Nektar Therapeutics Presents New Clinical and Preclinical Data for its Immuno-Oncology Pipeline at the 2018 Society for Immunotherapy of Cancer (SITC) Annual Meeting

November 9, 2018

New Efficacy, Safety and Biomarker Data Presented for Stage IV I-O Naïve Melanoma Patients in PIVOT-02 Study of NKTR-214 with nivolumab

Additional Preclinical Data Presentations Showcase Nektar's Immuno-Oncology (I-O) Pipeline Programs

SAN FRANCISCO, Nov. 9, 2018 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) announced today a presentation of new clinical and preclinical data for its I-O pipeline at the 2018 Society for Immunotherapy of Cancer (SITC) Annual Meeting.

New clinical study results from the PIVOT-02 Phase 1/2 Study were shared in an oral presentation titled, "Immune monitoring after NKTR-214 plus nivolumab (PIVOT-02) in previously untreated patients with metastatic Stage IV melanoma" (Abstract #O4) by Adi Diab, MD, Assistant Professor, Department of Melanoma Medical Oncology, Division of Cancer Medicine, University of Texas MD Anderson Cancer Center during the Cytokines Reinvented Session on Friday, November 9th.

Additional preclinical data presented at the annual meeting showed that NKTR-214 may drive, sustain and expand anti-tumor response when combined with therapies with complementary mechanisms of action including NKTR-262, poly (ADP-ribose) polymerase (PARP) inhibitors, radiation therapy (RT) and other agents. When combined with these treatments, NKTR-214 showed the potential to lead to tumor clearance and tumor specific immunologic memory.

"The data presented at this year's SITC Annual Meeting showcase our pipeline of novel investigational I-O agents that target key components of the immune cycle in order to restore immune surveillance and harness the body's immune system to fight cancer," said Jonathan Zalevsky, Ph.D., Senior Vice President and Chief Scientific Officer at Nektar Therapeutics. "Clinical data presented for NKTR-214 show that NKTR-214 plus nivolumab give deep and durable responses in first-line IO-naive Stage IV melanoma patients, including a high rate of complete responses. For our TLR agonist candidate, NKTR-262, we presented data demonstrating alteration of the tumor micro-environment, including activating the innate and adaptive arms of the immune system along with encouraging anti-tumor activity."

Highlights from the oral presentation on Stage IV 1L Melanoma patients include:

Clinical Efficacy (*Response measured per RECIST 1.1 by central independent radiology review for efficacy-evaluable patients treated at the recommended Phase 2 dose and with ≥1 on treatment scan). Response and median time on study calculated from data cut as of October 1, 2018*:

- Confirmed best overall response rate (ORR) was 53% (20/38) in efficacy-evaluable patients, with a 24% (9/38) complete response (CR) rate. Median time of follow-up was 7.2 months and median time to response was 2 months. 85% (17/20) patients with responses have ongoing responses. DCR, also known as disease control rate (CR+ PR + SD) was 76%.
- Amongst the 33 patients with known pre-treatment PD-L1 status, ORR in PD-L1 negative patients was 6/14 (43%) and in PD-L1 positive patients was 13/19 (68%). One patient with unknown PD-L1 baseline status experienced a CR.

Clinical Safety *(1L Melanoma safety database as of October 1, 2018):*

- A total of 41 patients have been treated at the RP2D. The most common (>30%) treatment-related adverse events (TRAEs) were grade 1-2 flu-like symptoms (78%), rash (70.7%), fatigue (63.4%), pruritus (46.3%), nausea (43.9%), arthralgia (36.6%) and myalgia (31.7%). A total of 8/41 (19.5%) of patients experienced a Grade 3 (G3) or higher TRAE with 2/41 (4.9%) patients discontinuing treatment due to a TRAE. 2/41 (4.9%) of patients experienced a G3 or higher immune-mediated AE.
- A decreased frequency of Grade 1-2 cytokine related AEs was observed with continuous dosing.

Biomarkers and Mechanism of Action:

- Clear activation of the IL-2 pathway demonstrated by an increase in absolute lymphocyte count with activated and proliferating CD4, CD8 and NK cells in blood.
- Combination demonstrated T cell infiltration and activation in the tumor microenvironment.
- TCR repertoire analysis demonstrates the presence of newly trafficked clonal infiltrates after treatment with NKTR-214 plus nivolumab.

Opdivo is a programmed death-1 (PD-1) immune checkpoint inhibitor that is designed to uniquely harness the body's own immune system to help restore anti-tumor immune response. By harnessing the body's own immune system to fight cancer, *Opdivo* has become an important treatment option across multiple cancers. NKTR-214 is an investigational immuno-stimulatory therapy designed to expand and activate specific cancer-fighting T cells and natural killer (NK) cells directly in the tumor micro-environment and increase expression of cell-surface PD-1 on these immune cells. A Phase 3 trial evaluating NKTR-214 in combination with nivolumab versus nivolumab in first-line advanced melanoma patients is currently recruiting

patients (NCT03635983).

