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Nektar Announces Start of Phase 3 SUMMIT-07 Study of NKTR-181 in Patients with Chronic Low Back Pain

SAN FRANCISCO, Feb. 25, 2015 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) today announced the enrollment of the first patient in SUMMIT-07, its initial Phase 3 study of 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 current opioid analgesics.[1] SUMMIT-07 will evaluate the efficacy, safety and tolerability of NKTR-181 in patients with chronic low back pain who are also opioid-naïve (new to treatment).

"With millions of patients suffering from chronic pain, there is a clear unmet medical need for better and safer pain medications," said Dr. Nathaniel Katz, President of Analgesic Solutions and Adjunct Asst. Professor of Anesthesia at Tufts University School of Medicine. "As a mu-opioid agonist designed to have anti-abuse properties inherent to its molecular structure, NKTR-181 has the potential to have an important impact on the growing health care crisis of opioid abuse and diversion."

NKTR-181 is a new chemical entity (NCE) that was created using Nektar's proprietary small molecule polymer conjugate technology. NKTR-181 has several potential differentiating properties that are inherent to the structure of the molecule, including a slow rate of entry into the CNS as measured by pupillometry (contraction of the pupils) and a plasma pharmacokinetic profile that supports twice-daily oral dosing. NKTR-181 is not a reformulation of a marketed opioid, which is a commonly-used method to attempt to prevent the manipulation of existing long-acting opioid drugs into more abusable forms.

"The investigators are pleased to see the start of this important first study in the SUMMIT Phase 3 program to evaluate the efficacy and safety of NKTR-181 in patients with chronic low back pain," said Dr. Martin Hale, Medical Director of Gold Coast Research, LLC. "NKTR-181 holds great promise as it represents a completely new class of pain medicine that could allow us to maintain the efficacy of traditional opioids, while potentially reducing the risks of misuse, abuse and diversion."

NKTR-181 has been granted has been granted Fast Track designation for the treatment of moderate to severe chronic pain by the U.S. Food and Drug Administration.

SUMMIT-07 Study Design
The SUMMIT-07 Phase 3 trial utilizes an enriched-enrollment, randomized withdrawal (EERW) design and will enroll opioid-naïve patients ages 18 to 75 years who have had moderate to severe non-neuropathic chronic low back pain for at least six months. The study includes an open-label, dose titration period followed by a randomized, double-blind, placebo-controlled 12 week treatment period. During the open-label titration phase, study participants will be titrated on NKTR-181 tablets administered orally twice daily until they experience an adequate and sustained pain response. Patients who achieve this will then be randomized on a 1:1 basis to either continue to receive their analgesic dose of NKTR-181 or to receive placebo during the double-blind 12 week treatment period. A total of 208 patients will be randomized to each arm. No background NSAIDs are allowed throughout the study.

The primary endpoint of the study is a change in pain as measured by the change in a patient's weekly pain score from baseline to week 12 of the randomized, double-blind treatment period.

The SUMMIT Phase 3 program will also include a Phase 3 efficacy and safety trial in patients who are opioid-experienced (SUMMIT-12) as well as a 52-week long-term safety study (SUMMIT-LTS).

For more information on the SUMMIT-07 study, please visit https://www.clinicaltrials.gov/ct2/show/NCT02362672?term=nktr-181&rank=2

About Opioids and Pain Management
Pain is one of the most common reasons people seek medical treatment.[i] A study published in the American Pain Society's *The Journal of Pain* in October 2014 estimated that 19 percent of the U.S. population, or 39 million people, suffer from persistent pain.[ii]

Opioids are considered the most effective therapeutic option for pain with 270 million prescriptions written in the U.S. alone in

2013.[iii] [iv] The global opioid market for chronic pain, which includes chronic back pain, osteoarthritis, fibromyalgia and neuropathic pain, is estimated to be $12.6 billion. Opioids can cause serious side effects such as respiratory depression and sedation and have the potential for addiction, abuse and misuse. According to the Centers for Disease Control and Prevention (CDC), 420,040 emergency department visits in 2011 were related to opioid analgesics.[v] In the United States, prescription opioid abuse costs were about $55.7 billion in 2007, of which 46 percent was attributable to workplace costs (e.g., lost productivity), 45 percent to healthcare costs (e.g., abuse treatment), and 9 percent to criminal justice costs.[vi]

About Nektar

Nektar Therapeutics has a robust R&D pipeline in pain, oncology, hemophilia and other therapeutic areas. In the area of pain, Nektar has an exclusive worldwide license agreement with AstraZeneca for MOVANTIK™ (naloxegol), the first FDA-approved once-daily oral peripherally-acting mu-opioid receptor antagonist (PAMORA) medication for the treatment of opioid-induced constipation (OIC), in adult patients with chronic, non-cancer pain. The product is also approved in the European Union as MOVENTIG® and is indicated for adult patients with OIC who have had an inadequate response to laxatives. The AstraZeneca agreement also includes NKTR-119, an earlier stage development program that is a co-formulation of MOVANTIK™ and an opioid. NKTR-181, a wholly-owned mu-opioid analgesic molecule for chronic pain conditions, is in Phase 3 development. NKTR-171, a wholly-owned new sodium channel blocker being developed as an oral therapy for the treatment of peripheral neuropathic pain, is in Phase 1 clinical development. In oncology, NKTR-102 is being evaluated in a Phase 3 clinical study (the BEACON study) for the treatment of metastatic breast cancer. In hemophilia, BAX 855, a longer-acting PEGylated Factor VIII therapeutic is in Phase 3 development conducted by partner Baxter. 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 nine approved products in the U.S. or Europe through partnerships with leading biopharmaceutical companies, including AstraZeneca's MOVANTIK™, 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 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.

MOVANTIK™ is a trademark of the AstraZeneca group of companies.

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 therapeutic potential of NKTR-181 and the value and potential of our technology and 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) our drug candidates and those of our collaboration partners are in various stages of clinical development and the risk of failure is high and can unexpectedly occur at any stage prior to regulatory approval for numerous reasons including safety and efficacy findings even after positive findings in previous preclinical and clinical studies; (ii) the timing of the commencement or end of clinical trials and the commercial launch of drugs may be delayed or unsuccessful due to regulatory delays, slower than anticipated patient enrollment, manufacturing challenges, changing standards of care, evolving regulatory requirements, clinical trial design, clinical outcomes, competitive factors, or delay or failure in ultimately obtaining regulatory approval in one or more important markets; (iii) acceptance, review and approval decisions for new drug applications by health authorities is an uncertain and evolving process and health authorities retain significant discretion at all stages of the regulatory review and approval decision process; (iv) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of the application of our technology platform to potential new drug candidates is therefore highly uncertain and unpredictable and one or more research and development programs could fail; (v) patents may not issue from our patent applications for our drug candidates, 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 drug candidates and those of our collaboration partners. Other important risks and uncertainties set forth in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 7, 2014. 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.

[i] 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).

[ii] http://americanpainsociety.org/about-us/press-room/persistent-pain-incidence-news-release.

[iii] IMS, NSP, NPA and Defined Health 2013 Estimates.

[iv] Melnikova, I, Pain Market, Nature Reviews Drug Discovery, Volume 9, 589-90 (August 2010).

[v] http://www.cdc.gov/homeandrecreationalsafety/overdose/facts.html.

[vi] http://www.cdc.gov/homeandrecreationalsafety/overdose/facts.html.