December 7, 2024

# Nektar Therapeutics Announces NKTR-255 Following CD19-directed CAR-T Therapy Enhanced Complete Response Rates in Patients with Relapsed or Refractory Large B-cell Lymphoma at the 66th Annual ASH Meeting

*73% of the NKTR-255 treatment group compared to 50% of the placebo group achieved a complete response at 6 months*

*NKTR-255 enhanced CAR T-cell kinetics with improved CD8+ CAR-T area under the curve (AUC) 0-15 days post-administration being 5.8-fold greater than placebo-controls*

SAN FRANCISCO, Dec. 7, 2024 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced results of its Phase 2 proof-of-concept study evaluating NKTR-255 as an adjuvant treatment to enhance complete response rate (CRR) and durability following CD19-directed CAR-T therapy in patients with relapsed/refractory (R/R) Large B-cell Lymphoma (LBCL) at the 66$^{th}$ ASH Annual Meeting and Exposition in San Diego, California.

NKTR-255 is an investigational polymer-conjugated IL-15 agonist, that activates, proliferates and expands natural killer (NK) and CD8+ T-cells *in vivo*, as well as promotes the survival and expansion of memory CD8+ T cells intended to increase duration and level of response for CAR-T and cellular therapies.[1,2]

In this multicenter, double-blind Phase 2 study, patients were randomized to receive one of three dose regimens of NKTR-255 or placebo intravenously starting 14 days after CAR-T infusion. In the fifteen-person clinical trial, the NKTR-255 combined treatment group demonstrated an improved CRR at six months, achieving 73% compared to 50% for the placebo, as assessed by a blinded independent central radiology review. Additionally, two patients treated with NKTR-255 converted from stable disease or partial response to complete responses at six months. No conversions from stable disease or partial response to complete response were observed in the placebo arm of the trial.

"The majority of patients currently receiving CAR-T therapies fail to achieve durable disease remission," said Sairah Ahmed, M.D., Associate Professor, Director of CAR-T Program at the Department of Lymphoma/Myeloma, Division of Cancer Medicine at University of Texas MD Anderson Cancer Center. "The results of this study demonstrated that NKTR-255 enhanced CAR T-cell counts and increased the number of patients who achieve a CR at 6 months post infusion. This finding is highly significant since, in multiple pivotal trials, patients who achieved complete response at 6 months were highly likely to remain in complete response beyond 2 years translating to improved progression-free survival."

The reported clinical benefit surpasses the published historical benchmark data from multiple pivotal trials and real-world meta-analyses of currently available commercial CD19 CAR-T cell therapies, which demonstrate 6-month complete response rates of 41% to 44%.

"This study is the first randomized trial demonstrating adjuvant treatment with NKTR-255 can enhance the durability of response to standard-of-care commercial CAR T-cell therapy by modifying CAR T-cell kinetics," said Mary Tagliaferri, M.D., Chief Medical Officer of Nektar. "These results contribute to the growing body of evidence demonstrating the broad applicability of NKTR-255 in combination with cellular therapies, and, as new data emerge, we continue to explore the best path forward for this program."

NKTR-255 was safe and well-tolerated in patients with relapsed/refractory LBCL in combination with FDA-approved CD19 CAR T-cell products.

Details of the presentation can be found on Nektar's website at www.nektar.com under Scientific Posters, Presentations and Publications.

**Title: 2068 NKTR-255 Vs Placebo to Enhance Complete Responses and Durability Following CD19-Directed CAR-T Therapy in Patients with Relapsed/ Refractory (R/R) Large B-Cell Lymphoma (LBCL)**
Poster: 2068
Program: Oral and Poster Abstracts
Session: 704. Cellular Immunotherapies: Early Phase Clinical Trials and Toxicities: Poster I
Hematology Disease Topics & Pathways: Research, Clinical trials, Clinical Research
Time & Date: Saturday, December 7, 2024, 5:30 PM-7:30 PM

**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.

In addition to studies in combination with CAR T cell therapies, NKTR-255 is being studied in a Phase 1 clinical trial sponsored by AbelZeta Pharma, Inc., which is evaluating C-TIL051, a tumor-infiltrating lymphocyte therapy, in anti-PD1 resistant metastatic non-small cell lung cancer (NCT05676749). The JAVELIN Bladder Medley study (NCT05327530), sponsored by Merck KGaA, is also ongoing to evaluate NKTR-255 in combination with avelumab as a maintenance treatment in patients with locally advanced or metastatic urothelial carcinoma (NCT05327530).

**About Nektar Therapeutics**

Nektar Therapeutics is a clinical-stage biotechnology company focused on developing treatments that address the underlying immunological dysfunction in autoimmune and chronic inflammatory diseases. Nektar's lead product candidate, rezpegaldesleukin (REZPEG, or NKTR-358), is a novel, first-in-class regulatory T cell stimulator being evaluated in two Phase 2b clinical trials, one in atopic dermatitis and one in alopecia areata. Nektar's pipeline also includes a preclinical bivalent tumor necrosis factor receptor type II (TNFR2) antibody and bispecific programs, NKTR-0165 and NKTR-0166, and a modified hematopoietic colony stimulating factor (CSF) protein, NKTR-422. Nektar, together with various partners, is also evaluating NKTR-255, an investigational IL-15 receptor agonist designed to boost the immune system's natural ability to fight cancer, in several ongoing clinical trials. Nektar is headquartered in San Francisco, California. For further information, visit www.nektar.com and follow Nektar on LinkedIn.

***Cautionary Note Regarding Forward-Looking Statements***

This press release contains forward-looking statements which can be identified by words such as: "will," "expect," "develop," "potential," "advance," "anticipate," "can," and similar references to future periods. Examples of forward-looking statements include, among others, statements regarding the therapeutic potential of, and future 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, 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 are based on preclinical and clinical findings and observations and are subject to change as research and development continue; (ii) NKTR-255 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 future clinical studies (notwithstanding positive findings in earlier preclinical and clinical studies); (iii) NKTR-255 is 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 November 8, 2024. 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. Shah, N., Perales, M. A., Turtle, C. J., Cairo, M. S., Cowan, A. J., Saeed, H., … Patel, K. K. (2021). Phase I Study Protocol: NKTR-255 as Monotherapy or Combined with Daratumumab or Rituximab in Hematologic Malignancies. *Future Oncology*, *17*(27), 3549–3560. https://doi.org/10.2217/fon-2021-0576
2. Miyazaki T, Maiti M, Hennessy M, et al. NKTR-255, a novel polymer-conjugated rhIL-15 with potent antitumor efficacy. *Journal for ImmunoTherapy of Cancer 2021*;9:e002024. doi:10.1136/jitc-2020-002024