NEKTAR

News Release

Nektar Presents Positive Proof-of-Concept Clinical Data for Its New Opioid Molecule, NKTR-181, at American Academy of Pain Medicine's 28th Annual Meeting

NKTR-181 demonstrates reduced rate of entry into CNS, sustained analgesic responses, and excellent tolerability profile in humans

San Francisco, Calif, February 27, 2012 – Nektar Therapeutics (Nasdaq: NKTR) today announced a presentation of positive clinical data for NKTR-181, its new oral opioid analgesic molecule, at the 2012 American Academy of Pain Medicine's 28th Annual Meeting (AAPM). NKTR-181 is a novel mu-opioid agonist molecule, which was designed to have a slow rate of entry into the brain to reduce the attractiveness of the molecule as a target of abuse and to reduce its CNS-mediated side effects. NKTR-181 was created using Nektar's proprietary polymer conjugate technology and its differentiating properties are inherent to the design of the new molecule. As a new molecular structure, NKTR-181 is unique in that it does not rely on a formulation approach to prevent its conversion into a more abusable form of an opioid.

Clinical results were presented at AAPM from a human Phase 1 study which evaluated the pharmacokinetics, pharmacodynamics, and safety of oral doses of NKTR-181 as compared to placebo over an 8-day treatment period in healthy subjects. Using pupil constriction as a measure of the onset of central opioid effect, the study showed that NKTR-181 enters the brain slowly and produces centrally-mediated opioid effects that are dose-dependent and statistically meaningful ($P<0.001$) following twice daily oral doses of 200-400 mg. Further, NKTR-181 enters the CNS from the plasma at a rate approximately ten-times slower than historical published rates for oxycodone.[1] NKTR-181's slow rate of entry into the CNS may reduce the euphoria and other CNS side effects that are associated with rapid CNS uptake of current standard opioid therapies.

"NKTR-181 is an exciting new approach to opioid analgesia," said Lynn R. Webster, MD, Medical Director of Lifetree Clinical Research. "The human data now show us that NKTR-181 crosses into the brain slowly across a wide range of doses, over multiple days of dosing, and also achieves a sustained analgesic response. By slowing the rate of entry into the brain,

NKTR-181 is designed to have less euphoria, sedation and respiratory depression than traditional opioid compounds. Individuals with a higher risk of abusing opioids prefer rapid onset of euphoria, which means NKTR-181 should be less attractive as a drug of abuse. NKTR-181 represents an exciting developmental advance in pain. This new human data support its further clinical development as a compelling therapeutic for the treatment of chronic pain."

Data presented at AAPM show the positive analgesic properties of NKTR-181 in humans. NKTR-181 produced dose-dependent analgesic responses in two separate models of pain used to measure central and peripheral analgesic activity in healthy subjects. In a cold-pressor test pain model measuring latency-to-hand-removal (LHR), the 200 mg dose of NKTR-181 given twice-daily over the 8-day dosing period demonstrated the extent and duration of analgesic effect of NKTR-181 administration. Results show a significant analgesic effect as compared to placebo ($P<0.01$, $n=12$) over the entire dosing period. In addition, a model of induced UVB injury was also used to demonstrate the extent and duration of analgesic effect produced by NKTR-181. Results show that NKTR-181 has both centrally-mediated and peripherally-mediated analgesic effects. In this model, data was presented on NKTR-181 at doses of 300 mg and 400 mg demonstrating its significant analgesic and anti-hyperalgesic effect (measured as change from baseline) following mechanical and thermal stimulation, with p-values of $P<0.009$ and $P<0.03$, respectively ($n=12$).

“The data from this study reinforce our belief that NKTR-181 could potentially transform the treatment of chronic pain,” said Robert Medve, MD, Chief Medical Officer at Nektar Therapeutics. “Unique to this new mu-opioid analgesic molecule is that it does not rely on a formulation to decrease its abuse liability. With a ten-fold slower entry into the brain as compared to oxycodone, NKTR-181 avoids the rush into the brain associated with euphoria. Adding to our excitement is the data that shows the peripheral analgesic and anti-hyperalgesic effects of NKTR-181 in multiple pain models. We will seek to capitalize on the properties of this unique molecule as we advance NKTR-181 into Phase 2 development this year.”

In a separate presentation of preclinical data at the AAPM Meeting, NKTR-181 resulted in less sedation and abuse liability as compared to oxycodone in multiple animal models across a wide range of doses. As predicted from its molecular design, NKTR-181 has a reduced rate of entry into the brain in rodents. This feature contributed to a 30-fold shift in the dose-response for abuse liability and a 10-fold shift in the dose response for sedation relative to oxycodone.

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.[2]

About the NKTR-181 Phase 1 Multiple Ascending Dose Study

This Phase 1, double-blind, randomized, placebo-controlled, ascending multiple dose study of NKTR-181 was conducted in the U.S. at Lifetree Clinical Research. The study enrolled a total of 60 healthy subjects over an eight-day treatment period. Four dose cohorts were evaluated with 15 subjects in each dose cohort (100 mg, 200 mg, 300 mg, 400 mg). Subjects in each cohort received oral twice-daily doses of NKTR-181 (n=12) in aqueous solution or placebo (n=3) following an overnight fast. Pharmacokinetics were determined through serial blood samples. Serial opioid pharmacodynamic tests included the cold-pressor test (CPT) and a UVB injury model to assess both centrally-mediated and peripherally-mediated analgesic effects. A pupillometry test was used as an indicator of the onset of opioid effect. Statistical analyses are based on a repeated-measure mixed model analysis of variance.

