Nektar Announces New Clinical Collaboration with Merck KGaA Darmstadt, Germany and Pfizer Inc. to Combine NKTR-255, a Novel Interleukin-15 Agonist, with Avelumab in the JAVELIN Bladder Medley Study

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SAN FRANCISCO, Sept. 21, 2021 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) announced it has entered into a new oncology clinical collaboration with Merck KGaA, Darmstadt, Germany and Pfizer Inc. to evaluate the maintenance regimen of NKTR-255, Nektar's interleukin-15 (IL-15) receptor agonist, in combination with avelumab, a PD-L1 inhibitor, in patients with locally advanced or metastatic urothelial carcinoma (UC) in the Phase II JAVELIN Bladder Medley study.

NKTR-255 is wholly owned by Nektar and is currently being evaluated in two separate clinical studies in both liquid and solid tumors. The novel IL-15 agonist is designed to activate the IL-15 pathway to expand both natural killer (NK) cells and memory CD8+ T cell populations.[1] Avelumab, which is marketed in the U.S. as BAVENCIO®, is co-developed and co-commercialized by Merck KGaA, Darmstadt, Germany and Pfizer Inc.

"We are excited to partner with Merck KGaA, Darmstadt, Germany and Pfizer Inc. to evaluate the combination of NKTR-255 with avelumab in urothelial carcinoma," said Jonathan Zalevsky, Ph.D., Chief Research & Development Officer at Nektar. "Preclinical studies suggest that avelumab may induce lysis of tumor cells via antibody-dependent cell-mediated cytotoxicity, or ADCC, indicating an additional mechanism of action, and providing an opportunity for potential synergy when combined with an NK cell stimulator, such as NKTR-255."

Under the new collaboration, Merck KGaA, Darmstadt, Germany and Pfizer Inc. will include the combination of NKTR-255 plus avelumab in the new JAVELIN Bladder Medley study. The study is a recently designed global, multi-center Phase II umbrella trial evaluating different avelumab-based combinations, compared with avelumab monotherapy, as potential maintenance therapy regimens for patients with locally advanced or metastatic UC that has not progressed with a first-line platinum-containing chemotherapy regimen. Nektar will supply NKTR-255 for the trial. Nektar and the Merck KGaA, Darmstadt, Germany-Pfizer alliance will each maintain existing global commercial rights to their respective medicines. The study is expected to begin enrolling patients in the first quarter of 2022.

BAVENCIO® (avelumab) is indicated in the U.S. and Europe for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-containing chemotherapy.

NKTR-255 is an investigational agent in clinical development and is not approved alone or in combination with avelumab (or any other agent) for use in any country.

About Urothelial Carcinoma

Bladder cancer is the 10th most commonly diagnosed cancer worldwide, with approximately 573,000 new cases and 213,000 deaths.[2] It is more common in men than in women, representing the 6th most common cancer and the 9th leading cause of cancer death among males. Incidence rates for men and women are respectively 9.5 and 2.4 per 100,000. Mortality rates for men and women are respectively 3.3 and 0.9 per 100,000.[2] Noninvasive cancers reflect a large proportion of all bladder cancers[2], and only 25% to 55% of patients receive any second-line therapy after first-line chemotherapy.[3-9] In the U.S. and EU5 markets, approximately 40% to 50% of patients receive an immune checkpoint inhibitor in second-line therapy.[10]

BAVENCIO Important Safety Information from the US FDA-Approved Label

The warnings and precautions for avelumab (BAVENCIO®) include immune-mediated adverse reactions (such as pneumonitis and hepatitis [including fatal cases], colitis, endocrinopathies, nephritis, and other immune-mediated adverse reactions as a single agent or in combination with axitinib [which can be severe and have included fatal cases]), infusion-related reactions, hepatotoxicity in combination with axitinib, major adverse cardiovascular events (MACE) in combination with axitinib [which can be severe and have included fatal cases], and embryo-fetal toxicity.

Common adverse reactions (reported in at least 20% of patients) in patients treated with BAVENCIO® monotherapy include fatigue, musculoskeletal pain, diarrhea, nausea, infusion-related reaction peripheral edema, decreased appetite, urinary tract infection and rash. Common adverse reactions (reported in at least 20% of patients) in patients receiving BAVENCIO® in combination with axitinib include diarrhea, fatigue, hypertension, musculoskeletal pain, nausea, mucositis, palmar-plantar erythrodysesthesia, dysphonia, decreased appetite, hypothyroidism, rash, hepatotoxicity, cough, dyspnea, abdominal pain and headache. Grade 3-4 hematology laboratory value abnormalities reported in at least 10% of patients with Merkel cell carcinoma treated with BAVENCIO® monotherapy include lymphopenia; in patients receiving BAVENCIO® in combination with axitinib, grade 3-4 clinical chemistry abnormalities include blood triglyceride increased and lipase increased.

For full US Prescribing Information and Medication Guide for BAVENCIO®, please see http://www.BAVENCIO.com.

About NKTR-255
NKTR-255 is a novel polyethylene glycol (PEG)-conjugate of recombinant human interleukin-15 (rhIL-15), which was designed to retain all known receptor binding interactions of the IL-15 molecule. The investigational candidate is uniquely designed to overcome known challenges of recombinant IL-15 and other IL-15 agonists, which are rapidly cleared from the body and have shown diminishing response to successive doses. Through an extended circulating half-life and optimal engagement of the IL-15Rα/IL-2Rβγ receptor complex, NKTR-255 enhances functional NK cell populations and formation of long-term CD8+ mediated immunological memory, which may lead to sustained anti-tumor immune response.

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.

BAVENCIO is a registered trademark of Merck KGaA, Darmstadt, Germany.

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Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "will", "may," "design," "potential," "provide," "expect," "indicate," "suggest" 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-255 in both liquid and solid tumors and as alone or in combination with other agents (such as avelumab), the potential benefits of clinical collaborations and the timing and the availability of results from 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-255 are based on preclinical and clinical findings and observations and are subject to change as research and development continue; (ii) NKTR-255 is an investigational agent and continued research and development for this drug candidate 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-255 is in early 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 or competitive factors; (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 August 6, 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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