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Nektar Presents Preclinical Study Findings for Etirinotecan Pegol (NKTR-102) in Combination with a PARP Inhibitor in BRCA1-deficient Cancer Model

SAN FRANCISCO, Nov. 20, 2014 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) today announced results of a study investigating the preclinical anti-tumor activity and tolerability of etirinotecan pegol (NKTR-102) in combination with the PARP inhibitor rucaparib in a BRCA1-deficient MX-1 breast tumor model. The preclinical study results demonstrated that all dose combinations of NKTR-102 and rucaparib were well-tolerated, synergistic, and led to 100% prolonged survival in this tumor model. These data were presented during the Symposium on Molecular Targets and Cancer Therapeutics in Barcelona, Spain, sponsored by the European Organisation for Research and Treatment of Cancer (EORTC), the National Cancer Institute (NCI) and the American Association for Cancer Research (AACR).

"We are encouraged by these results which demonstrate that NKTR-102 in combination with the PARP inhibitor rucaparib has a synergistic effect resulting in 100% prolonged survival in a BRCA 1-deficient tumor model," said Stephen K. Doberstein, Ph.D., senior vice president and chief scientific officer of Nektar Therapeutics. "As a next-generation topo-I inhibitor with broad anti-tumor activity, NKTR-102 has the potential to be combined with a number of targeted agents in multiple tumor settings."

NKTR-102 is the first long-acting topoisomerase I inhibitor with an extended half-life and a unique structure that is also designed to concentrate the drug in tumors. In patients, NKTR-102 leads to greatly prolonged plasma SN38 exposure compared to irinotecan (elimination half-life of 50 days compared to 2 days) yet peak SN38 concentrations are at least 5- to 10-times less, which may also result in a favorable tolerability profile.

Preclinical Study Design and Results
Study investigators initiated tumor xenografts with MX-1 human breast carcinomas maintained by serial subcutaneous transplantation in female athymic nude (Crl:NU(Ncr)-Foxn1nu), 8-week-old mice. On the day of tumor implant, each test mouse received a 1-mm^3 MX-1 fragment implanted subcutaneously in the right flank. Animals were randomized into treatment groups (n=10/grp) when their tumors reached 63-196 mm^3 and subsequently received either vehicle, NKTR-102, rucaparab, or combinations of NKTR-102 + rucaparib. Doses selected were known to provide clinically relevant exposure levels. Twice weekly, animals were weighed, and tumor volumes were measured until the endpoint (2000 mm^3 or Day 88) was met. Efficacy was measured by tumor growth delay and regression response rate.

NKTR-102 and rucaparib in combination exhibited marked synergy, demonstrated by durable complete responses, even at the lowest doses of both agents dosed in combination. The combination of NKTR-102 and rucaparib was tolerated at all dose levels. Doses used in this study provide exposures of NKTR-102 (SN38 trough) and rucaparib that are achievable clinically, underscoring the translational relevance of these results.

Combination studies of NKTR-102 and rucaparib are ongoing in patient-derived xenograft models in collaboration with Professor Paul Haluska at Mayo Clinic and Clovis Oncology.

About NKTR-102

NKTR-102 is currently being evaluated in a Phase 3, open-label, randomized, multicenter study called the BEACON study. BEACON enrolled 852 women with locally recurrent or metastatic breast cancer, who have previously been treated with anthracycline, taxane or capecitabine (ATC), and is being conducted at approximately 150 sites worldwide including North America, Western Europe, Russia and the Republic of Korea. Nearly half of the patients enrolled in BEACON were located in North America. Patients were randomized on a 1:1 basis to receive 145 mg/m2 of single-agent NKTR-102 once every three weeks or a single agent of physician's choice. The physician's choice agents include: ixabepilone, vinorelbine, gemcitabine, eribulin, or a taxane. Randomization was stratified by geographic region, prior use of eribulin and receptor status.

The primary endpoint of the BEACON study is overall survival; secondary endpoints include progression-free survival, objective tumor response rates, clinical benefit rate, duration of response, pharmacokinetics, safety, quality-of-life measurements, and pharmacoeconomic implications. The study is also evaluating specific biomarker data to assess correlation with objective tumor response rates, progression-free survival, overall survival and selected toxicities.

About Nektar

Nektar Therapeutics has a robust R&D pipeline in pain, oncology, hemophilia and other therapeutic areas. In the area of pain, Nektar has an exclusive worldwide license agreement with AstraZeneca for MOVANTIK™, the first FDA-approved once-daily oral peripherally-acting mu-opioid receptor antagonist (PAMORA) medication for the treatment of opioid-induced constipation (OIC), in adult patients with chronic, non-cancer pain. The AstraZeneca agreement also includes NKTR-119, an earlier stage development program that is a co-formulation of MOVANTIK™ and an opioid. NKTR-181, a wholly-owned mu-opioid analgesic molecule for chronic pain conditions, has completed Phase 2 development. NKTR-171, a wholly-owned new sodium channel blocker being developed as an oral therapy for the treatment of peripheral neuropathic pain, is in Phase 1 clinical development. In oncology, etirinotecan pegol (NKTR-102) is being evaluated in a Phase 3 clinical study (the BEACON study) for the treatment of metastatic breast cancer. In hemophilia, BAX 855, a longer-acting PEGylated Factor VIII therapeutic is in Phase 3 development conducted by partner Baxter. In anti-infectives, Amikacin Inhale is in Phase 3 studies conducted by Bayer Healthcare as an adjunctive treatment for intubated and mechanically ventilated patients with Gram-negative pneumonia.

Nektar's technology has enabled nine approved products in the U.S. or Europe through partnerships with leading biopharmaceutical companies, including AstraZeneca's MOVANTIK™, UCB's Cimzia® for Crohn's disease and rheumatoid arthritis, Roche's PEGASYS® for hepatitis C and Amgen's Neulasta® for neutropenia.

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.

MOVANTIK™ is a trademark of the AstraZeneca group of companies.

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "expect," "believe," "should," "may," "will" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the therapeutic potential of etirinotecan pegol (NKTR-102) in combination with the PARP inhibitor rucaparib; and the value and potential of our technology and research and development pipeline. 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 drug candidates and those of our collaboration partners 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 for numerous reasons including safety and efficacy findings even after positive findings in previous preclinical and clinical studies; (ii) the timing of the commencement or end of clinical trials and the commercial launch of drug candidates 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; (iii) acceptance, review and approval decisions for new drug applications by health authorities is an uncertain and evolving process and health authorities retain significant discretion at all stages of the regulatory review and approval decision process; (iv) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of the application of our technology platform to potential new drug candidates 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, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required; and (vi) the outcome of any existing or future intellectual property or other litigation related to our drug candidates and those of our collaboration partners. Other important risks and uncertainties set forth in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 7, 2014. 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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