Nektar Announces Poster Presentations at the 64th American Society of Hematology (ASH) Annual Meeting

December 12, 2022

-- Unveils Trial Design for Nektar Phase 2/3 Study Combining NKTR-255 with CAR-T Therapies --

-- Presents First Data for NKTR-255 in Combination with Daratumumab in Patients with Relapsed/Refractory Multiple Myeloma --

SAN FRANCISCO, Dec. 12, 2022 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced two presentations of NKTR-255 at the 64th American Society of Hematology (ASH) Annual Meeting.

NKTR-255 is an investigational IL-15 receptor agonist designed to boost antitumor immunity by increasing the proliferation and survival of natural killer (NK) and memory CD8^{+} T cells, thereby enhancing the formation of long-term immunological memory, which may lead to sustained antitumor immune response.

The study design of an upcoming Phase 2/3, randomized, double-blind, placebo-controlled, multicenter clinical trial of NKTR-255 following CD19-directed chimeric antigen receptor T (CAR-T) cell therapy in patients with relapsed/refractory (R/R) large B-cell lymphoma (LBCL) was presented by Miguel-Angel Perales, M.D., Chief, Adult Bone Marrow Transplant Service, at Memorial Sloan Kettering Cancer Center on Sunday, December 11th. Pre-clinical studies demonstrate that NKTR-255 can potentiate the effects of CAR-T therapies and a number of early clinical studies are currently underway to evaluate the role of NKTR-255 following CAR-T cell treatment for different hematologic malignancies.

Additionally, results from the ongoing Phase 1 study of NKTR-255 as a monotherapy and in combination with daratumumab in patients with R/R multiple myeloma (MM) or non-Hodgkin's lymphoma (NHL) were presented by Krina Patel, M.D., Associate Professor, Department of Lymphoma-Myeloma, at the University of Texas MD Anderson Cancer Center on Monday, December 12th. The data showed that NKTR-255 resulted in an expansion and proliferation of NK cells following daratumumab's on-target depletion of CD38-expressing NK cells.

"NKTR-255 administration one-day following dara resulted in a 4-fold expansion of the NK cells, returning NK cells to the same baseline level seen before dara administration. This exciting result shows that NKTR-255 can restore dara-induced NK cell depletion and may potentiate its ADCC mechanism. Moreover, NKTR-255 treatment resulted in NK cell expansion and induction of NK-cell activation markers across multiple cycles further validating NKTR-255's effect," said Jonathan Zalevsky, Ph.D., Head of Research and Development at Nektar. "Additional work presented at ASH highlights our new trial evaluating NKTR-255 as a unique potentiator of cellular therapy in a Phase 2/3 study in relapsed or refractory lymphoma patients who are seeking long-term efficacy from currently available CAR-T cell therapy."

2022 ASH presentations are available for download at www.nektar.com/science/scientific-posters-and-presentations.

Key details and takeaways from the presentation are as follows:

Abstract 3335 (Trial in Progress): "A Phase 2/3, Randomized, Double Blind, Placebo-Controlled, Multicenter Study of NKTR-255 Vs Placebo Following CD-19 Directed CAR-T Therapy in Patients with Relapsed/Refractory Large B-Cell Lymphoma", Perales M., et al.

- Based on preclinical and clinical evidence, NKTR-255 has the potential to improve efficacy of currently approved cellular therapy by enhancing antitumor effect and durability of responses.
- The upcoming Phase 2/3 study will enroll eligible patients with R/R LBCL who have received an FDA-approved CAR-T cell product. Patients will receive NKTR-255 intravenously, starting approximately 14 days following CAR-T therapy, with continued dosing every 21 days.
- The primary objective of the Phase 2 portion of the study is to identify the dose of NKTR-255 for the Phase 3 portion of the study based on safety, tolerability, and complete response rate (CRR) at month 6, the primary efficacy endpoint.

Abstract 4652: "Safety, Tolerability, PK/PD and Preliminary Efficacy of NKTR-255, a Novel IL-15 Receptor Agonist, in Patients with Relapsed/Refractory Hematologic Malignancies", Patel K., et al.

- NKTR-255 was well tolerated in heavily pre-treated patients with hematologic malignancies (NHL and MM) in doses up to 12 µg/kg and in combination with daratumumab in doses up to 9 µg/kg (in MM). The majority of treatment-related adverse events (TRAE) were low-grade, transient, and easily managed. The maximum tolerated dose (MTD) was not reached.
- No new safety signals or overlapping toxicities were observed with the doublet and dose escalation is ongoing.
- Early evidence of clinical activity was observed in this heavily pre-treated and highly refractory patient population with the

doublet (NKTR-255 + daratumumab).

- Peak fold-changes of ~17-fold NK cell and ~2-fold in $CD8^+$ T cell expansion were observed in the first 2 cycles with NKTR-255 monotherapy doses up to 12 µg/kg. Sustained proliferative ability of NK and $CD8^+$ T cells across multiple cycles indicated no evidence of tachyphylaxis.
- Preliminary data from patients previously treated with off-the-shelf allogenic CAR-T cells indicate that allo-CAR-T cells persisted with NKTR-255 monotherapy, suggesting no alloreactivity to off-the-shelf allo-CAR-T cells.
- With combination therapy, NK cell rescue was observed with sustained increases in NK and $CD8^+$ T cells despite daratumumab's on-target depletion of CD38 expressing NK cells.

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

Nektar has initiated a Phase 1 dose escalation and expansion clinical study of NKTR-255 in adults with relapsed or refractory non-Hodgkin lymphoma or multiple myeloma (NCT04136756), as well as a Phase 1/2 clinical study of NKTR-255 in patients with relapsed or refractory head and neck squamous cell carcinoma or colorectal cancer (NCT04616196).

There are two ongoing investigator sponsored 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).

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.

Nektar Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "will," "may," "design," "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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