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

SAN FRANCISCO, Sept. 8, 2011 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced that dosing began in a Phase 1 clinical study to evaluate multiple ascending doses of NKTR-181, the company's novel opioid analgesic drug candidate. NKTR-181 is in development as a once- or twice-daily oral tablet for the treatment of chronic pain, and is designed to address the abuse liability and serious central nervous system (CNS) side effects associated with current opioid therapies. Chronic pain conditions, such as osteoarthritis, back pain and cancer pain, affect at least 126 million adults in the U.S. annually and contribute to over $100 billion a year in lost productivity(1).

The multiple ascending dose study is the second study in the Phase 1 clinical program for NKTR-181. The first study, a single ascending dose trial in 110 healthy subjects, was completed in July 2011. Results from the first Phase 1 study will be presented at the 2011 American Academy of Pain Management (AAPM) Annual Clinical Meeting on September 21, 2011.

NKTR-181, a novel mu-opioid agonist with an extended pharmacokinetic profile, was created using Nektar's proprietary small molecule polymer conjugate technology. With slower entry into the CNS when compared to published oxycodone data, NKTR-181 has the potential to greatly reduce the euphoria that underlies opioid abuse liability and dependence. In addition, NKTR-181 is intended to reduce the other serious CNS-related side effects such as respiratory depression and sedation which are associated with current opioid therapies. NKTR-181 is a new chemical entity created by small molecule polymer conjugation with unique properties that are inherent to its molecular structure. As a result, NKTR-181 is also specifically designed to prevent its conversion into a more abusable opioid.

The primary objective of this Phase 1 multiple ascending dose study is to establish the safety, tolerability and pharmacokinetic profile of NKTR-181 upon repeat administration in preparation for Phase 2 clinical development in chronic pain patients. Four dose levels of NKTR-181 will be evaluated in approximately 60 healthy subjects over an eight-day treatment period. Endpoints in this multiple dose Phase 1 study will also include assessment of pharmacodynamic effects including pupillometry, exploratory pain measures, and respiratory parameters. The study is being conducted in the U.S. at the Lifetree Pain Clinic in Salt Lake City, Utah and is expected to be completed by the end of 2011.

"NKTR-181 is an exciting program because it represents a completely new approach to opioid analgesia, with a truly unique molecular structure designed to mitigate the inherent risks associated with current opioid formulations on the market or in development," said Robert Medve, MD, Chief Medical Officer at Nektar Therapeutics. "In our first Phase 1 study, NKTR-181 demonstrated a clinical profile that should enable once or twice daily dosing with an excellent safety profile. This second Phase 1 trial will help us further characterize the profile of the drug and establish dose ranges for Phase 2 development in patients with chronic pain, which is planned for 2012."

About NKTR-181

NKTR-181 is a novel mu-opioid analgesic investigational drug candidate created using Nektar's advanced small molecule polymer conjugate technology. The unique molecular design of the polymer conjugate is designed to prevent conversion of NKTR-181 into a more abusable form of an opioid. As a result, NKTR-181 has the potential to be an effective analgesic with a wider therapeutic window, favorable safety profile and reduced potential for abuse, misuse and diversion compared to available opioids.

Data Presentations for NKTR-181 at 2011 AAPM Meeting

Two data presentations for NKTR-181 are planned at the American Academy of Pain Management (AAPM) Annual Clinical Meeting:

SESSION TYPE: Poster Session
DATE: September 21, 2011
TIME: 3:25 PM Pacific time
TITLE: "*Phase 1 Study of Oral NKTR-181, a Novel Opioid Analgesic Molecule with Reduced Abuse Potential and Favorable Safety Profile*"
AUTHOR/SPEAKER: Lynn Webster, M.D.

SESSION TYPE: Poster Session
DATE: September 21, 2011
TIME: 3:25 PM Pacific time
TITLE: "NKTR-181: A Novel Mu-Opioid Agonist That Exhibits Reduced Abuse Potential and Maintains Full Analgesic Activity Following Repeat Dosing in Preclinical Rodent Models"
AUTHOR/SPEAKER: Stephen Harrison, Ph.D.

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 health-care expenditures and lost work time(1). 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's technology and drug development expertise have enabled seven approved products in the U.S. or Europe for leading biopharmaceutical company partners, including UCB's Cimzia(R) for Crohn's disease and rheumatoid arthritis, Roche's PEGASYS(R) for hepatitis C and Amgen's Neulasta(R) for neutropenia.

Nektar has created a robust pipeline of potentially high-value therapeutics to address unmet medical needs by leveraging and expanding its technology platforms to improve and enable molecules. In addition to the releasable polymer technology, Nektar is the first company to create a permanent small molecule-polymer conjugate with enhanced oral bioavailability and restricted entry into the CNS. Nektar is currently conducting clinical and preclinical programs in oncology, pain and other therapeutic areas. Nektar has an exclusive worldwide license agreement with AstraZeneca for its oral NKTR-118 program to treat opioid-induced constipation and its NKTR-119 program for the treatment of pain without constipation side effects. NKTR-102 is being evaluated in Phase 2 clinical studies for the treatment of ovarian, breast and colorectal cancers.

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 therapeutic potential of NKTR-181, the value 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 statements regarding the potential therapeutic potential of NKTR-181 are based on preclinical data and data from the first Phase 1 clinical study and future clinical studies may not confirm one or more of these potential therapeutic benefits; (ii) although Nektar has conducted various experiments using laboratory and home-based chemistry techniques that have so far been unable to convert NKTR-181 into a rapidly-acting, more abusable opioid, there is a risk that an alternative chemistry technique or process may be discovered in the future that would enable the conversion of NKTR-181 into a more abusable opioid; (iii) NKTR-181 is in early stage clinical development and could fail at any time due to numerous unpredictable and significant risks related to safety, efficacy and other important findings that can negatively impact clinical development; (iv) the U.S. Food and Drug Administration and other regulatory agencies could impose burdensome risk mitigation requirements that hamper market acceptance of NKTR-181, even if approved for commercialization; (v) 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 could unexpectedly fail at any time; (vi) patents may not issue from Nektar's patent applications for NKTR-181, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required; and (vii) 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 Form 10-Q for the quarter ended June 30, 2011, filed on August 5, 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. 2011 National Academy of Sciences. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research, 2010 Decision Resources, and 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