Nektar Therapeutics Presents New Data from Its Immuno-Oncology Pipeline at the 2020 Society for Immunotherapy of Cancer (SITC) Annual Meeting

November 11, 2020

Updated Clinical Data for Patients with Metastatic Melanoma Treated in PIVOT-02 Study of Bempegaldesleukin with Nivolumab Show Durable Clinical Benefit with Median Progression-Free Survival of 30.9 Months

New Clinical Data Presentations for NKTR-255, a Novel IL-15 Agonist, and NKTR-262, a TLR 7/8 Agonist, Showcase Nektar's Immuno-Oncology (I-O) Pipeline

SAN FRANCISCO, Nov. 11, 2020 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced four data presentations for its I-O pipeline from three separate clinical-stage investigational agents at the 2020 Society for Immunotherapy of Cancer (SITC) Annual Meeting.

New clinical results were presented for bempegaldesleukin (BEMPEG; NKTR-214), NKTR-262 and NKTR-255. Data for BEMPEG and NKTR-262 were featured in two oral presentation sessions presented by Adi Diab, MD, Associate Professor, Department of Melanoma Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center during, respectively, the Concurrent Rapid Oral Abstract Presentation Session and the Combinatorial Therapies Session on Wednesday, November 11th. Clinical data for NKTR-255 and preclinical data for NKTR-262 were also featured in poster presentations by Dr. Nina Shah, Associate Professor, Department of Medicine, at the University of California San Francisco and Dr. Annah Rolig, Earle A. Chiles Research Institute, Providence Cancer Institute on Monday, November 9th.

Adi Diab, MD, lead investigator of the PIVOT-02 study noted: "These updated PIVOT-02 clinical data further validate our prior results that BEMPEG plus nivolumab provides both deep and durable responses in first-line metastatic Stage IV melanoma patients. We observed a total overall response rate of 53%, with 34% achieving a complete response, and now we have also observed a median depth of response of 78.5%, as well as a median progression free survival for the entire cohort of 30.9 months."

"The data presented at this year's SITC Meeting highlight that, by targeting key immunological processes, we have the opportunity to more effectively harness the body's immune system to fight cancer," said Jonathan Zalevsky, Ph.D., Head of Research and Development at Nektar Therapeutics. "In the PIVOT-02 study of BEMPEG plus nivolumab, we observed that 90% or 18 of the 20 metastatic melanoma patients who responded went on to achieve a 100% reduction in their RECIST target lesions, and, importantly for the first time, we reported a two year survival rate of 77% from this study, and median OS has not yet been reached."

"For our TLR agonist candidate, we presented data demonstrating that the combination of NKTR-262 and bempegaldesleukin alters the tumor micro-environment through activation of both the innate and adaptive arms of the immune system," continued Zalevsky. "Data presented for NKTR-255 demonstrated this novel IL-15 agonist was biologically active in patients. We observed durable and sustained increases in Natural Killer and CD8+ T cells as well as disease stabilization in the first patients who were treated in the lowest dose cohorts, which included patients with highly-refractory and heavily pre-treated multiple myeloma and Non-Hodgkin's lymphoma."

Clinical presentations at 2020 SITC are available for download at https://www.nektar.com/science/scientific-posters-and-presentations.

Highlights from the presentations are as follows:

Abstract 420: "*Progression-free survival and biomarker correlates of response with BEMPEG plus NIVO in previously untreated patients with metastatic melanoma: results from the PIVOT-02 study*", Diab, A., et al. **(Concurrent Rapid Oral Abstract Presentation Session: Clinical):**

- Confirmed best overall response rate (ORR) was 53% (20/38) in efficacy-evaluable patients, with a 34% (13/38) complete response (CR) rate. 47% (18/38) of patients achieved 100% reduction in RECIST target lesions. 80% (16/20) of patients had ongoing responses and median duration of response was not reached at a 29-month follow-up. (*Response was measured per RECIST 1.1 by blinded independent central radiology review for efficacy-evaluable patients treated. Data cut as of September 1, 2020).*
- Median progression-free survival (PFS) observed was 30.9 months. Median overall survival (OS) was not reached. Based upon a Kaplan-Meier Estimate of OS, the OS rates at 12 months, 24 months and 36 months are 82%, 77%, and 71%, respectively.
- New biomarker translational data presented show non-invasive, on-treatment biomarkers (CD8+ PSD* and eosinophils) predicted response to the combination.
- BEMPEG plus NIVO was well tolerated; treatment-related AEs are predictable and consistent with previous reports.

