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Nektar Therapeutics Presents Positive Data from Human Abuse Liability Study for NKTR-181, a First-in-Class Investigational Opioid to Treat Chronic Pain, at 2013 Annual Meeting of The College on Problems of Drug Dependence

NKTR-181 rates similar to placebo on "drug liking" and "feeling high" scores at all doses studied and differentiates from the widely abused drug oxycodone with high statistical significance (p<0.0001)

SAN DIEGO, June 19, 2013 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced positive top-line results from a human abuse liability (HAL) study for NKTR-181, a first-in-class, opioid analgesic molecule with a slow rate of entry into the brain. This slow rate of entry is designed to reduce the euphoria that can lead to the abuse of and addiction to current opioid analgesics.[1] In the study data being presented today, NKTR-181 was rated similar to placebo in "drug liking" and "feeling high" scores and had highly statistically significant lower "drug liking" scores and reduced "feeling high" scores as compared to oxycodone at all doses tested ($p < 0.0001$).

Prescription opioids are critical in the management of moderate-to-severe chronic pain. However, the abuse and misuse of these opioids have led to a serious public health crisis. HAL studies are clinical studies that assess the relative abuse potential of a medicine. These studies are conducted in a non-dependent, recreational drug abuser population and are designed to predict how probable it is that a particular medicine will be attractive to abusers (i.e., "liked"). The primary endpoint for the NKTR-181 HAL study was drug-liking measured on a bi-polar visual analogue scale (VAS). This endpoint is known to correlate most directly with a drug's potential for abuse.[2]

"It is clear that there is a pressing societal need for better and safer analgesics," said Dr. Lynn Webster, President of the American Academy of Pain Medicine and lead investigator for the study at CRI Lifetree. "We know that speed of entry into the brain is important in abuse. When we look at the critical period following dosing when the commonly abused drug oxycodone reaches maximum liking, NKTR-181 was not distinguished from placebo with respect to both drug-liking and feeling high. These are two of the most important metrics that help us understand the abuse potential of a medicine. Importantly, NKTR-181 was dosed as an oral liquid, which underscores that its less rewarding properties are inherent to this NCE and independent of any abuse-deterrent formulation. These data, along with previous efficacy data, suggest NKTR-181 may be a major advance towards safer opioid therapy for the treatment of moderate to severe chronic pain."

The HAL study compared drug liking between each treatment group (oxycodone 40 mg, Placebo, and NKTR-181 100 mg, 200 mg, and 400 mg). On the bipolar VAS scale (0-100), a score of 50 indicates that the subject "neither likes nor dislikes" the drug. In the study, 40 mg of oxycodone oral solution resulted in a maximum mean drug liking score of 85, indicating a "strong liking" for the effects of oxycodone. The oxycodone liking score was significantly different from placebo as early as 15 minutes after dosing and peaked at 60 minutes. In the placebo arm, the maximum mean drug liking score was 50, indicating that the subjects neither liked nor disliked the effects. NKTR-181 dosing was similar to placebo with maximum mean drug liking VAS scores of 58, 58 and 63 for 100 mg, 200 mg and 400 mg, respectively.

"The data from this study are remarkable and clearly demonstrate that drug abusers could not discriminate NKTR-181 from placebo at doses that we know produced analgesia in the validated pain models from our Phase 1 studies," said Robert Medve MD, SVP and Chief Medical Officer of Nektar Therapeutics. "These data suggest that NKTR-181 could change the way we think about opioids and how we treat patients with chronic pain."

Additional Study Results

- *Assessment of "Feeling High"*

All oral doses of NKTR-181 scored similar to placebo in a Drug Effects Questionnaire (DEQ) assessing the treatment's effect on how "high" the subject felt (on a scale of 0 (not at all) to 100 (extremely)). Oxycodone oral solution resulted in a maximum mean DEQ score of 81. NKTR-181 maximum mean DEQ scores were 14, 14 and 23 for 100 mg, 200 mg tablet and 400 mg, respectively, with p-values < 0.0001 as compared to oxycodone. Placebo achieved a maximum mean DEQ score of 9.

