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Preclinical Data Presented at AACR Demonstrate that Combining NKTR-214 with Checkpoint Blockade is Superior to Dual Checkpoint Inhibition in Increasing Clonality of the T Cell Receptor (TCR) Repertoire and T Cell Tumor Infiltration

SAN FRANCISCO, April 18, 2016 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) today announced new preclinical data for the company's investigational immuno-stimulatory cytokine therapy, NKTR-214, which demonstrate both its activity as a single-agent and its synergistic activity with checkpoint blockade. In a TCR repertoire analysis conducted to assess both anti-tumor T cell clonality and T cell tumor infiltration (TIL clonality and infiltration), the combination of NKTR-214 and a checkpoint inhibitor resulted in dramatically higher increases for both parameters as compared to dual checkpoint inhibition. These data were presented at the American Association for Cancer Research (AACR) Annual Meeting in New Orleans, LA on April 17, 2016.

TIL clonality establishes the frequency of T cells with a specific TCR Vβ and TCR Jβ chain usage at the tumor site, which suggests increased CD8-positive effector T cell function against the specific tumor.[1] The concomitant presence of both TIL clonality and infiltration has been significantly correlated with clinical response and better survival outcomes in patients.[1] In a CT26 colon carcinoma model, sequencing for TCRs in the tumor was conducted using Adaptive Biotechnologies' ImmunoSEQ platform. Measurements of TIL clonality and infiltration were assessed seven days after treatment. NKTR-214 as a single-agent led to superior increases in TIL clonality and infiltration as compared to either anti-CTLA-4 or anti-PD-1 therapy alone. The combination of NKTR-214 with either mode of checkpoint inhibition led to superior increases in both TIL clonality and infiltration relative to the combination of CTLA-4 and PD-1 inhibitors. The highest increases occurred when NKTR-214 was added to an anti-PD-1 therapy.

"We are particularly excited by these new preclinical data for the combination of NKTR-214 with a checkpoint inhibitor which show an induced oligoclonal T cell response along with high TIL infiltration, "said Dr. Jonathan Zalevsky, Vice President of Biology at Nektar Therapeutics. "These data demonstrate that the addition of NKTR-214 to either an anti-CTLA-4 or anti-PD-1 agent could improve T cell clonality differences over checkpoint blockade therapies."

NKTR-214 is an investigational CD122-biased agonist currently in Phase 1/2 clinical development. NKTR-214 is 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 studies conducted in multiple established tumor models presented at AACR, NKTR-214 demonstrated activity as both a single-agent and when co-dosed with either an anti-PD-1 agent or an anti-CTLA-4 agent. In a tumor re-challenge study conducted in an EMT6 colon carcinoma model, sequential dosing of anti-CTLA-4 followed by NKTR-214 resulted in durable immunity, with complete responders resisting a tumor re-challenge. Following a second re-challenge, 100% of the animals remained tumor-free without additional treatment.

"Our latest preclinical findings continue to show that treatment with NKTR-214 either as a single-agent or in combination with checkpoint blockade is superior to single or dual checkpoint inhibition in multiple models," added Steve Doberstein, PhD, Senior Vice President and Chief Scientific Officer of Nektar Therapeutics. "These new data emphasize the cellular mechanisms underlying the remarkable efficacy of NKTR-214 in our preclinical models of cancer."

The data presentation at AACR entitled, "*Durable antitumor activity of the CD122-biased immuno-stimulatory cytokine NKTR-214 combined with immune checkpoint blockade*," can be accessed at http://www.nektar.com/product_pipeline/oncology_nktr-214.html

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 tumor-infiltrating lymphocytes (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 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 ten 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-K filed with the Securities and Exchange Commission on February 29, 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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