A copy of Dr. Diab's presentation of PIVOT-02 data is available on Nektar's corporate website at https://www.nektar.com/download_file/629/0.

Details of the preclinical poster presentations at SITC are as follows and each will be available for download at the time of presentation at http://www.nektar.com/science/scientific-posters:

Poster/Abstract #P364: *"Systemic anti-tumor immunity and immune memory formation by a novel TLR7/8 targeting agent NKTR-262 combined with CD122-biased immunostimulatory cytokine NKTR-214",* Kivimae, S., et al.

- NKTR-262 and NKTR-214 in combination showed efficacy in all tested preclinical tumor models, correlated with sustained systemic expansion of tumor antigen specific CD8+ T cells.
- Combining NKTR-262 with NKTR-214 coordinates tumor antigen presentation and costimulatory signaling with tumor antigen recognizing CD8+ T cell expansion to produce a sustained systemic anti-tumor immune response.

Poster/Abstract #P378: *"NKTR-214 (CD122-biased agonist) and NKTR-262 (TLR7/8 agonist) combination treatment pairs local innate immune activation with systemic CD8+ T cell expansion to enhance anti-tumor immunity"*, Rolig, A., et al.

- NKTR-214 and NKTR-262 resulted in systemic CD8+ T cell expansion, enhanced intratumoral CD8+ T cell effector function, and favorable myeloid polarization.
- This robust anti-tumor immunity resulted in improved tumor regression and tumor-free survival in preclinical models.

Poster/Abstract #P368: *"Combination of a Dipeptidyl Peptidase Inhibitor BXCL701 and Biased CD122 Agonist NKTR-214 with Anti-PD1 Provides Functional Immunological Memory through Inflammatory Cell Death",* MacDougall, J., et al.

- In a triple combination with NKTR-214 and an anti-PD-1 antibody, BXCL701 generated complete and durable responses in models with high densities of tumor associated. macrophages, validating the importance of engaging multiple cell types of the immune system required for complete anti-tumor response.

Poster/Abstract #P348: *"Survival and immune modulation in homologous recombination deficient murine ovarian tumors using the PARP inhibitor, rucaparib and immune agonist, NKTR-214"*, Charych, D., et al.

- NKTR-214 paired with rucaparib provided significantly increased survival and durable complete response than either treatment alone in murine models of ovarian cancer.
- Preclinical results suggest the activity of this combination is through antigen priming of infiltrating memory T cells, increased NK cell recruitment and enhanced cytotoxicity of tumor infiltrates.

Poster/Abstract #P418: *"Pre-clinical investigation of NKTR-255, a polymer-conjugated IL-15 with a potent NK cell dependent anti-tumor efficacy",* Miyazaki, T., et al.

- NKTR-255 demonstrated powerful immune stimulation of NK cells with dose-dependent effect in the proliferation and activation of NK cells and enhanced anti-metastatic activity in mouse lung metastasis models.
- Results suggest NKTR-255 has high promise as a novel anti-tumor agent that boosts NK cell expansion and survival.

Poster/Abstract #P419: *"NKTR-214 in combination with radiation produces a potent in situ vaccine in the syngeneic B78 melanoma model"*, Sondel, P., et al.

- In a murine melanoma model study, the combination of NKTR-214 and radiation therapy (RT) resulted in significant tumor regression, higher rates of complete response, and stronger immunologic memory compared with radiation RT, RT plus IL-2, or NKTR-214 alone.

Poster/Abstract #P422: *"A polymer-associated human IL-15 (NKTR-255) has optimized biological activity and unique mechanisms of action on CD8 T Cells and NK Cells",* Robinson T., et al.

- Preclinical findings highlighted the ability of NKTR-255 to impact different mechanisms of action on CD8 T cells and NK cells leading to novel therapeutic effects.

Poster/Abstract #P424: *"NKTR-214, an engineered IL-2, selectively depletes intratumoral Tregs and expands immunotherapy-induced effector T cell responses"*, Sharma, M., et al.

- NKTR-214 showed synergy with both checkpoint blockade and peptide-vaccination resulting in improved overall survival and cure of mice in models of colon carcinoma and melanoma.
- The synergistic mechanism led to proliferation and tumor infiltration of effector CD8+ T cells while promoting selective intratumoral depletion of Tregs to establish effective anti-tumor immunity.

Poster/Abstract #P557: *"Overcoming genetically-based resistance mechanisms to PD-1 blockade"*, Torrejón, D., et al.
[NOTE: *These data were also presented in an oral presentation titled "Overcoming genetically-based resistance mechanisms to PD-1 blockade" by Davis Torrejón, M.D., UCLA Hematology-Oncology, during the Rapid Oral Abstract Presentations Session on Friday, November 9th.*]

- Genetic models of resistance to anti-PD-1 therapy were assessed using *JAK1, JAK2,* and *B2M* knockout (KO) models.
- NKTR-214 overcame resistance to anti-PD-1 in the *B2M*-KO tumor model and significantly increased survival.

