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Nektar Therapeutics Presents New Clinical Data from Ongoing Phase 1 Dose-Escalation Study of NKTR-214 at the Society for Immunotherapy of Cancer (SITC) 2016 Annual Meeting

Single-agent, anti-tumor activity observed in 7/18 evaluable patients with solid tumors, including one unconfirmed partial response per RECIST 1.1
NKTR-214 is well-tolerated with a once every three-week or once every two-week outpatient dosing regimen
Robust elevations in immune cell frequency and activation observed in both tumor and blood following treatment with NKTR-214

SAN FRANCISCO, Nov. 9, 2016 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced that new Phase 1 clinical data for Nektar's lead immuno-oncology agent, NKTR-214, were presented at the SITC 2016 Annual Meeting. NKTR-214 is an investigational immuno-stimulatory therapy designed to expand specific cancer-fighting T cells and Natural Killer (NK) cell abundance directly in the tumor micro-environment and increase expression of PD-1 on these immune cells. The results were presented by Adi Diab, MD, Assistant Professor, Department of Melanoma Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center in an oral presentation during today's session entitled "New Cancer Immunotherapy Agents in Development."

Interim results presented were from the ongoing Phase 1 dose-escalation, first-in-human, trial of single-agent NKTR-214 in patients with locally advanced or metastatic solid tumors, including melanoma, renal cell carcinoma (RCC), bladder, colorectal and other solid tumor cancers. A total of 20 patients were treated in four separate every three-week (q3w) dose cohorts (ranging from 0.003 mg/kg q3w to 0.012 mg/kg q3w) with 18 of these patients evaluable for anti-tumor activity. Based upon encouraging anti-tumor activity and tolerability of NKTR-214 observed at the 0.006 mg/kg q3w dose, an every two week (q2w) cohort of the 0.006 mg/kg dose began enrolling in September 2016 with an additional 5 patients enrolled to this cohort, all of which are continuing on therapy.

"NKTR-214 resulted in robust activation of the immune system and encouraging anti-tumor activity, including a partial response observed in a patient who continues to be treated with NKTR-214," said Dr. Ivan Gergel, Senior Vice President, Drug Development & Chief Medical Officer of Nektar. "NKTR-214 was also well tolerated in patients when administered as an every two-week or every three-week outpatient therapy. We are very encouraged by the clinical profile emerging for NKTR-214 and the totality of the data from this ongoing single-agent trial of NKTR-214."

Preliminary encouraging evidence of anti-tumor activity has been observed to date in the ongoing study:

- 12/18 (67%) evaluable patients had stable disease at the initial 8 week scan
- 7/18 (39%) evaluable patients had radiographic reductions in tumor size per RECIST 1.1 on NKTR-214
- One patient with metastatic melanoma (prior treatment with ipilimumab and a BRAF inhibitor) has received 13 cycles of treatment (0.003 mg/kg q3w) with stable disease and continues on therapy with NKTR-214
- In the 18 evaluable patients, a total of 5 patients with metastatic RCC who had progressed on 1 prior tyrosine kinase inhibitor (TKI) were treated with NKTR-214 at the 0.006 mg/kg q3w dose level:
  - 1/5 (20%) of these RCC patients had a uPR per RECIST 1.1 (at 16 week scan) and treatment with NKTR-214 is ongoing
  - 2/5 of these RCC patients had additional tumor reductions of 6% and 10% per RECIST 1.1 while on NKTR-214

NKTR-214 also demonstrated a favorable safety and tolerability profile with convenient, outpatient q2w or q3w administration in 25 patients evaluable for safety to-date:

- No immune-related AEs were observed (e.g. colitis, dermatitis, hepatitis pneumonitis, adrenal insufficiency)
- No deaths or grade 4 AEs related to NKTR-214
- No capillary leak syndrome was observed at any dose
- One patient experienced a dose-limiting toxicity (DLT) of hypotension/syncope at 0.012 mg/kg q3w and continued on treatment at 0.006 mg/kg q3w

- 3/25 patients experienced grade 3 hypotension, which was rapidly reversed with fluid administration and all patients continued on treatment with NKTR-214
- Most common grade 1-2 adverse events were fatigue, pruritis, cough, decreased appetite, pyrexia, and hypotension

Immune pheno-typing was conducted and biomarkers of immune activation were measured in patients with evaluable tumor biopsies and blood samples. Treatment with NKTR-214 produced a robust elevation in immune cell frequency and activation, including:

