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Clinical Data from Phase 1 Dose-Escalation Study of Single-Agent NKTR-214 in Patients with Renal Cell Carcinoma Presented at the ASCO 2017 Genitourinary Cancers Symposium

SAN FRANCISCO and ORLANDO, Fla., Feb. 18, 2017 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced that positive Phase 1 clinical data for Nektar's lead immuno-oncology agent, NKTR-214, in patients with renal cell carcinoma (RCC) were presented at ASCO GU 2017. 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 Michael Hurwitz, MD, PhD, Assistant Professor of Medicine, Department of Medical Oncology at Yale Cancer Center and were entitled "*A Novel Immune Agonist, NKTR-214, Increases the Number and Activity of CD8+ Tumor Infiltrating Lymphocytes in Patients with Advanced Renal Cell Carcinoma.*"

"NKTR-214 resulted in dramatic increases in tumor-infiltrating lymphocytes (TILs) and also demonstrated encouraging anti-tumor activity, with 40% of RCC patients experiencing tumor reductions, including one patient with a partial response," said Dr. Mary Tagliaferri, Vice President, Clinical Development at Nektar. "We know that high TIL levels are correlated with clinical response and longer survival in patients treated with checkpoint inhibitor therapies and can be the best predictor of response. NKTR-214's unique mechanism, favorable safety profile and clinical activity support our combination trials of NKTR-214 with existing checkpoint inhibitors, such as nivolumab and atezolizumab, but also with other I-O mechanisms in development."

Clinical benefit and safety data were presented on 15 patients from the trial with renal cell carcinoma who were treated with single-agent NKTR-214:

- 6/15 (40%) patients with RCC had radiographic reductions in tumor size per RECIST 1.1 on NKTR-214, including:
  - 3 patients who had progressed on 1 prior tyrosine kinase inhibitor (TKI) and had also progressed on 1 prior checkpoint therapy
  - 3 patients who had progressed on 1 prior tyrosine kinase inhibitor (TKI) and were checkpoint therapy naïve, including 1 patient who experienced an unconfirmed partial response (*u*PR)
- NKTR-214 continues to demonstrate a favorable safety and tolerability profile with convenient, outpatient q3w or q2w administration in all patients evaluable for safety to-date.

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 lymphocytes and newly proliferating (Ki67+) CD4+ T cells, CD8+ T cells, and NK cells, with increases greater than 50-fold observed
- Increase in CD8+ T 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)
- Increase in expression of cell-surface PD-1 on T cell subsets of up to 2-fold in the tumor micro-environment

Nektar and Bristol-Myers Squibb are collaborating to develop NKTR-214 as a potential combination treatment regimen with Bristol-Myers Squibb's *Opdivo (*nivolumab*)* in five tumor types and eight potential indications. The Phase 1/2 clinical program 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 in the indications of first-line melanoma, second-line RCC checkpoint therapy-naïve, and second-line non-small cell lung cancer (NSCLC) checkpoint therapy-naïve.

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 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.

The ASCO GU 2017 poster can be downloaded at the following url:

http://www.nektar.com/application/files/1414/8701/4816/2017_ASCOGU_NKTR-214-clinical_poster.pdf

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.

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,"continue" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the potential safety, tolerability, and 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); (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

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/clinical-data-from-phase-1-dose-escalation-study-of-single-agent-nktr-214-in-patients-with-renal-cell-carcinoma-presented-at-the-asco-2017-genitourinary-cancers-symposium-300409873.html

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