- *Assessment of "Sleepiness"*

Sedation was measured using a DEQ assessment of sleepiness (on a scale of 0 (not at all) to 100 (extremely). All doses of NKTR-181 scored lower on sleepiness when compared to oxycodone. The maximum mean DEQ sleepiness score for oxycodone was 44 as compared to the maximum mean DEQ scores for NKTR-181 100 mg, 200 mg and 400 mg of 10, 9, and 18, respectively ($p < 0.0001$).

Study Design

The randomized, double-blind, placebo- and active-controlled, 5-way crossover trial, compared the effects of three doses of NKTR-181 oral solution (100 mg, 200 mg, and 400 mg), to the effects of 40 mg of oxycodone oral solution and placebo. Participants were healthy adults (N=42) who were not currently physically opioid-dependent but had used opioids to attain non-medical effects on at least 10 occasions during the past year and at least once in the 12 weeks before the study. Study participants sequentially received the five treatments, administered in a randomized, double-blinded fashion, with each treatment separated by a washout period. The study also utilized a Williams Square cross-over design, which uses a series of randomized sequences for each individual subject.

About NKTR-181

NKTR-181 is currently being evaluated in Phase 2 development as a twice-daily oral tablet to treat chronic pain. The NKTR-181 Phase 2 study is a double-blind, placebo-controlled, randomized withdrawal study design evaluating the investigational drug candidate in patients with moderate to severe chronic pain from osteoarthritis of the knee. Approximately 200 patients will be randomized to receive either NKTR-181 or placebo in the study.

NKTR-181 is an NCE (new chemical entity) which was created using Nektar's proprietary small molecule polymer conjugate technology and its potential differentiating properties are inherent to its molecular design. In June of 2012, the U.S. Food and Drug Administration (FDA) granted Fast Track Designation to NKTR-181 for the treatment of moderate to chronic pain.

A Phase 1 clinical program for NKTR-181 has been completed in approximately 160 healthy volunteers. These studies showed that NKTR-181 produced sustained and dose-dependent analgesic responses with twice-daily dosing over a period of 8 days. These studies also measured the contraction of pupils over time following dosing with NKTR-181 and the data confirmed that NKTR-181 has a slow rate of entry into the CNS (central nervous system). This slow rate of entry is designed to reduce the euphoria that can lead to abuse and addiction to current opioid analgesics.[1]

Analyst Call to be Held 10:00 AM Pacific Time/1:00 PM Eastern Time on Wednesday, June 19, 2013

The company will be hosting a call to discuss these data with analysts and investors at 10:00 AM Pacific time/1:00 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 Sidney H. Schnoll, MD, PhD of PinneyAssociates, an internationally recognized expert in addiction and pain management.

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: 97974070 (Nektar Therapeutics is the host)

The webcast replay of the conference call will be available through June 24, 2013.

About Opioids and Pain Management

Pain is one of the most common reasons people seek medical treatment.[1] 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.[3] Opioids are considered the most effective therapeutic option for pain, with sales exceeding over $10 billion a year in the U.S. alone.[4,5] 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.[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 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. This agreement 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 opioid therapy with reduced abuse potential, and the value and potential of our technology and 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 earlier stages of 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; (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, 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; (iii) the statements regarding the therapeutic potential of NKTR-181 as an opioid analgesic are based on preclinical data and data from Phase 1 clinical studies and results from future clinical studies, including the ongoing placebo-controlled Phase 2 efficacy clinical study for NKTR-181, may fail to confirm these earlier analgesic findings; (iv) 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; (v) 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 (vi) certain other important risks and uncertainties set forth in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 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) Source: January 2013 Guidance for Industry: Abuse-Deterrent Opioids — Evaluation and Labeling — Draft Guidance distributed by the U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER)

(3) 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).

(4) IMS, NSP, NPA and Defined Health 2010 Estimates.

(5) Melnikova, I, Pain Market, *Nature Reviews Drug Discovery*, Volume 9, 589-90 (August 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).

SOURCE Nektar Therapeutics