NKTR-181, A Mu-Opioid Analgesic With a Novel Molecular Structure, Demonstrates Slower Entry Rate Into the Brain and Reduced CNS Side Effects

Preclinical Data Presented in Oral Abstract Presentation at Pain 2010 Conference

SAN CARLOS, Calif., Oct 015, 2010 /PRNewswire via COMTEX News Network/ -- Nektar Therapeutics (Nasdaq: NKTR) presented promising data today from preclinical studies of NKTR-181, a next-generation mu-opioid analgesic candidate with a novel molecular design. NKTR-181 is being developed to effectively treat pain while addressing the abuse liability and serious side effects associated with traditional opioid therapies. The data are being featured in an oral abstract session and poster presentation today at the 5th Annual Frontiers of Clinical Investigation Symposium - Pain 2010: From Bench to Bedside in La Jolla, CA.

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 eliminate not only the euphoria that underlies opioid abuse liability and dependence, but also 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 rapid-acting abusable form of an opioid. NKTR-181 is currently in IND-enabling studies and Nektar plans to begin Phase 1 clinical studies in the first part of 2011.

"Opioid analgesics represent the gold standard in pain control but they pose significant safety risks, and their misuse and abuse have been cited as serious public health issues. NKTR-181 is the first mu-opioid analgesic with a novel molecular structure specifically engineered to eliminate the euphoric high and dangerous side effects associated with this class of painkillers," said Stephen K. Doberstein, Ph.D., Senior Vice President and Chief Scientific Officer of Nektar Therapeutics. "In highly-predictive preclinical models of analgesia and abuse liability, NKTR-181 has shown comparable analgesia to oxycodone with minimal CNS side effects and as a result, we are enthusiastic about the potential of this new therapeutic to dramatically advance the field of pain management."

NKTR-181 Data Highlights from Pain 2010

Data presented includes receptor binding and function studies that demonstrate NKTR-181 binds specifically to the mu-opioid receptor and acts as a full agonist. In standard preclinical models of pain, NKTR-181 demonstrated full suppression of pain symptoms comparable to oxycodone. NKTR-181 also displayed slowed kinetics of entry to the brain *in vivo* as compared to oxycodone, with a 90% reduction in the rate of entry into the brain versus oxycodone. The slower rate of brain-uptake correlated with dramatically diminished abuse liability and CNS side effects. At analgesic doses, NKTR-181 displayed no significant CNS side effects and in a self-administration model of abuse liability, NKTR-181 displayed no reinforcing properties up to the highest dose tested.

The oral and poster presentations from the Pain 2010 meeting can be found on Nektar's website at www.nektar.com:

- Fishburn et. al., "NKTR-181: A Novel Opioid With Slowed Brain Entry Shows Low Abuse Liability and Reduced CNS Side Effects"

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. 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 Centers 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 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 unique molecular design of the polymer conjugate also prevents conversion of NKTR-181 into free opioid or an abusable form of an 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 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 Nektar's oral NKTR-118 development program to treat opioid-induced constipation and its NKTR-119 development program for the treatment of pain without constipation side effects. The company has additional pain compounds in preclinical studies. In oncology, NKTR-102, a novel topoisomerase I-inhibitor, is being evaluated in Phase 2 clinical studies for the treatment of ovarian, breast 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 nine approved products in the U.S. or Europe through partnerships with leading biopharmaceutical companies, 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.


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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 timing of the start of Phase 1 clinical studies 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 preclinical data for NKTR-181 described in this press release and presented at the Pain 2010 Conference may not be predictive of future success in clinical trials; (ii) the commencement of a Phase 1 clinical study for NKTR-181 could be delayed due to regulatory factors, the need to successfully complete certain toxicology studies, drug manufacturing challenges, or other important factors that can impact clinical development efforts; (iii) 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; (iv) 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 (v) 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, 2010, filed on July 29, 2010. Nektar undertakes no obligation to update forward-looking statements, whether as a result of new information, future events or otherwise.

References:

(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