June 6, 2016

Preclinical Data Presented at ASCO 2016 Annual Meeting Demonstrate that Single-Agent NKTR-214 Produces a Large Increase in Tumor-Infiltrating Lymphocytes to Provide Durable Anti-Tumor Activity

SAN FRANCISCO, June 6, 2016 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) today announced new preclinical data for NKTR-214, an immuno-stimulatory CD-122 biased cytokine currently being evaluated in cancer patients with solid tumors in a Phase 1/2 clinical trial being conducted at MD Anderson Cancer Center and Yale Cancer Center. The new preclinical data presented demonstrate that treatment with single-agent NKTR-214 mobilizes tumor-killing T cells into colon cancer tumors. In addition, mouse pharmacodynamics data demonstrated that a single dose of NKTR-214 can increase and sustain STAT5 phosphorylation (a marker of IL-2 pathway activation) through one week post-dose. These data were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL from June 3-7, 2016.

"These latest data build upon our growing body of preclinical evidence demonstrating the unique mechanism of NKTR-214," added Jonathan Zalevsky, PhD, Vice President, Biology and Preclinical Development at Nektar Therapeutics. "The studies presented at ASCO show that NKTR-214 promotes tumor-killing immune cell accumulation directly in the tumor, providing a mechanistic basis for its significant anti-tumor activity in multiple preclinical tumor models. The ability to grow TILs[1] in vivo and replenish the immune system is exceptionally important. We've now learned that many human tumors lack sufficient TIL populations and the addition of the NKTR-214 TIL-enhancing MOA could improve the success of many checkpoint inhibitors and other agents, and allow more patients to benefit from immuno-therapy."

In studies previously published for NKTR-214, when mice bearing established breast cancer tumors are treated with NKTR-214 and anti-CTLA4 (a checkpoint inhibitor therapy known as ipilimumab for human treatment), a large proportion of mice become tumor-free. Anti-tumor immune memory was demonstrated when tumor-free mice were re-challenged by implant with a new breast cancer tumor and then found to clear the new tumor, without further therapy. The new data presented at ASCO demonstrate that upon re-challenge, there is a rapid expansion of newly proliferative CD8 T cells and particularly CD8 effector memory T cells. Both cell populations were readily detectable in multiple tissues (blood, spleen, and lymph nodes) and likely contribute to the anti-tumor effect observed in these animals. Adoptive transfer studies confirmed the immune-memory effect as transplant of splenocytes from tumor-free mice into naïve recipients provided the ability to resist tumor growth.

"NKTR-214 provides a highly unique immune activation profile that allows it to access the IL-2 pathway without pushing the immune system into pathological overdrive," said Dr. Steve Doberstein, Senior Vice President and Chief Scientific Officer. "NKTR-214's unique immune-stimulatory profile and antibody-like dosing schedule positions it as a potentially important medicine within the immuno-oncology landscape."

The data presentation at ASCO entitled, "Immune memory in nonclinical models after treatment with NKTR-214, an engineered cytokine biased towards expansion of CD8+ T cells in tumor," can be accessed at http://www.nektar.com/2016_NKTR-214_ASCO_poster.pdf

NKTR-214 is a CD122-biased agonist designed to stimulate the patient's own immune system to kill tumor cells by preferentially activating production of specific immune cells which promote tumor killing, including CD8-positive T cells and Natural Killer (NK) cells, within the tumor micro-environment. CD122, which is also known as the Interleukin-2 receptor beta subunit, is a key signaling receptor that is known to increase proliferation of these types of T cells.[2]

In preclinical studies, NKTR-214 demonstrated a highly favorable mean ratio of 450:1 within the tumor micro-environment of CD8-positive effector T cells relative to regulatory T cells.[3] Furthermore, the pro-drug design of NKTR-214 enables an antibody-like dosing regimen for an immuno-stimulatory cytokine.[4]

About the NKTR-214 Phase 1/2 Clinical Study
A Phase 1/2 clinical study is underway to evaluate NKTR-214 in patients with advanced solid tumors, including melanoma, renal cell carcinoma and non-small cell lung cancer. The first stage of this study, which is expected to be complete in the second half of 2016, is evaluating escalating doses of single-agent NKTR-214 treatment in approximately 20 patients with solid tumors. The primary objective of the first stage of the study is to evaluate the safety and efficacy of NKTR-214 and to

identify a recommended Phase 2 dose. In addition, the study will also assess the immunologic effect of NKTR-214 on TILs and other immune cells in both blood and tumor tissue, and it will also include TCR repertoire profiling. Dose expansion cohorts are planned to evaluate NKTR-214 in specific tumor types, including melanoma, renal cell carcinoma and non-small cell lung cancer.