- In July of 2019, this novel combination was awarded US FDA Breakthrough Therapy Designation for the treatment of patients with previously untreated unresectable or metastatic melanoma.
- In melanoma, registrational Phase 3 trials evaluating BEMPEG plus NIVO are enrolling patients in the first-line metastatic setting (PIVOT IO 001; NCT03635983) and in the adjuvant setting (PIVOT-12; NCT04410445).

Abstract 368: *"REVEAL: Phase 1 dose-escalation study of NKTR-262, a novel TLR7/8 agonist, plus bempegaldesleukin: local innate immune activation and systemic adaptive immune expansion for treating solid tumors"*, Diab, A., et al. **(Combinatorial Therapies):**

- Safety, pharmacokinetics (PK), pharmacodynamics (PD) and biomarker data supported selection of NKTR-262 3.84 mg Intra-Tumoral (IT) plus BEMPEG 0.006 mg IV q3w as the RP2D. A maximum-tolerated dose was not reached.
- Robust TLR 7/8 engagement was observed upon administration of NKTR-262 IT.
- NKTR-262 plus BEMPEG induced systemic activation of T cells and Natural Killer (NK) cells demonstrating engagement of the entire immune activation cascade required for systemic tumor clearance.
- Induction of TLR7/8-responsive genes significantly correlated with CD11c+ baseline density. CD11c+ target cells are significantly more abundant in baseline melanoma biopsies vs other tumor types.
- NKTR-262 IT, as monotherapy or in combination with BEMPEG, showed early signs of clinical activity and an acceptable safety profile in a highly relapsed/refractory, heavily pre-treated melanoma patient population.

Abstract 355*: "First-in-human phase I study of NKTR-255 in patients with relapsed/refractory hematologic malignancies,"* Shah, N., et al.

- NKTR-255 was biologically active and demonstrated consistent expansion of lymphocytes, with durable and sustained increases in NK and CD8+ T cells in this highly refractory population of patients with multiple myeloma (MM) and non-Hodgkin lymphoma (NHL).
- NKTR-255 was well tolerated with low-grade, cytokine-related AEs that were transient and easily managed.
- NKTR-255 exhibited a long half-life with no evidence of accumulation.
- These data support continued dose escalation of NKTR-255 and subsequent evaluation in combination with other anticancer agents.

Abstract 451: "*Combining Bempegaldesleukin (CD122-preferential IL-2 pathway agonist) and NKTR-262 (TLR7/8 agonist) pairs local innate activation with systemic CD8+ T cell expansion to enhance anti-tumor immunity*", Rolig, A., et al.

- BEMPEG/NKTR-262 treatment produces a higher fraction of activated tumor antigen-specific cytotoxic CD8 T cells systemically, correlating with superior anti-tumor efficacy relative to BEMPEG combined with radiotherapy (RT).
- BEMPEG/NKTR-262 combination therapy depends on CD8 T cells and NK cells.
- BEMPEG/NKTR-262 combination therapy induces intra-tumoral CD8+ T cells that have increased activity as demonstrated by increased granzyme expression and increased tumor killing, and reduced conversion to an exhausted phenotype (PD-1, Tim3, Lag3).
- Loss of NK cells reduces CD8+T cell percentages and function in the peripheral blood and in the tumor, suggesting a connection between early NK cell function and anti-tumor adaptive immune responses.

Analyst Call with Panel of Oncology Experts:

Nektar will webcast an analyst and investor conference call that will include SITC authors and presenters, Dr. Adi Diab, Associate Professor, Melanoma Medical Oncology at The University of Texas MD Anderson Cancer Center; Dr. Brendan Curti, Director of the Melanoma Program, Cytokine and Adoptive Immunotherapy and Genitourinary Oncology Research at Providence Cancer Institute; Dr. Nina Shah, Associate Professor, Department of Medicine, at the University of California San Francisco; and Dr. Alan Tan, Assistant Professor, Department of Internal Medicine, Division of Hematology, Oncology and Cell Therapy at Rush Medical College.

