Nektar Therapeutics Presents New Preclinical Data for its Immuno-Oncology Programs at the American Association for Cancer Research (AACR) Annual Meeting 2018

April 15, 2018

Four Preclinical Data Presentations Showcase Nektar's Immuno-Oncology Programs, NKTR-214 and NKTR-262

SAN FRANCISCO, April 15, 2018 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced that it is presenting new preclinical data for its immuno-oncology programs at the American Association for Cancer Research (AACR) Annual Meeting 2018. Nektar researchers and collaborators will present new preclinical data on NKTR-214, a CD122-biased agonist, as well as on NKTR-262, a novel toll-like receptor (TLR) agonist.

"The preclinical studies being presented at AACR by both Nektar scientists and our collaborators highlight the potential of NKTR-214 as a backbone therapy in immuno-oncology," said Jonathan Zalevsky, Ph.D., Nektar's Senior Vice President and Chief Scientific Officer. "NKTR-214 is designed to stimulate the number and functional activity of cancer-fighting T cells which are often limited in patients with cancer and necessary for immunotherapy to be fully effective. These data show that NKTR-214 synergizes with multiple modalities including TLRs, HDAC and ACT. With regard to TLR biology, the combination of NKTR-214 and NKTR-262 engages both the innate and adaptive immune system to initiate antigen release, expand T cells and drive them into the tumor. This novel immuno-oncology combination is now being evaluated in a Phase 1/2 study."

NKTR-214 is an investigational immuno-stimulatory therapy designed to expand specific cancer-fighting CD8+ effector T cells and natural killer (NK) cells directly in the tumor micro-environment and increase expression of PD-1 on these immune cells. NKTR-214 targets CD122 receptors found on the surface of cancer-fighting immune cells in order to stimulate the proliferation and activation of these cells. In clinical and preclinical studies, treatment with NKTR-214 resulted in expansion of these cell populations and their mobilization into the tumor.[1,2] NKTR-214 has an antibody-like dosing regimen similar to the existing checkpoint inhibitor class of approved medicines.

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.[3] 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.[4]

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

Immunology

Abstract 3755/Poster 5: "*Comprehensive antitumor immune activation by a novel TLR7/8 targeting agent NKTR-262 combined with CD122-biased immunostimulatory cytokine NKTR-214*", Kivimae, S., et al.
Session: Immunomodulatory Agents and Interventions 1
Session Date and Time: Tuesday, April 17, 2018, 8:00 a.m. - 12:00 p.m. Central Time
Location: McCormick Place South, Exhibit Hall A, Poster Section 32

- The combination of NKTR-262 and NKTR-214 demonstrates efficacy in a broad range of syngeneic tumor models with diverse histologies.
- 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.

Abstract 2755/Poster 17: *"NKTR-262: Prodrug pharmacokinetics in mice, rats, and dogs*", Lee, M., et al.
Session: Immune Mechanisms Invoked by Therapies 1
Session Date and Time: Monday, April 16, 2018, 1:00 p.m. - 5:00 p.m. Central Time
Location: McCormick Place South, Exhibit Hall A, Poster Section 33

- NKTR-262 was effectively retained in the injected tumor after intratumoral injection.
- NKTR-262's prodrug design was demonstrated *in vitro* by the formation of active species.
- Compared to intratumoral injection of an unmodified TLR agonist, intratumoral injection of NKTR-262 resulted in elevated cytokine levels in the tumor and reduced systemic cytokine induction.

Tumor Biology

Abstract 123/Poster 13: "*Enhanced anti-tumor activity of the combination of entinostat and NKTR-214 in renal and colon cancer tumor models*", Wang, L., et al.
Session: Role of the Innate Immune System in Tumorigenesis
Session Date and Time: Sunday, April 15, 2018, 1:00 p.m. - 5:00 p.m. Central Time
Location: McCormick Place South, Exhibit Hall A, Poster Section 5

- The combination of NKTR-214 and entinostat, an HDAC inhibitor, significantly inhibited tumor growth in CT26 colon carcinoma and RENCA renal cell carcinoma models producing greater levels of IFNγ and granzyme B to enhance T cell cytotoxicity.
- Preclinical results presented suggest that NKTR-214 and entinostat is a promising combination to explore in patients with CRC or renal cell carcinoma.

Clinical Research

Abstract 3566/Poster 4: "*Enhanced expansion and tumor targeting of adoptively transferred T cells with NKTR-214*", Parisi, G., et al.
Session: Adoptive Cell Therapy 3
Session Date and Time: Tuesday, April 17, 2018, 8:00 a.m. - 12:00 p.m. Central Time
Location: McCormick Place South, Exhibit Hall A, Poster Section 24

- NKTR-214 + ACT was well tolerated and provides a robust anti-tumor response in the aggressive B16F10 melanoma tumor model.
- Treatment with NKTR-214 + ACT mobilizes T cells into the tumor where they durably persist without expanding T cells in the periphery.
- The robust and long-lasting effect of NKTR-214 supports its potential use in combination with cell-based therapeutics.

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, autoimmune 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: "design," "may," and "will" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the therapeutic potential of NKTR-214 and NKT-262, alone and in combination with each other as a doublet, and the anticipated progress and outcomes of our clinical studies. 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 NKTR-214 and NKTR-262 are based on findings and observations from preclinical findings; (ii) NKTR-214 and NKTR-262, both alone and in combination with other agents are in early stages of research and clinical development and the risk of failure remains high and failure can unexpectedly occur due to efficacy, safety or other unpredictable factors prior to regulatory approval for numerous reasons, including negative safety and efficacy findings even after positive findings in previous clinical and preclinical studies; (iii) 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, competitive factors, or delay or failure in ultimately obtaining regulatory approval in one or more important markets; (iv) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of applying our technology platform to potential new drug candidates (such as NKTR-214 and NKTR-262) is therefore highly uncertain and unpredictable and one or more research and development programs could fail; (v) patents may not issue from our patent applications for our drug candidates including NKTR-214 and NKTR-262, 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 Annual Report on Form 10-K for the year ended December 31, 2017 filed with the Securities and Exchange Commission on March 1, 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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1. Charych, D., et al., Clin Can Res; 22(3) February 1, 2016
2. Diab, A., et al., Journal for ImmunoTherapy of Cancer 2016, 4(Suppl 1):P369
3. Adams S. Toll-like receptor agonists in cancer therapy. *Immunotherapy*. 2009;1(6):949-964. doi:10.2217/imt.09.70.
4. Kivimae, S., et al., Journal for ImmunoTherapy of Cancer 2017, 5(Suppl 2):P275

View original content:http://www.prnewswire.com/news-releases/nektar-therapeutics-presents-new-preclinical-data-for-its-immuno-oncology-programs-at-the-american-association-for-cancer-research-aacr-annual-meeting-2018-300630025.html

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