

Nektar Therapeutics Presents Preclinical Data from Novel PEGylated Interferon Gamma Program, NKTR-288, at the Society for Immunotherapy of Cancer (SITC) Annual Meeting

November 10, 2022

NKTR-288 upregulated MHC Class I and PD-L1 expression on tumors, enhancing anti-tumor activity when combined with anti-PD-1 or anti-PD-L1 antibodies

SAN FRANCISCO, Nov. 10, 2022 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced the first presentation of preclinical data for NKTR-288 at the 2022 Society for Immunotherapy of Cancer (SITC) Annual Meeting.

NKTR-288 is a novel polyethylene glycol (PEG)-conjugate of interferon gamma (IFN- γ), designed to modify binding of IFN- γ to its substrates and optimize the duration of IFN- γ signaling. IFN- γ is a cytokine that induces cellular antigen presentation and enhances tumor antigen-specific cytotoxic T cell response, and may have applications in a number of therapeutic areas, including oncology and infectious diseases, among others.

The presentation today showed the sustained pharmacological properties of NKTR-288 relative to native cytokine, including durable exposure and induction of the well characterized interferon gamma response. These data support further evaluation of NKTR-288 as a monotherapy or in combination with checkpoint inhibitors in the clinical setting.

"The results presented at SITC clearly demonstrate that NKTR-288 has differentiated pharmacokinetic and pharmacodynamic properties compared to native IFN- γ , leading to durable *in vivo* anti-tumor activity in preclinical models," said Jonathan Zalevsky, Ph.D., Senior Vice President and Chief Research & Development Officer at Nektar. "Particularly promising were data that show NKTR-288 upregulates PD-L1 expression in tumor tissue, supporting potential combination therapy with checkpoint inhibitors by enhancing checkpoint blockade efficacy in low-MHC Class I 'cold' tumor models. It highlights the potential of NKTR-288 to augment currently available PD-1 or PD-L1 treatment strategies and possibly broaden the responsive patient population."

Also presented at SITC by Nektar's partner, Merck KGaA, is a trials in progress poster of the Phase 2 JAVELIN Bladder Medley study ([NCT05327530](https://clinicaltrials.gov/ct2/show/study/NCT05327530)). The ongoing clinical trial includes evaluation of BAVENCIO[®] (avelumab), Merck's anti-PD-L1 therapy, in combination with NKTR-255, Nektar's IL-15 receptor agonist designed to increase the proliferation and survival of natural killer (NK) cells and memory CD8⁺ T cells to enhance anti-tumor immunity. Merck KGaA is running this study and is on track to generate comparative progression-free survival (PFS) data for this study by the end of 2024.

Key details and takeaways from the presentation are as follows:

Abstract 1086: "NKTR-288, a PEGylated Interferon Gamma Drug Candidate for the Treatment of Cancer", Hamel, D., et al.

- NKTR-288 demonstrated reduced affinity to both IFN- γ receptor and heparin, decreasing target mediated drug disposition (TMDD) and increasing bioavailability compared to native IFN- γ .
- Induced sustained upregulation of major histocompatibility complex class I (MHC Class I) expression in fast-growing, low-MHC Class I "cold" syngeneic tumor models, as well as T cell-mediated anti-tumor activity, alone and in combination with checkpoint inhibitors.
- NKTR-288 also upregulated PD-L1 expression in tumor tissue as a monotherapy, while significant anti-tumor activity was observed when combined with anti-PD-1 or anti-PD-L1 antibodies.
- Well tolerated at pharmacologically active doses in preclinical models well below maximum tolerated dose (1 mg/kg).
- These results support the development of NKTR-288, a novel, optimized IFN- γ pathway agonist, to treat cancer as a monotherapy or in combination with PD-1/PD-L1 therapy.