Date and Time: Wednesday, November 11, 2020, at 4:15 p.m. EST

Dial-in: 877-881-2183 (toll-free) or 970-315-0453 (enter access code 2090614)

Investors and analysts can also view slides and listen to the live audio webcast of the presentation at https://edge.media-server.com/mmc/p/25u4g5o7. The event will also be available for replay for two weeks on the company's website, www.nektar.com.

Dr. Adi Diab

Adi Diab, M.D., serves as Associate Professor of Melanoma Medical Oncology at The University of Texas MD Anderson Cancer Center. Dr. Diab is one of the lead investigators in PIVOT-02, the Phase 1/2 study of BEMPEG plus nivolumab, and in REVEAL, the Phase 1/2 study of NKTR-262 and BEMPEG. He is also on the steering committee for the BMS-sponsored Phase 3 registrational study, PIVOT IO 001, which is ongoing, in patients with previously untreated metastatic melanoma. His research is focused on developing new immunotherapeutic strategies that will improve clinical outcomes in patients. He has authored or co-authored over thirty scientific publications and abstracts and serves as a reviewer for *Cancer Discovery*, *Journal of Clinical Oncology*, *Nature Reviews Journal of Immunotherapy* and *Journal of the American Society of Hematology*.

Dr. Brendan D. Curti

Brendan D. Curti, M.D., is the Robert W. Franz Chair for Clinic Research and Member in the Earle A. Chiles Research Institute at Providence Cancer Institute. He serves as the Director of Cytokine and Adoptive Immunotherapy, Melanoma Program and Genitourinary Oncology Research. His clinical research focuses on developing new immunotherapies for melanoma, renal cell carcinoma, prostate cancer and bladder cancer. He previously served as a Senior Investigator in the Biological Response Modifiers Program at the National Cancer Institute and was an Associate Professor at the Penn State College of Medicine before joining the Earle A. Chiles Research Institute at Providence Cancer Institute.

Dr. Nina Shah

Nina Shah, M.D., is an Associate Professor in the Department of Medicine at the University of California San Francisco and a specialist in blood diseases who focuses on treating multiple myeloma, a type of cancer affecting certain cells in the bone marrow. Her areas of professional interest include the intersection of immunology and oncology as well as helping patients fight multiple myeloma by boosting their immune systems. She is an investigator in the NKTR-255 Phase 1/2 study in hematological malignancies. She belongs to the American Society of Clinical Oncology, American Society of Hematology and American Society for Transplantation and Cellular Therapy.

Dr. Alan Tan

Alan Tan, MD, is an Assistant Professor in the Division of Hematology, Oncology and Cell Therapy at Rush Medical College. He specializes in kidney cancer, bladder cancer, prostate cancer and melanoma. He also has an extensive background in hematologic malignancies. Dr. Tan has clinical research interest in designing and implementing clinical trials to test novel immunotherapies and targeted therapies for renal cell carcinoma and GU malignancies. He is an investigator in the NKTR-255 Phase 1/2 study in hematological malignancies. He also has interest in precision genomic cancer medicine, identifying molecular alterations that will serve as targets for individualized treatment strategies.

About Bempegaldesleukin (NKTR-214)

Bempegaldesleukin (BEMPEG: NKTR-214) is an investigational CD122-preferential IL-2–pathway agonist that leverages the clinically validated IL-2 pathway to stimulate an antitumor immune response.[1] BEMPEG was engineered to deliver a controlled, sustained, and preferential IL-2 pathway signal, with the goals of stimulating an antitumor immune response while minimizing toxicity, thereby allowing for outpatient administration.[1,2] In a phase 1 trial of BEMPEG in combination with the checkpoint inhibitor nivolumab (NIVO; PIVOT-02), the combination was well tolerated and produced durable responses that deepened over time in multiple advanced solid tumor types.[3]

In July of 2019, Bristol-Myers Squibb and Nektar Therapeutics announced that the U.S. Food and Drug Administration granted Breakthrough Therapy Designation for investigational agent bempegaldesleukin in combination with nivolumab for the treatment of patients with previously untreated unresectable or metastatic melanoma.

