Nektar Therapeutics Announces Presentation of Preclinical Data for NKTR-255, its Novel IL-15 Agonist, at the American Society of Hematology (ASH) 2020 Annual Meeting

December 7, 2020

SAN FRANCISCO, Dec. 7, 2020 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) today announced two nonclinical data presentations for NKTR-255, its IL-15 pathway agonist, at the 62nd American Society of Hematology (ASH) Annual Meeting. The presentations include an oral presentation of translational research studies conducted in collaboration with researchers from Dana-Farber Cancer Center.

NKTR-255 is an interleukin-15 (IL-15) receptor agonist that is designed to expand both natural killer (NK) cells and memory CD8 T cell populations. It is currently being evaluated in multiple clinical studies in both hematological and solid tumors in combination with agents that induce antibody-dependent cellular toxicity (ADCC). In the hematological setting, NKTR-255 is being tested in a Phase 1b/2 clinical study as monotherapy and in combination with rituximab or daratumumab in patients with multiple myeloma (MM) and non-Hodgkin's lymphoma (NHL). It is also being evaluated in a Phase 1b/2 solid tumor trial in combination with cetuximab for the treatment of colorectal cancer and head and neck squamous cell carcinoma (HNSCC).

"Inhibition of NK cell effector functions is a mechanism for immune evasion in patients with multiple myeloma and therefore restoring and enhancing NK cell functionality is a key goal for new immunotherapeutic approaches, " said Nikhil C. Munshi, MD, Professor of Medicine at Harvard Medical School, Director of Basic and Correlative Science, and Associate Director of the Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute. "In our studies, we found the novel IL-15 receptor agonist, NKTR-255, was effective in reverting the inhibitory status observed in NK cells from MM patients, leading to enhanced direct NK cytotoxicity against several MM cell lines and primary MM cells. In addition, we saw a significant increase in ADCC activity *in vitro* with NKTR-255 in combination with myeloma-targeting antibodies as compared to activity with those antibodies alone. These data accentuate the potential for NKTR-255 as an innovative immunotherapeutic agent in the treatment of multiple myeloma."

"The ASH presentations add to the growing body of data for NKTR-255 that highlight its ability to enhance NK cell effector function and greatly potentiate the ADCC mechanisms of targeted antibodies," said Jonathan Zalevsky, Ph.D., Chief Research & Development Officer at Nektar. "We are excited about the development potential of NKTR-255, especially as we've already observed biological activity in the first multiple myeloma and non-Hodgkin's lymphoma patients treated in the monotherapy dose-escalation phase of our liquid tumor study."

Details of the preclinical data presentations at ASH are listed below and are available on the scientific section of Nektar's website at http://www.nektar.com/science/scientific-posters-and-presentations:

Abstract 667: "*Restoring NK Cell Activities in Multiple Myeloma with IL-15 Receptor Agonist NKTR-255,"* Fernández, R. A., et al. (This study was conducted in collaboration with Dr. Nikhil C. Munshi at the Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute.)

- **Oral Session:** 652. Myeloma: Pathophysiology and Pre-Clinical Studies, excluding Therapy
- **Date:** Monday, December 7, 2020, 2:30 p.m. Eastern Standard Time
    - The induction of an activated profile in NK cells by NKTR-255 results in an effective enhancement of their anti-myeloma effector function in *ex vivo* assays.
    - *In vivo* studies confirmed superiority of the combination of daratumumab and NKTR-255 compared to single agents in controlling MM growth.
    - NKTR-255 improves the immune cell compartment both in the tumor tissue and blood following anti-CD38 treatment.

Abstract 825: "*Optimizing Ex-Vivo Expanded NK Cell- Mediated Antibody-Dependent Cellular Cytotoxicity (ADCC) Combined with NKTR-255 in Chronic Lymphocytic Leukemia (CLL), Follicular Lymphoma (FL), and Burkitt Lymphoma (BL),"* Chu, Y., et al. (This study was conducted in collaboration with Dr. Mitchell Cairo at New York Medical College.)

- **Poster Session:** 203. Lymphocytes, Lymphocyte Activation, and Immunodeficiency, including HIV and Other Infections: Poster I
- **Date:** Saturday, December 5, 2020, 7:00 a.m. – 3:30 p.m. Eastern Standard Time
    - NKTR-255 significantly enhanced the *in vitro* cytotoxicity of expanded NK cells when combined with rituximab against MEC-1, PGA-1, and DOHH2 as compared to the control groups.
    - NKTR-255 also significantly enhanced the *in vitro* cytotoxicity of expanded NK cells when combined with obinutuzumab against rituximab-resistant BL cells like Raji-2R and Raji-4RH as compared to the control groups.
    - NKTR-255 significantly enhanced the ADCC of expanded NK cells with anti-CD20 type I and type II antibodies against CLL, FL and rituximab-resistant BL cells in vitro with enhanced IFN-γ, granzyme B and perforin release.

About NKTR-255

NKTR-255 is an IL-15 receptor agonist designed to activate the IL-15 pathway and expand NK cells and promote the survival and expansion of memory CD8+ T cells without inducing suppressive regulatory T cells. Through optimal engagement of the IL-15Rα/IL-2Rβγ receptor complex, NKTR-255 enhances functional NK cell population and formation of long-term immunological memory, which may lead to sustained anti-tumor immune response. NKTR-255 is uniquely designed to overcome the challenges of recombinant IL-15 and other IL-15 agonists, which are rapidly cleared from the body and have shown diminishing response to successive doses.[1] NKTR-255 was designed using Nektar's polymer conjugation technology to extend circulating half-life.

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: "potential," "design," "enhance," "may," "test," "evaluate" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the expected benefits of NKTR-255 (both alone as a single agent as well as in combination with other agents, such as targeted antibodies), the ability to obtain useful data from the Phase 1b/2 clinical study of NKTR-255, and the future clinical development plans for NKTR-255. 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, 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-255 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/2 clinical study notwithstanding positive preclinical findings; (ii) clinical study outcomes, including the Phase 1b/2 clinical study outcome of NKTR-255, 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, and competitive factors; (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-255) is therefore highly uncertain and unpredictable; (v) patents may not issue from our patent applications for NKTR-255, 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 6, 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.

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1. Blood 2018 Jun 7;131(23):2515-2527

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