

Nektar Therapeutics Announces Presentation of New Preclinical Data for its IL-15 Agonist, NKTR-255, at the American Society of Hematology (ASH) 2019 Annual Meeting

December 9, 2019

SAN FRANCISCO, Dec. 9, 2019 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) today announced three presentations at the 61st American Society of Hematology (ASH) Annual Meeting & Exposition for its IL-15 agonist and investigational candidate, NKTR-255. Data were presented from a number of preclinical studies conducted in collaboration with researchers from the Dana-Farber Cancer Institute and the Fred Hutchinson Cancer Research Center.

NKTR-255 is an interleukin-15 (IL-15) receptor agonist, which is currently being evaluated in a Phase 1 clinical study in patients with multiple myeloma (MM) and non-Hodgkin's lymphoma (NHL). NKTR-255 is designed to work by selectively targeting the IL-15 pathway to expand both natural killer (NK) cells and memory CD8 T cell populations.

"The preclinical data being recognized at ASH demonstrate NKTR-255's promise in hematological malignancies through its potential to restore both NK cell and memory CD8 T cell compartments in patients," said Loui Madakamutil, Ph.D., Senior Vice President and Head of Discovery and Research at Nektar Therapeutics. "In studies presented by the laboratory of Dr. Nikhil Munshi at Dana-Farber, NKTR-255 enhanced the number and function of NK and CD8+ effector memory T cell populations in peripheral blood and bone marrow from patients with multiple myeloma and, also increased expression of activating receptors found on those NK cells. Separately, researchers from the laboratory of Dr. Cameron Turtle at Fred Hutchinson demonstrated NKTR-255 prevented tumor growth and increased survival of CAR T cells when added to a CD19-targeted CAR T cell regimen in models of B cell lymphoma. This preclinical data reinforces the basis of our ongoing clinical trial evaluating the potential of NKTR-255 in patients with multiple myeloma and non-Hodgkin's lymphoma."

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

Abstract 2866: *"Combination of NKTR-255, a polymer conjugated human IL-15, with CD19 CAR T cell immunotherapy in a preclinical lymphoma model,"* Chou, C., et al. (This study was conducted in collaboration with the Turtle Laboratory in the Fred Hutchinson Cancer Research Center.)

- **Session:** 625. Lymphoma: Pre-Clinical – Chemotherapy and Biologic Agents: Poster II
- **Date:** Sunday, December 8, 2019, 6:00 p.m. – 8:00 p.m. Eastern Standard Time
 - CAR T cells treated with NKTR-255 demonstrate increased proliferation and survival both in vitro and in vivo which may in part be due to increased expression of bcl-2.
 - Tumor bearing mice treated with NKTR-255 and CAR T cells have decreased tumor burden and increased survival compared to mice treated with CAR T cells alone.
 - Tumor-bearing mice previously treated with NKTR-255 and CAR T cells are able to reject tumor re-challenge supporting persistence of functional CAR T cells.

Abstract 4398: *"Restoring innate and adaptive immune repertoire in multiple myeloma for therapeutic application,"* Fernandez, R., 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.)

Note: Dr. Rafael Fernandez was recognized with a 2019 ASH Abstract Achievement Award for this abstract.

- **Session:** 652. Myeloma: Pathophysiology and Pre-Clinical Studies, Excluding Therapy: Poster III
- **Date:** Monday, December 9, 2019, 6:00 p.m. – 8:00 pm. Eastern Standard Time
 - Multiple myeloma patients are known to experience impaired innate immunity and a decline in function of NK cells along with lower expression of activating receptors found on these cells.
 - Treatment with NKTR-255 enhanced the number and function of both NK and CD8+ effector memory T cell populations in peripheral blood from healthy donors and MM patients in a dose dependent manner.
 - NKTR-255 was also able to revert the inhibitory status of NK cells from MM patients and showed synergy with daratumumab and elotuzumab to significantly increase status of NK susceptibility of the MM cells.
 - Findings suggest NKTR-255 delivers a significant impact on the activation of effector cell function to efficiently target MM cells.

Details of the *Trials in Progress* poster presentation are as follows:

Abstract 4459: *"A Phase 1, Open-Label, Multi-Center, Dose Escalation and Dose Expansion Study of NKTR-255 As a Single Agent in Relapsed or Refractory Hematologic Malignancies and in Combination with Daratumumab As a Salvage Regimen for Multiple Myeloma,"* Shah, N., et al.

- **Session:** 704. Immunotherapies: Poster III
- **Date:** Monday, December 9, 2019; 6:00 p.m. – 8:00 p.m. Eastern Standard Time

About the Phase 1 Study of NKTR-255 (NCT04136756)

NKTR-255 is currently being evaluated in an open-label Phase 1, dose escalation and dose expansion study in patients with select hematological malignancies (relapsed or refractory NHL or MM). The dose escalation phase of the study will evaluate the safety and tolerability of NKTR-255 as monotherapy in approximately 40 patients in order to establish a recommended Phase 2 dose (RP2D) for NKTR-255. The dose expansion phase of the study will enroll patients with MM or NHL (relapsed/refractory salvage) to evaluate the NKTR-255 RP2D in combination with targeted antibodies, including anti-CD38 monoclonal antibody, daratumumab in MM and anti-CD20 monoclonal antibody, rituximab in NHL. These studies are designed to assess pharmacokinetic and pharmacodynamic effects, anti-tumor activity and a range of biomarker assessments associated with NK and memory T cell populations.

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-15R α /IL-2R $\beta\gamma$ receptor complex, NKTR-255 enhances functional NK cell repopulation 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 Designed using Nektar's polymer conjugation technology to extend circulating half-life, NKTR-255 can be dosed every 14 or 21 days.

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: "promise," "potential," "design," "enhance," "may," "will" 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 1 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 1 clinical study notwithstanding positive preclinical findings; (ii) clinical study outcomes, including the Phase 1 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 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.

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

 View original content: <http://www.prnewswire.com/news-releases/nektar-therapeutics-announces-presentation-of-new-preclinical-data-for-its-il-15-agonist-nktr-255-at-the-american-society-of-hematology-ash-2019-annual-meeting-300971422.html>

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