The Nektar-Bristol-Myers Squibb joint clinical development program for BEMPEG+NIVO includes registrational and other studies of BEMPEG plus NIVO in select tumor types (melanoma, renal cell carcinoma or RCC, and bladder cancer). This includes a Phase 3 trial in first-line advanced melanoma (NCT03635983), a Phase 3 trial in adjuvant melanoma (NCT04410445), a Phase 3 trial in advanced RCC (NCT03729245), a Phase 3 trial in muscle-invasive bladder cancer (NCT04209114), a Phase 2 trial in cisplatin-ineligible urothelial carcinoma (NCT03785925) and a Phase 1/2 trial in combination with a tyrosine kinase inhibitor in advanced RCC (NCT04540705).

BEMPEG is also being evaluated by Nektar in the PROPEL study in combination with pembrolizumab in non-small cell lung cancer (NCT03138889) and in collaboration with Vaccibody in the DIRECT-01 study in combination with VB10.NEO in squamous cell carcinoma of the head and neck (NCT03548467).

About NKTR-255

NKTR-255 is an IL-15 receptor agonist designed to activate the IL-15 pathway, expand NK cells and promote the survival and expansion of memory CD8+ T cells. Through optimal engagement of the IL-15Rα/IL-2Rβγ receptor complex, NKTR-255 enhances formation of long-term immunological memory, which may lead to sustained anti-tumor immune response. NKTR-255 is uniquely designed to overcome the challenges of recombinant IL-15, which is rapidly cleared from the body and must be administered frequently and in high doses, limiting its utility due to toxicity and convenience of use.

About NKTR-262

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.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit us at BMS.com or follow the company on LinkedIn, Twitter, YouTube, Facebook, and Instagram.

About Nektar

Nektar Therapeutics is a biopharmaceutical company with a robust, wholly owned R&D pipeline of investigational medicines in oncology, immunology and virology as well as a portfolio of approved partnered medicines. 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.

1. Bentebibel S-E, et al. A First-in-Human Study and Biomarker Analysis of NKTR-214, a Novel IL2Rβγ -Biased Cytokine, in Patients with Advanced or Metastatic Solid Tumors. *Cancer Discovery* 2019;9:711-21.
2. Charych D, et al. Modeling the receptor pharmacology, pharmacokinetics, and pharmacodynamics of NKTR-214, a kinetically controlled interleukin-2 (IL2) receptor agonist for cancer immunotherapy. *PLoS ONE* 2017;12.
3. Diab A, et al. Bempegaldesleukin (NKTR-214) plus nivolumab in patients with advanced solid tumors: Phase 1 dose-escalation study of safety, efficacy and immune activation (PIVOT-02). *Cancer Discovery* 2020
4. Adams S. Toll-like receptor agonists in cancer therapy. *Immunotherapy*. 2009;1(6):949-964. doi:10.2217/imt.09.70.

*Polynomial Strength Difference (PSD): difference in PSI between C1D1 and C1D8; PSI, polyfunctional strength index, using IsoPlexis technology

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "will," "develop," "may," "design" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the therapeutic potential of bempegaldesleukin in combination with other agents, and the therapeutic potential of each of NKTR-255 and NKTR-262, as well as the availability of results and outcomes from clinical and preclinical studies of our 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 our drug candidates are based on preclinical and clinical findings and the expected therapeutic potential for each of our drug candidates is subject to change as research and development continue; (ii) our drug candidates are in clinical development and the risk of failure remains high and failure can unexpectedly occur at any stage for one or more of the indications being studied prior to regulatory approval due to lack of sufficient efficacy, safety considerations or other factors that impact drug development; (iii) data reported from ongoing preclinical and clinical trials are necessarily interim data only and the final results will change based on continuing observations; (iv) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of potential new drug candidates (such as bempegaldesleukin, NKTR-255 and NKTR-262) is therefore very uncertain and unpredictable; (v) the timing of the commencement or end of clinical studies and the availability of clinical data 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, delays caused by our collaboration partners, and enrollment competition; (vi) 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 (vii) 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 6, 2020. 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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