Analyst Call with Melanoma Specialists
Nektar will webcast an analyst and investor conference call with melanoma specialists and company management on Saturday, November 10, 2018 at 9:00 a.m. EST in Washington, D.C. during the 2018 Society for Immunotherapy of Cancer (SITC) Annual Meeting. The event follows today's oral presentation of new efficacy, safety and immune monitoring data from the first-line Stage IV metastatic melanoma patient cohort in the PIVOT-02 study of NKTR-214 in combination with nivolumab.

Date and Time: Saturday, November 10, 2018 at 9:00 a.m. EST
Dial- in: 877-881-2183 (toll-free) or 970-315-0453 (enter access code 7865989)

Clinical investigators on the conference call will include Dr. Harriet Kluger, Professor of Medicine, Medical Oncology at the Yale Cancer Center and Dr. Adi Diab, Assistant Professor, Melanoma Medical Oncology at the University of Texas MD Anderson Cancer Center. Investors and analysts can also view slides and listen to the live audio webcast of the presentation at https://edge.media-server.com/m6/p/mjtntqda. The event will also be available for replay for two weeks on the company's website, www.nektar.com.

About NKTR-214
NKTR-214 is a CD122-biased agonist designed to stimulate the patient's own immune system to fight cancer. NKTR-214 is designed to grow specific cancer-killing T cells and natural killer (NK) cell populations in the body which fight cancer, which are known as endogenous tumor-infiltrating lymphocytes (TILs). NKTR-214 stimulates these 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. 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 effector T cells.[1] In clinical and preclinical studies, treatment with NKTR-214 resulted in expansion of these cells and mobilization into the tumor micro-environment.[2,3] NKTR-214 has an antibody-like dosing regimen similar to the existing checkpoint inhibitor class of approved medicines.

About NKTR-262
Cancer treatments that couple pharmacological activation of tumor antigen presentation with activation and expansion of CD8+ T and natural killer (NK) cells in the tumor environment have the potential to induce an effective anti-tumor immune response in patients. NKTR-262 is a novel small molecule agonist designed to activate toll-like receptors (TLRs). Intratumoral delivery of NKTR-262 promotes TLR activation to induce the development of antigen-specific immunity by initiating the process by which the immune system generates antigen-specific cytotoxic T cells to the patient's specific tumor.[4] NKTR-214 targets CD122 specific receptors found on the surface of these cancer-killing immune cells, known as CD8+ effector T cells. By first generating antigen-specific cytotoxic T cells with NKTR-262 and then growing these CD8+ effector T cells with NKTR-214, the patient's entire immunity cycle can potentially be engaged to fight cancer. In preclinical studies, a single intratumoral dose of NKTR-262, administered in combination with NKTR-214, resulted in complete abscopal tumor regressions in multiple mouse syngeneic tumor models.[5]

About NKTR-255
NKTR-255 is a memory T cell stimulating cytokine designed to engage the IL-15 pathway to induce long-term T cell activation and improve the quality of T cell memory response to treat cancer. Through optimal engagement of the IL-15Rα/IL-2Rγ receptor complex, NKTR-255 stimulates proliferation and survival of CD8+ T cells, natural killer (NK) cells and enhances formation of long-term immunological memory which may lead to sustained anti-tumor immune response. Native rhIL-15 is rapidly cleared from the body and must be administered frequently and in high doses limiting its utility due to toxicity. NKTR-255 is designed with IL-15 receptor alpha specificity to optimize biological activity and is uniquely engineered to provide optimal exposure and an improved safety profile.

About Nektar
Nektar Therapeutics is a research-based development stage biopharmaceutical company whose mission is to discover and develop innovative medicines to address the unmet medical needs of patients. Our R&D pipeline of new investigational medicines includes treatments for cancer, auto-immune disease and chronic pain. We leverage Nektar's proprietary and proven chemistry platform in the discovery and design of our new therapeutic candidates. 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: "will," "believe," "designed" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the therapeutic potential NKTR-214 in combination with other therapeutic agents, and the availability of results and outcomes from clinical and preclinical studies of our new drug candidates. 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, 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 and clinical findings and observations to date from ongoing clinical studies; (ii) 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 negatively impact drug development; (iii) data reported from ongoing clinical trials is necessarily interim data only and the final results will change based on continuing observations from patients that currently remain enrolled in the trials and/or new observations from patients enrolling in the trials; (iv) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of potential new drug candidates (such as NKTR-214, NKTR-262, and NKTR-255) is therefore very uncertain and unpredictable; (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 Nektar's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 8, 2018. 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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