Details of the Trials in Progress poster presentation are as follows:

Abstract 665: "JAVELIN Bladder Medley: a phase 2 trial of avelumab in combination with other antitumor drugs as first-line maintenance therapy for advanced urothelial carcinoma", Hoffman-Censits, J., et al.

- The objective of the phase 2, multicenter, randomized, open-label parallel-arm JAVELIN Bladder Medley umbrella trial (NCT05327530) is to assess the safety and efficacy of avelumab in combination with other antitumor agents, including NKTR-255, as first-line (1L) maintenance treatment for patients with advanced urothelial carcinoma (UC).
- When completed, the ongoing JAVELIN Bladder Medley study will show whether 1L maintenance treatment with avelumab-based combinations can improve PFS vs avelumab alone and report the safety and tolerability of the combination regimens.

Details of the data presentations at SITC are available on the Science section of Nektar's website at <http://www.nektar.com>

About NKTR-288

NKTR-288 is a PEG-conjugate of the protein, IFN- γ , a cytokine that induces cellular antigen presentation and has great potential in cancer treatment through enhancement of tumor antigen specific cytotoxic T cell response. NKTR-288 was designed utilizing a site-specific conjugation approach to modify binding of IFN- γ with one of its substrates, and overall, to optimize the duration of IFN- γ signaling. This program has applications in a number of therapeutic indications including oncology as well as in infectious disease and others.

About NKTR-255

NKTR-255 is a biologic that targets the IL-15 pathway in order to activate the body's innate and adaptive immunity. Through optimal engagement of the IL-15 receptor complex, NKTR-255 is designed to enhance functional NK cell populations and formation of long-term immunological memory, which may lead to sustained and durable anti-tumor immune response.

Preclinical findings suggest NKTR-255 has the potential to synergistically combine with antibody-dependent cellular cytotoxicity molecules as well as to enhance CAR-T therapies. Nektar has initiated a Phase 1 dose escalation and expansion clinical study of NKTR-255 in adults with relapsed or refractory non-Hodgkin lymphoma or multiple myeloma, as well as a Phase 1/2 clinical study of NKTR-255 in patients with relapsed or refractory head and neck squamous cell carcinoma or colorectal cancer. Nektar is also continuing its oncology clinical collaboration with Merck KGaA and Pfizer Inc. to evaluate the maintenance regimen of NKTR-255 in combination with avelumab, a PD-L1 inhibitor, in patients with locally advanced or metastatic urothelial carcinoma in the Phase 2 JAVELIN Bladder Medley study. Nektar is also currently designing a Nektar-sponsored Phase 2/3 study combining NKTR-255 with approved CAR-T cell therapies in diffuse large B-cell lymphoma, which it aims to initiate in the first quarter of 2023.

About Nektar Therapeutics

Nektar Therapeutics is a biopharmaceutical company with a robust, wholly owned R&D pipeline of investigational medicines in oncology and immunology as well as a portfolio of approved partnered medicines. Nektar is headquartered in San Francisco, California, with additional operations in Huntsville, Alabama. Further information about the company and its drug development programs and capabilities may be found online at <http://www.nektar.com>.

Nektar Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "will," "may," "demonstrate," "potential," "designed," "initiate," "generate" 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 NKTR-288, NKTR 255 and our other drug candidates in research programs, the prospects and plans for our collaborations with other companies, and the timing of the initiation of clinical studies and the data readouts for 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 NKTR-288, NKTR-255 and our other drug candidates are based on preclinical and clinical findings and observations and are subject to change as research and development continue; (ii) NKTR-288, NKTR-255 and our other drug candidates 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) NKTR-288, NKTR-255 and our other drug candidates 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 challenges caused by the COVID-19 pandemic, 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) we may not achieve the expected costs savings we expect from our corporate restructuring and reorganization, (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 our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 4, 2022. 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.

Contact:

For Media:

David Rosen of Argot Partners


(212) 600-1902

david.rosen@argotpartners.com

For Investors:

Vivian Wu of Nektar Therapeutics

628-895-0661

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