Nektar Therapeutics Announces First Publication of NKTR-358, a Novel Molecule Designed to Selectively Stimulate Expansion and Selective Function of T Regulatory Cells, in the Journal of Translational Autoimmunity

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-- NKTR-358 Elicited Sustained and Preferential Proliferation of Regulatory T Cells Without Corresponding Effects on T Effector Cells in Preclinical Models, Supporting Development in a Broad Range of Autoimmune Disorders --

SAN FRANCISCO, May 20, 2021 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced the publication of preclinical data in the *Journal of Translational Autoimmunity* describing NKTR-358, a first-in-class, composition of stable PEG conjugates of native IL-2 designed to selectively stimulate T regulatory (Treg) cell function. NKTR-358 is currently in development for the treatment of a range of autoimmune and inflammatory disorders. These published data demonstrate that NKTR-358 has the ability to elicit sustained and preferential proliferation and activation of Tregs *in vivo* without corresponding increases in T effector cells.

"The publication in the *Journal of Translational Autoimmunity* demonstrates, by a variety of measures, and across species, that NKTR-358 induces sustained, selective proliferation and activation of regulatory T cells with minimal effects on T effector cells. This is an important finding that validates the mechanistic approach of NKTR-358 for the treatment of autoimmune diseases, and provides a strong rationale for its ongoing clinical development," said Dr. Richard Furie, NKTR-358 key investigator and Chief, Division of Rheumatology, Northwell Health and Professor, Zucker School of Medicine at Hofstra/Northwell.

"NKTR-358 preferentially binds to the high affinity trimeric receptor on T regulatory cells resulting in the downregulation of function and proliferation of T effector cells," said Jonathan Zalevsky, Ph.D., Chief Research & Development Officer at Nektar. "The findings in the *Journal of Translational Autoimmunity* deepen our understanding of the pharmacology of NKTR-358 and, together with the early promising clinical data, provide strong support for continued testing as a new therapeutic for patients with diseases that have an imbalance of T lymphocyte subsets leading to autoimmunity. We look forward to the continued progress of multiple NKTR-358 studies across numerous autoimmune and inflammatory diseases by our partner, Eli Lilly."

In the study, researchers investigated NKTR-358's selectivity for Tregs, receptor-binding properties, *ex vivo* and *in vivo* pharmacodynamics, ability to suppress T effector cell proliferation *in vivo* and functional activity in a murine model of systemic lupus erythematosus (SLE).

Key findings are summarized below:

- A single administration of NKTR-358 in mice promotes greater Treg expansion compared with multiple administrations of native IL-2, demonstrating enhanced specificity towards Treg induction and improved pharmacokinetics in comparison with native IL-2.
- In a murine model of SLE, treatment with NKTR-358 maintained elevated Tregs for the duration of treatment and ameliorated disease progression.
- Tregs isolated from NKTR-358-treated mice displayed a sustained and higher suppression of T effector cell proliferation versus those from vehicle-treated mice.
- Repeated NKTR-358 dosing in non-human primates over six months demonstrated expansion of Tregs following each dose. Importantly, no anti-drug antibodies were detected during the six months of dosing, indicating that NKTR-358 does not induce immunogenicity while maintaining its pharmacologic effects over time.

Phase 1b data presented at the European Congress of Rheumatology (EULAR) in June 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 Tregs that was maintained over multiple administrations. Additional Phase 1b data from the study presented at the annual American College of Rheumatology (ACR) meeting in November 2020 included key biomarkers of Treg function and assessment of disease characteristics in mild to moderate SLE patients.

As part of the broad development program for NKTR-358, Nektar's partner, Eli Lilly & Co., is conducting a Phase 2 study in patients with SLE, a Phase 2 study in patients with ulcerative colitis, as well as two separate Phase 1b studies in patients with atopic dermatitis and psoriasis.

A link to the publication can be found here.

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 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). A Phase 2 study of NKTR-358 is also underway in patients with moderate to severe ulcerative colitis (INSTRUCT-UC) (NCT04677179). 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, immunology, and virology 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," "design," "develop," "potential" 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, 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) our statements regarding the therapeutic potential of NKTR-358 are based on preclinical and clinical findings and observations and are subject to change as research and development continue; (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) NKTR-358 is currently 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 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 May 14, 2021. 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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