Nektar Presents Positive Data for Novel Opioid Analgesic, NKTR-181, at the 2011 American Academy of Pain Management Annual Meeting

NKTR-181 Exhibits Dose-Dependent Analgesic Response, Reduced Rate of Entry into the CNS and Extended Pharmacokinetic Profile

SAN FRANCISCO, Sept. 21, 2011 /PRNewswire/ -- Nektar Therapeutics (NASDAQ:NKTR) today announced that positive proof-of-concept data is being presented from its first Phase 1 clinical trial of NKTR-181 at the American Academy of Pain Management (AAPM) 22nd Annual Clinical Meeting. NKTR-181 is a new oral opioid analgesic candidate in development for the treatment of chronic pain. It is designed to address the abuse liability and serious central nervous system (CNS) side effects associated with current opioid therapies. NKTR-181 is a novel mu-opioid agonist created using Nektar's proprietary polymer conjugate technology and its differentiating properties are inherent to the design of its new molecular structure. 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 result of this Phase 1 study for NKTR-181 is very promising for clinicians in pain management," said Lynn R. Webster, MD, Medical Director of Lifetree Clinical Research. "The profile and properties observed with NKTR-181, particularly its extended pharmacokinetic profile and its slow rate of entry into the brain, are interesting because they appear to be a result of the molecule's novel structure. Further, the rapid rate of entry of most traditional opioids into the CNS causes euphoria, which can lead to their abuse, and usually cause unwanted CNS side effects. The clinical data for NKTR-181 demonstrate that it enters the CNS slowly, which should make it less attractive for abuse, while at the same time reduce its CNS-related side effects. This, combined with a remarkably consistent analgesic response that has a linear relationship to dose, makes NKTR-181 a tremendously interesting potential new pain therapy."

The data presentations at AAPM show that NKTR-181 produced a clear dose-dependent analgesic response in a cold pressor test, a model of pain used in healthy subjects to measure CNS analgesic activity. Importantly, pupillometry data from the study demonstrate that NKTR-181's centrally-mediated opioid effects are dose-linear and that the molecule enters the brain slowly. With this reduced rate of entry into the CNS, NKTR-181 has the potential to greatly reduce the euphoria that drives opioid abuse liability and dependence. Based on the pharmacodynamic data from the Phase 1 study and preclinical studies, NKTR-181 also has the potential to reduce other serious CNS-related side-effects associated with current opioid therapies.

NKTR-181 also achieved a predictable, dose-linear pharmacokinetic (PK) profile in the Phase 1 study with an average half-life of approximately 12 hours. The drug was well-tolerated at all doses in the study, displayed good oral bioavailability with rapid absorption, and its PK profile supports dosing on a once-daily (QD) or twice-daily (BID) schedule.

"Our Phase 1 results for NKTR-181 reinforce our belief that this novel mu-opioid analgesic could play a transformational role in the treatment of pain," said Robert Medve, M.D., Nektar's Chief Medical Officer. "NKTR-181 exhibits a wide therapeutic window that is inherent to its molecular structure, without the use of a formulation approach to achieve its clinical profile. As a result, it could provide potent analgesia for chronic pain patients while greatly reducing the abuse liability and dangerous CNS-related side effects of currently-available therapies. The exciting data from this first Phase 1 study support Nektar's continued rapid development of NKTR-181. We are planning to complete our multi-dose Phase 1 study in the second half of 2011 and advance the drug candidate into Phase 2 next year."

Nektar is also presenting preclinical data for NKTR-181 at today's AAPM meeting which highlighted the drug candidate's reduced abuse potential in several drug discrimination and self-administration studies, as well as its sustained analgesic activity in repeat dosing studies in animals.

The data presentations to be made during today's AAPM 22nd Annual Clinical Meeting will be available on Nektar's website at http://www.nektar.com/product_pipeline/cns_pain_nktr-181.html.

About the NKTR-181 Phase 1 Study

The Phase 1 study of NKTR-181 enrolled 105 healthy subjects. The study was designed to determine the safety, tolerability, pharmacokinetics and pharmacodynamics of single ascending doses of NKTR-181. Seven dose cohorts were evaluated with 15 subjects in each dose cohort (10, 20, 40. 80, 160, 320 and 500 mg). Subjects in each cohort received a single oral dose of

NKTR-181 (n=12) or placebo (n=3) following an overnight fast. Pharmacokinetics and pharmacodynamics were measured through serial blood samples and observations of cold pressor test response, as well as pupillometry to determine opioid-induced miosis of drug effect and exposure over time.

NKTR-181 was well tolerated at all doses, with very few reports of adverse events (AEs) until the highest dose level tested (500 mg), when transient non dose-limiting AEs characteristic of an active opioid agonist were reported. Most of these non dose-limiting AEs were mild, such as mild dizziness and nausea.

NKTR-181 is currently in a Phase 1 multiple ascending dose study and is being prepared for Phase 2 development in chronic pain patients in mid-2012.

About NKTR-181

NKTR-181 is a novel mu-opioid analgesic investigational drug candidate created using Nektar's small molecule polymer conjugate technology. In preclinical studies, NKTR-181 exhibits a reduced rate of entry into the central nervous system (CNS) providing effective pain relief with fewer CNS-related side effects, such as euphoria, sedation and respiratory depression. The physiochemical properties of NKTR-181 that slow its entry into the brain are inherent in the molecular design, which prevents conversion of NKTR-181 into a drug that rapidly enters the CNS. 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. Opioids are considered to be the most effective therapeutic option for pain and have over $8 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, a novel mu-opioid analgesic molecule, is being evaluated in Phase 1 clinical studies. In oncology, NKTR-102, a novel topoisomerase I-inhibitor, is being evaluated in Phase 2 clinical studies for the treatment of breast, ovarian and colorectal cancers.

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.

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This press release contains forward-looking statements reflecting Nektar's current views as to the therapeutic potential of NKTR-181, observations based on data from the first NKTR-181 Phase 1 clinical study and preclinical findings, the value of Nektar's PEGylation and advanced polymer conjugation technology platforms, 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 clinical data for NKTR-181 described in this press release are based on results from the first Phase 1 clinical study and there is a risk that future clinical results may not confirm one or more of these observations; (ii) although Nektar has conducted various experiments using laboratory and home-based chemistry techniques that have been unable to convert NKTR-181 into a rapidly-acting, more abusable opioid, there can be no assurance that an alternative chemistry technique or process to convert NKTR-181 into a more abusable opioid may not be discovered; (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 studies; (iv) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of the application of Nektar's technology platforms to potential new drug candidates such as NKTR-181 is therefore very uncertain and unpredictable and could unexpectedly fail at any time; (v) Nektar's patent applications for NKTR-181 may not issue, patents that do issue 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 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.

(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