



September 26, 2013

## **Nektar Announces Preliminary Topline Results from Phase 2 Efficacy Study for NKTR-181 in Chronic Pain Patients with Osteoarthritis of the Knee**

### **Company to Host Conference Call on Thursday, September 26th at 1:30 PM Pacific Time/4:30 PM Eastern Time to Discuss Results**

SAN FRANCISCO, Sept. 26, 2013 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) announced the preliminary topline results from a Phase 2 study of NKTR-181 for the treatment of moderate-to-severe chronic pain in patients with osteoarthritis of the knee. The Phase 2 study utilized a double-blind, placebo-controlled, randomized withdrawal study design to assess the efficacy, safety and tolerability of NKTR-181. Of the 295 patients that entered the study, only 9 (3%) patients were unable to achieve meaningful pain relief with NKTR-181. 53 (18%) patients discontinued treatment during the titration period because of adverse events, most of which are those commonly associated with opioids. A total of 213 patients achieved an average 40% reduction in pain and entered the randomized phase of the study.

Following the titration period, patients were randomized 1:1 to either continue to receive their analgesic dose of NKTR-181 or to receive placebo for 21 days. NKTR-181 performed as expected as an opioid analgesic throughout the study with patients continuing to show a reduction in pain scores throughout the randomized phase of the study as well. However, patients who were randomized to placebo did not show the expected increase in pain scores observed in similar enriched enrollment, randomized withdrawal studies. This unusual lack of a placebo rebound caused the Phase 2 study to miss the primary endpoint in the study, which was based upon the average change in a patient's pain score from pre-randomization baseline to the end of the double-blind, randomized treatment period of the study.

"We are experiencing a major public health problem with prescription opioids in this country, and need to find new ways to address this problem," said Dr. Lynn Webster, Chief Medical Officer of CRI Lifetree. "I have worked with NKTR-181 since this new molecule entered the clinic, and I believe that NKTR-181 could be an important advance in analgesia, maybe even a breakthrough. Although this Phase 2 study did not achieve its primary endpoint, this is not uncommon in opioid development. What is important is that the large majority of patients in this trial were able to achieve meaningful and long-lasting pain relief from NKTR-181. Providing analgesia without the pronounced CNS effects and euphoria of standard opioids is the future of analgesic development."

NKTR-181 was also well-tolerated over the entire treatment period. The most common adverse events observed for patients taking NKTR-181 were constipation (22.4%) and nausea (10.3%). Discontinuation for adverse events was 18% during the titration period with the most common adverse events cited for discontinuation of constipation (8.8%), nausea (4%) and somnolence (3%).

"The results from this Phase 2 trial provide a great deal of additional insight into the analgesic profile of NKTR-181 and will be invaluable as we continue the development of this molecule," said Howard W. Robin, President and Chief Executive Officer of Nektar Therapeutics. "We were very pleased that this drug clearly performs as an effective analgesic with only 3% of the patients who received NKTR-181 unable to titrate to meaningful pain relief. We are carefully evaluating the lack of post-randomization rebound in the placebo arm in order to design the optimal pivotal trials for this drug. Based upon the data from this trial, it is clear that NKTR-181 provides pain relief on par with existing opioids while achieving a very favorable safety profile that differentiates it from standard opioids. We are committed to bringing NKTR-181 to patients suffering from chronic pain."

NKTR-181 is a novel mu-opioid agonist molecule 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 other CNS-mediated side effects, such as sedation and respiratory depression.

### **Analyst Call to be Held 1:30 PM Pacific Time/4:30 PM Eastern Time on Thursday, September 26, 2013**

The company will be hosting a call to discuss these data with analysts and investors at 1:30 PM Pacific time/4:30 PM Eastern time today. Hosting the call will be Howard Robin, President and CEO of Nektar, and Robert Medve, MD, Chief Medical Officer. Joining company management will be Jeffrey Gudín, MD, Director of Pain Management and Palliative Care, Englewood Hospital & Medical Center and Clinical Instructor of Anesthesiology at Mt. Sinai School of Medicine.

