fold above baseline.
  - NKTR-358 increased the expression of Treg activation markers.
  - Epigenetic analysis of immune cells demonstrated a significant increase in demethylated FOXP3 gene following NKTR-358 treatment at 28.0 µg/kg, further reinforcing that NKTR-358 is expanding true Tregs.
  - NKTR-358 induced dose-dependent changes in other genes associated with Treg regulation.
- NKTR-358 was not associated with any measurable changes in numbers and percentages of conventional CD4+ and CD8+ T cells (Tcons) at all doses and low-level increases of natural killer (NK) cell numbers was observed at highest doses tested.

A copy of the poster presentation of NKTR-358 data is available on Nektar's corporate website at https://www.nektar.com/download_file/722/0.

NKTR-358 is also being evaluated in a multiple ascending dose (MAD) study in patients with systemic lupus erythematosus and two additional double-blind, randomized, placebo-controlled Phase 1b studies in adults with psoriasis and atopic dermatitis. For more information, please visit clinicaltrials.gov and search for NCT03556007 (SLE trial), NCT04119557 (Psoriasis trial) and NCT04081350 (Atopic Dermatitis trial).

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 resolution therapeutic that may address this underlying immune system imbalance in people with different 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, 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 as a self-administered injection for a number of autoimmune and inflammatory diseases.

About Nektar Therapeutics
Nektar Therapeutics is a research-based, development-stage biopharmaceutical company whose mission is to discover and develop innovative medicines to address the unmet medical needs of patients. Our R&D pipeline of new investigational medicines includes treatments for cancer, autoimmune disease and chronic pain. We leverage Nektar's proprietary and proven chemistry platform in the discovery and design of our new therapeutic candidates. 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: "potential," "design," "continue," "may," and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the expected benefits of NKTR-358, the ability to obtain useful data from the Phase 1a and 1b clinical studies of NKTR-358, and the future clinical development plans for NKTR-358. 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) NKTR-358 is in early-stage clinical development and there are substantial risks that can unexpectedly occur for numerous reasons including negative safety and efficacy findings in the Phase 1b clinical study notwithstanding positive findings in prior studies; (ii) clinical study outcomes, including the Phase 1b clinical study outcome of NKTR-358, remain very unpredictable and it is possible that a clinical study could fail due to efficacy, safety or other important clinical findings; (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, slower than anticipated patient enrollment, manufacturing challenges, changing standards of care, evolving regulatory requirements, clinical trial design, clinical outcomes, delays caused by our collaboration partners, and enrollment competition; (iv) scientific discovery of new therapeutics is an inherently uncertain process and the future success of applying our technology platform to potential new drug candidates (such as NKTR-358) is therefore highly uncertain and unpredictable; (v) patents may not issue from our patent applications for NKTR-358, 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 Nektar's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 7, 2019. 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.

Contact:

For Investors:
Vivian Wu of Nektar Therapeutics
628-895-0661

For Media:
Jodi Sievers of Nektar Therapeutics
415-482-5593

Dan Budwick of 1AB
973-271-6085
dan@1abmedia.com

*NKTR-358 is referred to as LY3471851 under Lilly-sponsored studies.

View original content:http://www.prnewswire.com/news-releases/nektar-therapeutics-presents-data-from-first-in-human-phase-1a-study-on-novel-t-regulatory-cell-stimulator-nktr-358-at-2019-annual-meeting-of-the-american-college-of-rheumatology-300955183.html

SOURCE Nektar Therapeutics