Nektar and Collaborators Announce Publication in Blood Advances of Preclinical Data Demonstrating NKTR-255, a Novel Polymer-conjugated Human IL-15, Improves Efficacy of CD19-targeted CAR-T Cell Immunotherapy

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-- Polymer-conjugated IL-15 (NKTR-255) induced CD8$^+$ T cell and natural killer cell proliferation *in vivo* --

-- NKTR-255 enhanced the efficacy of human CD19 CAR-T cells in a xenogeneic lymphoma model --

SAN FRANCISCO, Nov. 9, 2022 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced the publication of preclinical data in *Blood Advances*, the open-access journal of the American Society of Hematology, highlighting the effects of NKTR-255, a novel polymer-conjugated human IL-15, on the efficacy of human CD19 CAR-T cells in a xenogeneic lymphoma model and on CD8$^+$ T effector cell (Tcell) and natural killer (NK) cell proliferation in non-human primates.

"The findings published today reinforce the foundational rationale behind the clinical development program we're pursuing of NKTR-255 enhancing CAR-T cell therapies," said Jonathan Zalevsky, Ph.D., Chief Research & Development Officer at Nektar. "We are looking forward to progressing our research in combination with cell therapies and are excited to launch our Phase 2/3 clinical trial of NKTR-255 following approved CAR-T cell therapies in patients with relapsed or refractory diffuse large B-cell Lymphoma."

The data from this publication demonstrate that NKTR-255 not only enhanced *in vivo* proliferation and accumulation of T and NK cells in non-human primates, but also demonstrated enhanced *in vivo* antitumor efficacy of human CD19 CAR-T in lymphoma-bearing immunodeficient mice.

"In contrast to mice treated with CAR-T alone, those that received CAR-T and NKTR-255 had markedly higher CAR-T counts in blood and marrow that were sustained after tumor clearance, without evidence of persistent proliferation or ongoing activation/exhaustion assessed by Ki-67 and inhibitory receptor co-expression," said Dr. Cameron Turtle, senior author on the publication and CLEARbridge Chair of Cancer Immunotherapy at Sydney Medical School. "These data support the ongoing clinical research of combined CAR-T and NKTR-255 for B-cell malignancies."

Key findings are summarized below:

- Serum IL-15 concentration is independently associated with longer CD19 CAR-T persistence in humans
- NKTR-255 promotes CD8$^+$ effector and memory T and NK cell accumulation in non-human primates
- NKTR-255 enhances proliferation and survival of human CD19 CAR-T at low target cell abundance
- NKTR-255 enhances accumulation and efficacy of human CD19 CAR-T in lymphoma bearing immunodeficient mice

The full citation of this article can be accessed at: https://ashpublications.org/bloodadvances/article/doi/10.1182/bloodadvances.2022008697/486976/A-novel-polymer-conjugated-human-IL-15-improves.

About NKTR-255

NKTR-255 is a biologic that targets the IL-15 pathway in order to activate the body's innate and adaptive immunity. Through optimal engagement of the IL-15 receptor complex, NKTR-255 is designed to enhance functional NK cell populations and formation of long-term immunological memory, which may lead to sustained and durable anti-tumor immune response.

Preclinical findings suggest NKTR-255 has the potential to synergistically combine with antibody-dependent cellular cytotoxicity molecules as well as to enhance CAR-T therapies.

There are two ongoing investigator sponsor trials evaluating NKTR-255 following treatment with a CAR-T cell therapy. Fred Hutchinson Cancer Center is conducting a Phase 1 study evaluating NKTR-255 in combination with CD19 CAR-T cell therapy in patients with relapsed or refractory large B-cell lymphoma (NCT05359211), and Stanford University is conducting a Phase 1 study evaluating NKTR-255 in combination with CD19/22 CAR-T cell therapy in patients with relapsed or refractory B-cell acute lymphoblastic leukemia (NCT03233854).

Nektar is also currently designing a Nektar-sponsored Phase 2/3 study combining NKTR-255 with approved CAR-T cell therapies in diffuse large B-cell lymphoma, which it aims to initiate in the first quarter of 2023.

About Nektar Therapeutics

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. 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: "will," "may," "launch," "potential," "demonstrate," "initiate" 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-255 and our other drug candidates in research programs, the prospects and plans for our collaborations with other companies, the timing of the initiation of clinical studies and the data readouts for our drug candidates, and our expectations (including our expected charges and cost savings) following our corporate restructuring, reorganization and workforce reduction, and our expected working capital and our cash runway. 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-255 and our other drug candidates are based on preclinical and clinical findings and observations and are subject to change as research and development continue; (ii) NKTR-255 and our other drug candidates are investigational agents and continued research and development for these drug candidates 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-255 and our other drug candidates are in various stages of 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 challenges caused by the COVID-19 pandemic, 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) we may not achieve the expected costs savings we expect from the restructuring and reorganization, (vi) 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 (vii) certain other important risks and uncertainties set forth in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 4, 2022. 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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