Nektar Initiates Phase 1 Clinical Study Evaluating NKTR-181, A Novel Opioid Molecule, for Treatment of Pain

SAN FRANCISCO, March 21, 2011 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced that the first subjects were dosed in a new Phase 1 clinical study to evaluate NKTR-181, the company's next-generation opioid analgesic candidate. NKTR-181 is being developed to effectively treat pain while addressing the abuse liability and serious CNS side effects associated with currently available opioid therapies. The single-dose Phase 1 study is assessing the pharmacokinetics, pharmacology, safety and efficacy of NKTR-181 in up to 75 healthy subjects. The primary objective of the Phase 1 trial is to establish the effective analgesic dose range of NKTR-181 associated with minimal CNS side effects. The study is being conducted in the U.S. and Nektar expects to complete the study in the second half of 2011.

NKTR-181 was uniquely designed to cross the blood-brain barrier at a substantially slower rate than other opioid therapies. With a reduced rate of entry into the CNS, NKTR-181 has the potential to greatly reduce the euphoria that underlies opioid abuse liability and dependence, as well as the serious CNS-related side-effects of respiratory depression and sedation. The unique molecular design of the polymer drug conjugate also prevents conversion of NKTR-181 into a rapidly-acting, more abusable opioid.

"New pain medicines are desperately needed that are as powerful as opioids, but without the usual serious risks such as respiratory depression and disabling sedation," said Lynn R. Webster, MD, Primary Investigator for the Phase 1 Study and Medical Director of Lifetree Clinical Research and Senior Consultant to Omega Pain Clinic in Salt Lake City, Utah. "A novel opioid therapy, such as NKTR-181, that also has the potential to reduce the psychopharmacologic effects associated with drug dependence provides great promise for all physicians looking for safer and more effective pain management, and could help to address the significant public safety threat posed by existing opioid drugs."

Endpoints in the Phase 1 study include standard measurements of pain relief and standard measurements of CNS effects, such as euphoria, respiratory depression and pupillary response.

"We are excited about the initiation of the NKTR-181 clinical program," said Dr. Lorianne Masuoka, Senior Vice President and Chief Medical Officer of Nektar. "NKTR-181 represents a major step forward for our emerging pipeline of innovative and important new medicines."

About NKTR-181

A novel mu-opioid analgesic investigational drug candidate, NKTR-181 was created using Nektar's small molecule polymer conjugate technology. In addition to exhibiting a reduced rate of CNS entry while providing effective pain relief with fewer CNS-related side effects in preclinical studies, the unique molecular design of the polymer drug conjugate also prevents conversion of NKTR-181 into an abusable form of opioid.As a result, NKTR-181 has the potential to be a highly effective analgesic with a favorable safety profile and reduced potential for abuse, misuse and diversion.

About Opioids and Pain Management

Pain is the most common symptom for which patients seek medical attention.(1) According to the American Pain Society, the prevalence of chronic pain in the United States is estimated to be 35.5% or 105 million people. Chronic pain costs more than $100 billion per year in direct healthcare expenditures and lost work time. Opioids are considered to be the most effective therapeutic option for pain and have over $10 billion a year in sales in the U.S. alone.(2,3) However, opioids cause significant problems for physicians and patients because of their serious side effects such as respiratory depression and sedation, as well as the risks they pose for addiction, abuse, misuse, and diversion. The U.S. Food and Drug Administration has cited prescription opioid analgesics as being at the center of a major public health crisis of addiction, misuse, abuse, overdose and death.(4) A 2010 recent report from the Center for Disease Control and Prevention (CDC) notes that emergency room visits tied to the abuse of prescription painkillers is at an all-time high, having increased 111 percent over a five-year period.(5)

About Nektar

Nektar Therapeutics is a biopharmaceutical company developing novel therapeutics based on its PEGylation and advanced polymer conjugation technology platforms. Nektar has a robust R&D pipeline of potentially high-value therapeutics in oncology, pain and other areas. In the area of pain, Nektar has an exclusive worldwide license agreement with AstraZeneca for NKTR-

118, an investigational drug candidate, being evaluated in Phase 3 clinical studies as a once-daily, oral tablet for the treatment of opioid-induced constipation. The agreement also includes NKTR-119, an earlier stage development program that is a co-formulation of NKTR-118 and an opioid. NKTR-181, the company's wholly-owned novel mu-opioid analgesic molecule, is being evaluated in Phase 1 clinical studies. In oncology, NKTR-102, a proprietary novel topoisomerase I-inhibitor, is being evaluated in Phase 2 clinical studies for the treatment of breast, ovarian and colorectal cancers. NKTR-105, a novel anti-mitotic agent, is in a Phase 1 clinical study in cancer patients with refractory solid tumors.

Nektar's technology has enabled seven approved products in the U.S. or Europe through partnerships with leading biopharmaceutical companies, including 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 R&D 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.

This press release contains forward-looking statements that reflect Nektar's current views as to the potential of NKTR-181 to effectively treat pain while addressing the abuse liability and serious side effects associated with traditional opioid therapies, the estimated completion date of the Phase 1 study for NKTR-181, the potential of Nektar's polymer conjugate technology platform, and the potential for certain of Nektar's other drug candidates. These forward-looking statements involve substantial risks and uncertainties including but not limited to one or more of the following: (i) the future results from the NKTR-181 Phase 1 clinical study may not be consistent with preclinical findings previously reported by Nektar; (ii) NKTR-181 is in early stage clinical development where the risk of failure remains very high and failure can unexpectedly occur at any stage of development due to safety, efficacy, or other important and unpredictable causes; (iii) the timing and/or success of the commencement or end of clinical trials, including without limitation the projected completion date of the Phase 1 study for NKTR-181, may be delayed or unsuccessful due to regulatory delays, slower than anticipated patient enrollment, adverse patient outcomes, and other important factors; (iv) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of the application of Nektar's technology platform to potential new drug candidates such as NKTR-181 is therefore very uncertain and unpredictable and one or more research and development programs could unexpectedly fail; (v) Nektar's patent applications for its proprietary or partner drug candidates may not issue, 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 Nektar's proprietary drug candidates including without limitation NKTR-181. Other important risks and uncertainties are detailed in Nektar's reports and other filings with the Securities and Exchange Commission, including without limitation, those risks and uncertainties set forth in Nektar's Annual Report on Form 10-K filed on March 1, 2011. Nektar undertakes no obligation to update forward-looking statements, whether as a result of new information, future events or otherwise.

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(1) Harstall, C. How prevalent is chronic pain? *Pain Clinical Updates* X, 1—4 (2003).

(2) IMS, NSP, NPA and Defined Health 2010 Estimates.

(3) Melnikova, I, Pain Market, *Nature Reviews Drug Discovery*, Volume 9, 589-90 (August 2010).

(4) Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee, "*Risk Evaluation and Mitigation Strategies (REMS) for Extended-Release and Long-Acting Opioid Analgesics*", July 23-4, 2010.

(5) Morbidity and Mortality Weekly Report (MMWR), Emergency Department Visits Involving Nonmedical Use of Selected Prescription Drugs --- United States, 2004—2008, **59(23);705-709 (June 2010).**

SOURCE Nektar Therapeutics