A live audio-only Webcast of the conference call can be accessed through a link that is posted on the home page and Investor

Relations section of the Nektar website: <http://www.nektar.com>. To access the conference call live, follow these instructions:

Dial: (877) 881-2183 (U.S.); (970) 315-0453 (international)

Passcode: 71977583 (Nektar Therapeutics is the host)

The webcast replay of the conference call will be available through October 7, 2013, 2013.

### **About Opioids and Pain Management**

Pain is one of the most common reasons people seek medical treatment.<sup>1</sup> The American Pain Society estimates that 36 percent of the U.S. population, or 105 million people, suffer from chronic pain in the United States. 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 healthcare expenditures and lost work time.<sup>2</sup> Opioids are considered the most effective therapeutic option for pain, with sales exceeding over \$10 billion a year in the U.S. alone.<sup>3,4</sup> However, opioids can cause serious side effects such as respiratory depression and sedation and have the potential for addiction, abuse and misuse. In 2010, the Centers for Disease Control and Prevention (CDC) reported that emergency room visits for non-medical use of opioid analgesics increased 111 percent over a five-year period.<sup>5</sup>

### **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 naloxegol (NKTR-118), an investigational drug candidate, which has completed Phase 3 development as a once-daily, oral tablet for the treatment of opioid-induced constipation. For naloxegol, a Marketing Authorisation Application (MAA) in the EU and a New Drug Application (NDA) in the US have been submitted for filing. The agreement with AstraZeneca also includes NKTR-119, an earlier stage development program that is a co-formulation of naloxegol and an opioid. NKTR-181, a novel mu-opioid analgesic candidate for chronic pain conditions, is in Phase 2 development in osteoarthritis patients with chronic knee pain. NKTR-192, a novel mu-opioid analgesic in development to treat acute pain is in Phase 1 clinical development. In oncology, etirinotecan pegol (NKTR-102) is being evaluated in a Phase 3 clinical study (the BEACON study) for the treatment of metastatic breast cancer and is also in Phase 2 studies for the treatment of ovarian and colorectal cancers. In anti-infectives, Amikacin Inhale is in Phase 3 studies conducted by Bayer Healthcare as an adjunctive treatment for intubated and mechanically ventilated patients with Gram-negative pneumonia.

Nektar's technology has enabled eight 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 Baxter's BAX 855, a long-acting PEGylated rFVIII program, which is in Phase 3 clinical development.

Nektar is headquartered in San Francisco, California, with additional 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," "may," "will" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the potential for NKTR-181 as a potentially new analgesic opioid therapy for the treatment of chronic pain based on observations and findings from Phase 2 clinical data, potential future clinical development plans for NKTR-181, and the value and potential of our technology and other drug candidates in our research and development pipeline. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, anticipated events and trends, the economy and other future conditions. 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) NKTR-181 is in the clinical development stage 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 prior to approval of a drug candidate; (ii) future development plans for NKTR-181 are preliminary only and subject to change based on, among other factors, our continued review of the clinical study results and interactions with health authorities; (iii) the preliminary topline results reported in this press release are subject to change based on final audit and verification procedures; (iv) 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, it is possible 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; (v) the statements regarding the therapeutic potential of NKTR-181 as an opioid analgesic are based on our findings and observations from preclinical and clinical data and results from future clinical studies for NKTR-181 may fail to confirm these earlier findings and observations; (vi) 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 very uncertain and unpredictable and these potential new drug candidates could unexpectedly fail at any time; (vii) 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 (viii) certain other important risks and uncertainties set forth in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 9, 2013. Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. 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.*

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(1) Hyman, Steven E., *Harvard Review of Psychiatry*. 2(1):43-46, May/June 1994.

(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.

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(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).

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