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Nektar Announces Publication in Blood of Phase 1 Data for Novel IL-15 Agonist NKTR-255 in Combination with Autologous CD19-22 CAR-T Cell Therapy in Patients with B-cell Acute Lymphoblastic Leukemia

– Relapse-free/progression-free survival for NKTR-255 plus CD19-22 CAR-T cell therapy at 12 months was double that of historical controls (67% vs 38%) –

– Eight of nine patients achieved complete remission, all without detectable MRD –

SAN FRANCISCO, Oct. 17, 2024 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced the publication of the first clinical data from a Phase 1 study evaluating NKTR-255 in combination with an autologous bispecific chimeric antigen receptor (CAR)-T cell therapy targeting CD19 and CD22 in patients with relapsed or refractory B-cell acute lymphoblastic leukemia (B-ALL) in *Blood*, the peer-reviewed medical journal of the American Society of Hematology.

NKTR-255 is a novel IL-15 receptor agonist currently being studied in clinical trials in combination with cellular therapies and immune checkpoint inhibitors. NKTR-255 has shown in previous clinical studies that it can proliferate a range of immune cells and augment lymphocyte trafficking.[1,2]

The data published in *Blood* showed favorable efficacy with eight out of nine patients (89%) whom successfully received CAR19-22 followed by NKTR-255 achieving measurable residual disease (MRD) negative remission. The study further demonstrated that, at 12 months, relapse-free/progression-free survival for NKTR-255 in combination with the CD19-22 CAR-T cell therapy was double that of historical controls (67% vs 38%).

"We are encouraged by these first clinical data that clearly demonstrate the ability of NKTR-255 to potentiate CAR-T cell therapy," said Mary Tagliaferri, MD, Senior Vice President and Chief Medical Officer at Nektar. "Data showed NKTR-255 in combination with CD19-22 CAR-T cell therapy resulted in a 67% 12-month relapse-free survival rate in relapsed or refractory B-ALL and investigators observed significant increases in proinflammatory cytokines and chemokines which suggest lymphocyte trafficking to tissues."

The Phase 1 single-center, single-arm dose-escalation study was conducted by Stanford Medicine and evaluated NKTR-255 in combination with CD19-22 CAR-T cell therapy in patients with relapsed or refractory B-ALL (NCT03233854).

"While CAR-T cell therapies have transformed the treatment landscape for B-cell malignancies, there remains a significant unmet need to drive durable treatment outcomes as relapse occurs in the majority of patients," said David Miklos, MD, Chief of BMT and Cell Therapy Program at Stanford Medicine, Division of Blood and Marrow Transplantation and Cellular Therapy.

The primary outcomes of this study were feasibility and safety. Secondary endpoints were assessed for patients who received NKTR-255 (n=9) and included pharmacokinetics of NKTR-255 as measured by IL-15 levels in blood and efficacy as measured by remission free survival (RFS). Exploratory endpoints included cytokine profiling, CAR19-22 expansion in blood, bone marrow, and cerebrospinal fluid (CSF), and long-term CAR-T persistence.

Key findings are summarized below:

- No dose-limiting toxicities related to NKTR-255 were observed. The most common adverse events in patients receiving NKTR-255 in combination with the CD19-22 CAR-T cell therapy were fevers, chills, and myelosuppression, which were either self-limiting or manageable with supportive care. The toxicities observed with the combination treatment were similar to those seen after CD19-22 CAR-T cell therapy alone.
- Cytokine and chemokine profiling showed significant increases in IL-15 levels. Increase in CXCL9 and CXCL10 were associated with decreases in absolute lymphocyte counts and CD8+ CAR T-cells in blood, and ten-fold increases CAR-T cells in CSF, suggesting lymphocyte trafficking to tissue.
- Favorable efficacy was observed in patients with relapsed or refractory B-ALL treated with NKTR-255 in combination with CD19-22 CAR-T. Eight out of nine patients achieved complete remission with or without hematologic recovery, all without detectable MRD.
- Compared to Stanford's control group previously treated with the CD19-22 CAR-T cell therapy, NKTR-255 when added to the cell therapy increased the 12-month relapse free survival from 38% to 67%. The median RFS for the CAR T cell only cohort was 3.9 months. For the cohort treated with NKTR-255 and the CD 19-22 CAR-T cell therapy, the median RFS has not been reached with over 14 months of follow up. Only three patients who received combination therapy (33%) relapsed, suggesting administration of NKTR-255 to the CD19-22 CAR-T cell therapy helps prevent early disease recurrence.

The full citation of this article can be accessed here (Volume 144, Issue 16, Pages 1649-1753).

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. Our pipeline also includes a preclinical candidate NKTR-0165, which is a bivalent tumor necrosis factor receptor type II agonist antibody. 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 us on LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

Contact:

For Investors:

Vivian Wu of Nektar Therapeutics
628-895-0661

For Media:

David Rosen of Argot Partners
(212) 600-1902
david.rosen@argotpartners.com

1. Hirayama A. et al. Pharmacodynamic Analysis of CAR-T Cell Persistence in Patients with Hematologic Malignancies Treated with NKTR-255, an IL-15 Receptor Agonist That Enhances CD8 $^{+}$ T-Cells: Preliminary Results from a Phase 1 Study. Poster presented at: 63rd ASH Annual Meeting; Dec 11-13, 2021; Atlanta, GA
2. Altan M. et al. NKTR-255+cetuximab in patients with solid tumors: interim safety and efficacy results from the phase 1b dose-escalation study. Poster presented at: SITC 2021; Nov 10-14, 2021; Washington, D.C.