- Increase in total and newly proliferating (Ki67+) CD4+ T cells, CD8+ T cells, and Natural Killer (NK) cells in 9/9 patients with blood samples evaluated in the trial to-date, with increases of up to 30-fold observed
- Increase in frequency of PD-1+ T cell subsets of up to 9-fold in the blood
- Increase in CD8+ T cells and Natural Killer (NK) cells of up to 10-fold in the tumor micro-environment in patients with evaluable tumor biopsies (pre-dose and post-dose at week 3), with minimal intratumoral changes to T regulatory cells
- Increase in expression of cell-surface PD-1 on T cell subsets of up to 2-fold in the tumor micro-environment
- Induction of an activation gene signature in the tumor micro-environment, including increases of 5-fold or greater in expression of interferon γ, perforin and granzyme B genes
- Changes in T cell repertoire (TCR), which is a measure of T cell clonality, in the tumor micro-environment

"We are extremely pleased with the single-agent activity of NKTR-214 and the potential of NKTR-214 to transform the immuno-oncology landscape," said Howard W. Robin, President & CEO of Nektar Therapeutics. "As the first I-O agent to demonstrate that it can increase tumor-infiltrating lymphocytes (TILs) and increase PD-1 expression on immune cells in humans, NKTR-214 complements not only existing checkpoint inhibitors, such as nivolumab, but also other I-O mechanisms in development."

In September 2016, Nektar entered into a clinical collaboration with Bristol-Myers Squibb to evaluate NKTR-214 as a potential combination treatment regimen with Bristol-Myers Squibb's *Opdivo (*nivolumab*)* in five tumor types and seven potential indications. The Phase 1/2 clinical trials will enroll up to 260 patients and will evaluate the potential for the combination of *Opdivo* (nivolumab) and NKTR-214 to show improved and sustained efficacy and tolerability above the current standard of care in melanoma, kidney, triple-negative breast cancer, bladder and non-small cell lung cancer patients. The initial dose-escalation trial is underway with *Opdivo* (nivolumab) and NKTR-214.

NKTR-214 is an experimental therapy designed to stimulate cancer-killing immune cells in the body by targeting CD122 specific receptors found on the surface of these immune cells, known as CD8+ effector T cells and Natural Killer (NK) cells. In preclinical studies, treatment with NKTR-214 resulted in a rapid expansion of these cells and mobilization into the tumor micro-environment.[1] NKTR-214 has an antibody-like dosing regimen similar to the existing checkpoint inhibitor class of approved medicines. A Phase 1/2 clinical study is ongoing to evaluate single-agent NKTR-214 in cancer patients.

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, 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.

ADYNOVATE™ is a trademark of Baxalta Inc.

ONZEALD™ is a trademark of Nektar Therapeutics.

Cimzia® is a trademark of UCB.

Opdivo is a registered trademark of Bristol-Myers Squibb.

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 potential therapeutic benefit of NKTR-214 for cancer patients, the future clinical development plans for NKTR-214, the potential of NKTR-214 in combination with other immunotherapy agents including Bristol-Myers Squibb's Opdivo (nivolumab), and certain other statements regarding the prospects and potential of Nektar's business, technology platform and drug candidate 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) NKTR-214 is in early stage clinical development and the risk of failure remains high and failure can unexpectedly occur at any stage for one or more of the cancer indications being studied prior to regulatory approval due to lack of sufficient efficacy, safety considerations or other factors that impact drug development; (ii) data reported from the Phase 1 Trial is interim data only and the final results will change based on continuing observations from patients that currently remain enrolled in the trial (e.g., whether unconfirmed objective responses ultimately become confirmed responses) and additional patients to be enrolled in the trial; (iii) the Phase 1 Trial results for NKTR-214 remain subject to final data gathering and analysis review and confirmation procedures; (iv) the timing or success of the start or end of clinical trials such as those planned for NKTR-214 may be delayed or unsuccessful due to regulatory delays, clinical trial design issues, slower than anticipated patient enrollment, drug manufacturing challenges, changing standards of care, and clinical outcomes; (v) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of the application of Nektar's technology platform to potential new drug candidates such as NKTR-214 is therefore very uncertain and unpredictable and one or more research and development programs could fail; (vi) Nektar's patent applications for NKTR-214 may not issue in one or more jurisdictions, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required in the future; (vii) the outcome of any existing or future intellectual property or other litigation related to Nektar's proprietary product candidates, including, without limitation, NKTR-214, is unpredictable and could have a material adverse effect on our business; and (viii) certain other important risks and uncertainties set forth in Nektar's Quarterly Report on Form 10-Q for the quarter ended September 30, 2016 filed with the Securities and Exchange Commission on November 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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1. Charych, D., et al., Clin Cancer Res.; 22 (3) 2016

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