NKTR-181 was generally well-tolerated at all dose levels in the study: most adverse events were mild and no serious adverse events were reported. Most frequent adverse events (AEs) observed at the highest doses tested were mild and consistent with AEs characteristic of an opioid agonist, such as constipation, headache and nausea. There was no observed respiratory depression with NKTR-181 at doses up to 400 mg twice-daily.

The multiple ascending dose study is the second study in the Phase 1 clinical program for NKTR-181. Positive results from the first Phase 1 study, which was a single ascending dose trial in 110 healthy subjects, were presented at the American Academy of Pain Management (AAPM) Annual Meeting in September 2011.

NKTR-181 is currently being prepared for Phase 2 development in chronic pain patients in mid-2012.

Data Presentations at 2012 AAPM Meeting

Clinical data from the Phase 1 multiple ascending dose study for NKTR-181 is available on Nektar's website at http://www.nektar.com/product_pipeline/cns_pain_nktr-181.html:

- Poster #282B, Presentation Title: "Multiple Dose Pharmacokinetics and Pharmacodynamics of the New Oral Opioid Analgesic NKTR-181"

- Authors: Webster, et al.
- Program Track: Poster Session 2: Epidemiology/Health Policy/Education, Pharmacological, Translational
- Date and Time: Friday, February 24 starting at 5:45pm-7:15pm Pacific time through Saturday, February 25 at 11:15am Pacific

Preclinical data from multiple preclinical studies for NKTR-181 is available on Nektar's website at http://www.nektar.com/product_pipeline/cns_pain_nktr-181.html:

- Poster #258B, "NKTR-181: An Orally Available Mu-Opioid Agonist with Slow Rate of Uptake into the CNS, Exhibits Comparable Analgesic Efficacy with Reduced Abuse Liability and CNS Mediated Side Effects Compared to Oxycodone"
- Authors: Gogas, et al.
- Program Track: Poster Session 2: Epidemiology/Health Policy/Education, Pharmacological, Translational
- Date and Time: Friday, February 24 starting at 5:45pm-7:15pm Pacific time through Saturday, February 25 at 11:15am Pacific

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. 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.

About Opioids and Pain Management

Pain is the most common symptom for which patients seek medical attention.[2] 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 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 direct health-care expenditures and lost work time.[2] 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.[3,4] 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.[5] 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.[6]

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 therapeutic areas. In the area of pain, Nektar has an exclusive worldwide license agreement with AstraZeneca for NKTR-118, an investigational drug candidate, which is being evaluated in Phase 3 clinical studies as a once-daily, oral tablet for the treatment of opioid-induced constipation. This license 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, has completed Phase 1 development and is being prepared for a Phase 2 study. In oncology, NKTR-102 is being evaluated in a Phase 3 clinical study for the treatment of metastatic breast cancer and in Phase 2 studies for the treatment of 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. Additional development stage products that leverage Nektar’s proprietary technology platform include peginesatide, for which Affymax and partner Takeda submitted an new drug application to the United States Food and Drug Administration in May 2011, and Baxter’s BAX 855, a long-acting PEGylated rFVIII program which is in Phase 1 clinical development.

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.

Cautionary Note Regarding Forward-Looking Statements

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," "could," "potential," "may" and similar references to future periods. Examples of forward-looking statements include our current views as to the potential of NKTR-181 as a new approach to opioid analgesia and pain therapy; the potential of NKTR-181 to exhibit reduced CNS-related side effects associated with standard opioid therapies; our plans to initiate a Phase 2 clinical study for NKTR-181; the value of our polymer conjugate technology platform; and the potential of certain of our other drug candidates and those of our collaboration partners. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations, observations and assumptions regarding the potential of our drug candidates and our technology. 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) the statements regarding the therapeutic potential of NKTR-181 are based on preclinical data and data from the completed Phase 1 clinical studies and future clinical studies may not confirm one or more of these potential therapeutic benefits; (ii) although we have conducted various experiments using laboratory and home-based chemistry techniques that have so far been unable to convert NKTR-181 into a rapid-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 significant risk mitigation requirements that hamper the commercial potential of NKTR-181, even if this drug candidate receives regulatory approval; (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 our 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 our proprietary drug candidates. Other important risks and uncertainties are detailed in our reports and other filings with the Securities and Exchange Commission ("SEC"), including without limitation, those risks and uncertainties set forth in Nektar's Form 10-Q for the quarter ended September 30, 2011, filed with the SEC on November 4, 2011 and our Form 8-K filed with the SEC on January 11, 2012. 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.

Nektar Investor Inquiries:

Jennifer Ruddock/Nektar Therapeutics *(415)482-5585*

Susan Noonan/SA Noonan Communications, LLC *(212) 966-3650*

Nektar Media Inquiries:

Karen Bergman/BCC Partners *(650) 575-1509*

Michelle Corral/BCC Partners *(415) 794-8662*

# # #

[1] Lalovic et al., Clinical Pharmacology and Therapeutics, 2006.
[2] 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).
[3] IMS, NSP, NPA and Defined Health 2010 Estimates.
[4] Melnikova, I, Pain Market, *Nature Reviews Drug Discovery*, Volume 9, 589-90 (August 2010).
[5] 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.
[6] *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).