Nektar Therapeutics Announces Initiation of First-in-Human Phase 1 Clinical Study of NKTR-255, an IL-15 Agonist, in Adults with Relapsed or Refractory Non-Hodgkin Lymphoma or Multiple Myeloma

October 16, 2019

SAN FRANCISCO, Oct. 16, 2019 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) today announced the initiation of a first-in-human, Phase 1 clinical study evaluating NKTR-255, an interleukin-15 (IL-15) receptor agonist, as monotherapy for patients with relapsed or refractory non-Hodgkin lymphoma (NHL) or multiple myeloma (MM). The study will also combine NKTR-255 with multiple targeted antibodies, that function through an antibody-dependent cell-mediated cytotoxicity (ADCC) mechanism, to evaluate the safety and efficacy in adults with relapsed or refractory MM. NKTR-255 is designed to activate the IL-15 pathway and expand functionally superior natural killer (NK) cells and promote the survival and expansion of memory CD8+ T cells without inducing suppressive regulatory T cells.

"We are excited to launch the first-in-human clinical study of NKTR-255, which has shown promising and substantial anti-tumor activity in our preclinical studies," said Wei Lin, M.D., Senior Vice President and Head of Development at Nektar Therapeutics. "By increasing the number and activity of NK cells, NKTR-255 has the potential to enhance the host's tumor-fighting response, both as a single agent and in combination with tumor-targeting antibodies, including daratumumab and rituximab."

One of the big challenges in treating cancer patients with targeted monoclonal antibodies is that the cancer patients have a deficiency in key effector cells like NK cells that are needed to work with the monoclonal antibodies.[1,2] In nonclinical studies, NKTR-255 exhibited anti-tumor activity and substantially enhanced *in vivo* proliferation and activation of NK cells to provide sustained cytotoxic function.[3] In a preclinical lymphoma model where single agent daratumumab was ineffective, NKTR-255 treatment, in combination with daratumumab, increased NK cell numbers and activity in bone marrow tissue and enhanced ADCC-mediated tumor cell clearance in the bone marrow compartment.[4]

NHL is one of the most common cancers in the United States, accounting for about 4% of all cancers. The American Cancer Society estimates that in 2019, approximately 74,200 people will be diagnosed with NHL in the U.S. and about 19,970 will die from this cancer. MM is a relatively uncommon cancer in the U.S., with a lifetime risk of getting MM of 1 in 132 (0.76%). The American Cancer Society estimates that in 2019, approximately 32,110 people will be diagnosed with MM and about 12,960 will die from this disease.

About the NKTR-255 Phase 1 Study
The NKTR-255 Phase 1 study is an open-label, dose escalation and dose expansion study in patients with select hematological malignancies (relapsed or refractory NHL or MM). The dose escalation phase of the study will evaluate the safety and tolerability of NKTR-255 as monotherapy in approximately 40 patients in order to establish a recommended Phase 2 dose (RP2D) for NKTR-255. The dose expansion phase of the study will enroll in two separate cohorts: the first cohort will enroll patients with MM or NHL (relapsed salvage) to evaluate the NKTR-255 RP2D as a monotherapy and the second cohort will enroll patients with MM or NHL (relapsed/refractory salvage) to evaluate the NKTR-255 RP2D in combination with targeted antibodies, including anti-CD38 monoclonal antibody, daratumumab. The study will also evaluate pharmacokinetic and pharmacodynamic effects, anti-tumor activity and biomarker assessments.

About NKTR-255
NKTR-255 is an IL-15 receptor agonist designed to activate the IL-15 pathway and expand NK cells and promote the survival and expansion of memory CD8+ T cells without inducing suppressive regulatory 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 Nektar Therapeutics
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: "promising," "potential," "design," "provide," "may," "will" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the expected benefits of NKTR-255 (both alone as a single agent as well as in combination with other agents, such as multiple targeted antibodies), the ability to obtain useful data from the Phase 1 clinical study of NKTR-255, and the future clinical development plans for NKTR-255. 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) NKTR-255 is in early-stage clinical development and there are substantial risks that can unexpectedly occur for numerous reasons including negative safety and efficacy findings in the Phase 1 clinical study notwithstanding positive preclinical findings; (ii) clinical study outcomes, including the Phase 1 clinical study outcome of NKTR-255, remain very unpredictable and it is possible that a clinical study could fail due to efficacy, safety or other important clinical findings; (iii) 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, and competitive factors; (iv) scientific discovery of new therapeutics is an inherently uncertain process and the future success of applying our technology platform to potential new drug candidates (such as NKTR-255) is therefore highly uncertain and unpredictable; (v) patents may not issue from our patent applications for NKTR-255, 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 Nektar's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 9, 2019. 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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2. Farnault, L., et al., *Hematological Malignancies Escape from NK Cell Innate Immune Surveillance: Mechanisms and Therapeutic Implications*. Clinical and Developmental Immunology Volume 2012, Article ID 421702, 8 pages

3. Journal for ImmunoTherapy of Cancer 2017 5(Suppl 2):87; P332.

4. Miyazaki T., et al.*, NKTR-255, a polymer-conjugated IL-15 enhances anti-tumor NK cell responses and synergizes with monoclonal antibodies to provide long-term survival in human lymphoma model.* In: Proceedings of the Annual Meeting of the AACR; 2019. Abstract 3265.