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Nektar Therapeutics Announces its First Publication of Preclinical Data Highlighting Anti-Tumor Properties of IL-15 Agonist, NKTR-255, in the Journal for ImmunoTherapy of Cancer (JITC)

-- Results demonstrate NKTR-255's differentiated pharmacologic profile versus precomplexed IL-15 agonists, supporting its potential as a potent immunotherapy agent --

SAN FRANCISCO, May 18, 2021 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced the publication of preclinical data from its second major immuno-oncology cytokine program, NKTR-255, in the *Journal for ImmunoTherapy of Cancer (JITC)*. NKTR-255 is a novel recombinant human Interleukin-15 (rhIL-15) receptor agonist designed to activate the IL-15 pathway to expand both natural killer (NK) cells and memory CD8+ T cell populations. The published data demonstrate that NKTR-255 retains the full spectrum of IL-15 biology but with improved pharmacologic properties and anti-tumor activity versus other rhIL-15 agonists. These preclinical findings support Nektar's robust clinical development program for NKTR-255 in patients with hematologic malignancies and solid tumors.

"These findings published today in the *Journal for ImmunoTherapy of Cancer* demonstrate IL-15's mechanism of action for engaging natural killer cell biology for the treatment of cancers," said Dr. Amita Patnaik, MD, FRCP(C), Co-Director of Clinical Research at the START Center for Cancer Care and a core investigator on the NKTR-255 clinical development program. "NKTR-255 may represent a particularly potent immunotherapeutic, and the data provide a strong rationale for clinical development."

"The findings in *JITC* describe the foundational science behind NKTR-255 and support its clinical advancement in both liquid and solid tumors," said Jonathan Zalevsky, Ph.D., Chief Research & Development Officer at Nektar. "We look forward to results from our two Phase 1/2 studies designed to evaluate NKTR-255 as a monotherapy as well as in combination with leading antibody-dependent cellular toxicity compounds, rituximab and daratumumab in hematological malignancies, and cetuximab in solid tumors."

Researchers analyzed *in vitro* pharmacological properties of rhIL-15, NKTR-255 and precomplexed IL-15 cytokines (rhIL-15/IL-15Ra and rhIL-15 N72D/IL-15Rα Fc) in receptor binding, cell signaling and cell function assays. *In vivo* pharmacokinetic (PK) and pharmacodynamic (PD) profiles of the cytokines were evaluated in normal mice, and immunomodulatory effect and anti-tumor activity were assessed in a model of lymphoma.

Key findings are summarized below:

- NKTR-255 maintained a similar receptor binding profile to that of rhIL-15, as compared to precomplexed IL-15 agonists.
- *In vivo*, NKTR-255 exhibited a PK profile with reduced clearance and a longer half-life (clearance: 2.31 mL/hour/kg; effective half-life: 15.2 hours) relative to rhIL-15 (clearance: 507 mL/hour/kg; effective half-life: 0.168 hours); NKTR-255 also demonstrated prolonged IL-15R engagement in lymphocytes compared with only transient engagement observed for rhIL-15 and precomplexed rhIL-15 N72D/IL-15Rα Fc.
- NKTR-255 was shown to provide a more durable and sustained effect on proliferation and activation of NK and CD8+ T cells than precomplexed cytokines.
- The properties of NKTR-255 promoted elevations in functionally competent cytotoxic NK cells in the tumor microenvironment and overall translated into increased survival rates and superior antitumor activity in a B-cell lymphoma model versus the precomplexed cytokines.

NKTR-255 is currently being evaluated in multiple clinical studies in both hematologic malignancies and solid tumors as a monotherapy and in combination with agents that induce antibody-dependent cellular toxicity (ADCC). In the hematological setting, NKTR-255 is being tested in a Phase 1b/2 clinical study as monotherapy and in combination with rituximab or daratumumab in patients with multiple myeloma (MM) and non-Hodgkin's lymphoma (NHL). It is also being evaluated in a Phase 1b/2 solid tumor trial in combination with cetuximab for the treatment of colorectal cancer (CRC) and head and neck squamous cell carcinoma (HNSCC).

In November 2020, Nektar reported encouraging early data from the NKTR-255 Phase 1/2 study in patients with relapsed/refractory hematologic malignancies at the 2020 Society for Immunotherapy of Cancer (SITC) Annual Meeting. NKTR-255 was administered intravenously (IV) every three weeks (Q3W), a similar dosing to that of checkpoint antibodies. These data indicated that NKTR-255 was biologically active and demonstrated consistent expansion of lymphocytes, with durable and sustained increases in NK and CD8+ T cells in the highly refractory population of patients with MM and NHL. NKTR-255 exhibited a long half-life and was well tolerated with low-grade, cytokine-related AEs that were transient in nature and easily managed. No anti-drug antibodies were reported.

About NKTR-255
NKTR-255 is a novel polyethylene glycol (PEG)-conjugate of recombinant human Interleukin-15 (rhIL-15), which was designed to retain all known receptor binding interactions of the IL-15 molecule.

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. Through an extended circulating half-life and optimal engagement of the IL-15Rα/IL-2Rβγ

receptor complex, NKTR-255 enhances functional NK cell populations and formation of long-term CD8+ mediated immunological memory, which may lead to sustained anti-tumor immune response.

The full citation of this article can be accessed at: 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;0:e002024. doi:10.1136/jitc-2020-002024.

About Nektar
Nektar Therapeutics is a biopharmaceutical company with a robust, wholly owned R&D pipeline of investigational medicines in oncology, immunology, and virology as well as a portfolio of approved partnered medicines. 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: "may," "design," "potential," "provide," "support" 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 in both liquid and solid tumors. 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 ongoing clinical studies (notwithstanding positive findings in earlier preclinical and clinical studies); (iii) NKTR-255 is in early 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 or competitive factors; (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 May 14, 2021. 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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