The NKTR-214 clinical study is being conducted initially at two primary investigator sites: MD Anderson Cancer Center under Drs. Patrick Hwu and Adi Diab; and Yale Cancer Center, under Drs. Mario Sznol and Michael Hurwitz. Patients and physicians interested in the ongoing NKTR-214 study can visit the "Clinical Trials" section of www.mdanderson.org using identifier 2015-0573 or visit https://medicine.yale.edu/cancer/research/trials/active/858.trial.

About Nektar
Nektar Therapeutics has a robust R&D pipeline and portfolio of approved partnered medicines in oncology, pain, immunology and other therapeutic areas. In the area of oncology, Nektar is developing NKTR-214, an immuno-stimulatory CD122-biased agonist, that is in Phase 1/2 clinical development for patients with solid tumors. ONZEALD™ (etirinotecan pegol), a long-acting topoisomerase I inhibitor, is being developed for patients with advanced breast cancer and brain metastases and is partnered with Daiichi Sankyo in Europe. In the area of pain, Nektar has an exclusive worldwide license agreement with AstraZeneca for MOVANTIK™ (naloxegol), the first FDA-approved once-daily oral peripherally-acting mu-opioid receptor antagonist (PAMORA) medication for the treatment of opioid-induced constipation (OIC), in adult patients with chronic, non-cancer pain. The product is also approved in the European Union as MOVENTIG® (naloxegol) and is indicated for adult patients with OIC who have had an inadequate response to laxatives. The AstraZeneca agreement also includes NKTR-119, an earlier stage development program that is a co-formulation of MOVANTIK and an opioid. NKTR-181, a wholly owned mu-opioid analgesic molecule for chronic pain conditions, is in Phase 3 development. In hemophilia, Nektar has a collaboration agreement with Baxalta for ADYNOVATE™ [Antihemophilic Factor (Recombinant)], a longer-acting PEGylated Factor VIII therapeutic approved in the U.S. and Japan for patients over 12 with hemophilia A. In anti-infectives, the company has two collaborations with Bayer Healthcare, Cipro Inhale in Phase 3 for non-cystic fibrosis bronchiectasis and Amikacin Inhale in Phase 3 for patients with Gram-negative pneumonia.

Nektar's technology has enabled nine approved products in the U.S. or Europe through partnerships with leading biopharmaceutical companies, including AstraZeneca's MOVANTIK™, Baxalta's ADYNOVATE™, UCB's Cimzia® for Crohn's disease and rheumatoid arthritis, Roche's PEGASYS® for hepatitis C and Amgen's Neulasta® for neutropenia.

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: "anticipate," "intend," "plan," "expect," "believe," "should," "may," "will" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the therapeutic potential of NKTR-214, the timing of availability of clinical data for NKTR-214, and the potential of our technology and drug candidates in our research and development pipeline. 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-214 are based on preclinical findings and observations, (ii) NKTR-214 is in early-stage clinical development and there are substantial risks that can unexpectedly occur for numerous reasons including negative safety and efficacy findings in the ongoing Phase 1 clinical study notwithstanding positive findings in preclinical studies; (iii) our drug candidates and those of our collaboration partners 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 for numerous reasons including negative safety and efficacy findings even after positive findings in previous preclinical and clinical studies; (iv) the timing of the commencement or end of clinical trials and the availability of clinical 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) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of

applying our technology platform to potential new drug candidates (such as NKTR-214) is therefore highly uncertain and unpredictable and one or more research and development programs could fail; (vi) patents may not issue from our patent applications for our drug candidates including NKTR-214, 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 May 4, 2016. 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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