Nektar Therapeutics Announces Data Presentations for Its Immuno-Oncology Pipeline at the 2021 Society for Immunotherapy of Cancer (SITC) Annual Meeting

November 12, 2021

Initial Safety and Efficacy Data for NKTR-255, a Novel IL-15 Agonist, in Combination with Cetuximab in Solid Tumors Presented in Late-Breaking Abstract Session

SAN FRANCISCO, Nov. 12, 2021 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced three data presentations for its I-O pipeline at the 2021 Society for Immunotherapy of Cancer (SITC) Annual Meeting.

Initial clinical results were presented from the dose-escalation stage of a Phase 1/2 study of NKTR-255 in combination with cetuximab in a late-breaking abstract presented by Mehmet Altan, MD, Assistant Professor, Department of Thoracic/Head and Neck Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center on Friday, November 12th. Collaborator presentations of translational data for bempegaldesleukin in combination with nivolumab and bempegaldesleukin in combination with NKTR-262 data were also featured in two poster presentations by Arika S. Feils at the Department of Human Oncology, University of Wisconsin School of Medicine and Public Health and Annah Rolig, PhD, Earle A. Chiles Research Institute, Providence Cancer Institute, respectively, on Friday, November 12th.

"The data presented at this year's SITC meeting highlight the strength of our cytokine portfolio and in particular the potential of NKTR-255 in the treatment of patients with solid tumors," said Jonathan Zalevsky, Ph.D., Senior Vice President and Chief Research & Development Officer at Nektar. "We were excited to see early evidence of clinical benefit in the first patients treated in the dose-escalation portion of the study for NKTR-255 in combination with cetuximab which reinforces the promising synergy of IL-15 in combination with an antibody-dependent cellular cytotoxicity agent for the treatment of solid tumors."

2021 SITC presentations are available for download at http://www.nektar.com/science/scientific-posters.

Highlights from the presentations are as follows:

Abstract 957: *"NKTR-255 Plus Cetuximab in Patients with Solid Tumors: Interim Safety and Efficacy Results from the Phase 1b Dose Escalation Study",* Altan, M., et al.

- The combination of NKTR-255 + cetuximab was well tolerated at NKTR-255 doses of 1.5 and 3.0 µg/kg every three weeks (Q21D) and treatment-related adverse events were generally low-grade, transient, and easily managed.
- Early evidence of on-target biological activity was observed with treatment with NKTR-255 leading to expansion and proliferation of Natural Killer (NK) cells and CD8+ T cells.
- Early evidence of clinical activity was observed in 9 patients that were evaluable for efficacy [6 colorectal (CRC) patients, 3 squamous cell carcinoma of head and neck (SCCHN) patients] with 1 CRC patient achieving a confirmed partial response (PR) with 52% tumor reduction by RECIST and 5 patients experiencing stable disease (SD) by RECIST [3 CRC, 2 SCCHN] in this heavily pre-treated and highly refractory patient population. 8 of the 9 patients evaluable for efficacy had also received prior treatment with an EGFR-targeted therapy and/or a checkpoint inhibitor.
- The maximum tolerated dose and recommended Phase 2 dose have not been reached yet and dose escalation of NKTR-255 + cetuximab is ongoing in patients with R/R SCCHN and CRC.

Abstract 59*: "Associations between KIR/KIR-ligand genotypes and clinical outcome for patients with advanced solid tumors receiving BEMPEG plus nivolumab combination therapy in the PIVOT-02 trial",* Feils, AS., et al.

- Individuals who were positive for KIR2DL2 and its HLA-C1 ligand had significantly greater TS (p=0.01) and longer PFS (p=0.04) with a trend towards increased ORR (p=0.07).
- No significant associations were found between an individual's clinical outcome and their KIR_3DL_1 and $HLA\text{-}Bw_4$ ligand status.
- Individuals who were positive for both KIR_2DL_2 and KIR_3DL_1 with their HLA-C1 and HLA-Bw4 ligands, respectively, had significantly greater TS (p=0.04) and increased ORR with a trend towards longer PFS (p=0.07).
- No significant associations were found between an individual's clinical outcome and their KIR/KIR-ligand present versus missing status.

Abstract 596: "*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 preclinical efficacy is superior to BEMPEG+RT efficacy and relies on CD8+ T cells.
- BEMPEG+NKTR-262 combination therapy produces a higher fraction of activated, tumor antigen-specific cytotoxic CD8+ T

cells systemically, correlating with superior anti-tumor efficacy relative to BEMPEG+RT in preclinical models.
- In preclinical models, BEMPEG+NKTR-262 therapy induces active (GzmA+, Ki-67+) AH1-A5-CD8+ T cell that are supported by type 1 IFN signaling, suggesting bystander T cell activity.
- In preclinical models, BEMPEG+NKTR-262 combination therapy induces intratumoral CD8+ T cells that have increased activity as demonstrated by increased granzyme expression, increased cytolytic capacity, and reduced conversion to an exhausted phenotype (PD-1+).

Analyst Call with Cancer Specialist:

Nektar management will host an analyst and investor conference call to review the data presentation for NKTR-255 at SITC 2021. The call will also include two invited speakers:

- Mehmet Altan, MD, Assistant Professor, Department of Thoracic/Head and Neck Medical Oncology, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center
- Alan Tan, MD, Director of GU Medical Oncology and Assistant Professor in the Division of Hematology, Oncology and Cell Therapy at Rush University Medical Center

Date and Time: Friday, November 12, 2021 at 12:00 p.m. EST

Dial-in: 877-881-2183 (toll-free) or 970-315-0453 (enter access code 1769208)

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/aqdnveeb. The event will also be available for replay for two weeks on the company's website, www.nektar.com.

Biography for Mehmet Altan, MD

Mehmet Altan, MD, is an Assistant Professor in the Department of Thoracic/Head and Neck Medical Oncology, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center. Dr. Altan is one of the lead investigators in the phase 1/2, dose-escalation and dose-expansion study of NKTR-255 in combination with cetuximab in patients with refractory 2nd and 3rd line metastatic colorectal cancer or metastatic head and neck cancer. His current research areas include identification of mechanisms for primary and secondary resistance to immunotherapies and predictive markers for immunotherapy toxicities. He also works on translational research projects for identification of spatiotemporal dynamics of the tumor microenvironment in response to immunotherapy to define potential therapeutic targets.

Biography for Alan Tan, MD

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 also has interest in precision genomic cancer medicine, identifying molecular alterations that will serve as targets for individualized treatment strategies.

About Nektar

Nektar Therapeutics is a biopharmaceutical company with a robust, wholly owned R&D pipeline of investigational medicines in oncology, immunology and virology 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 Discov* 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.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "will," "design," "develop," "potential" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the therapeutic potential of, and future development plans for, bempegaldesleukin, 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, 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 bempegaldesleukin, NKTR-255 and NKTR-262 are based on preclinical and clinical findings and observations and are subject to change as research and development continue; (ii) bempegaldesleukin, NKTR-255 and NKTR-262 are investigational agents and continued research and development for these drug candidates is subject to substantial risks, including negative safety and efficacy findings in ongoing clinical studies (notwithstanding positive findings in earlier preclinical and clinical studies); (iii) bempegaldesleukin, NKTR-255 and NKTR-262 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; (iv) the timing of the commencement or end of clinical trials 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, competitive factors, or delay or failure in ultimately obtaining regulatory approval in one or more important markets; (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 our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 5, 2021. 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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