Nektar Doses First Subjects in Phase 1 Clinical Study Evaluating NKTR-192, a New Short-Acting Opioid Molecule for the Treatment of Acute Pain

SAN FRANCISCO, April 2, 2012 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) announced today that the first subjects were dosed last week in a Phase 1 clinical study to evaluate the pharmacokinetics and safety of NKTR-192, the company's novel short-acting mu-opioid analgesic candidate. NKTR-192 is designed to have a short-acting profile with rapid onset of pain relief for the treatment of acute pain. With a reduced rate of entry into the central nervous system (CNS) as compared to other fast-acting opioid therapies in preclinical studies, NKTR-192 has the potential to greatly reduce the euphoria that underlies opioid abuse and dependence, as well as other unwanted CNS side effects, such as sedation. The unique characteristics of NKTR-192 are engineered into its new molecular design and are not the result of formulation techniques.

The single-dose Phase 1 clinical study will assess the pharmacokinetics and safety of NKTR-192 in up to 36 healthy subjects. The primary objective of the study is to assess the pharmacokinetic profile of various dosages in humans in order to design future clinical studies for the compound. This Phase 1 clinical study is being conducted in the United States at Lifetree Clinical Research.

"With prescription opioid abuse at epidemic levels in the United States, new approaches are desperately needed to address this serious problem," said Robert Medve, M.D., Chief Medical Officer of Nektar Therapeutics. "NKTR-192 is a highly compelling new opioid molecule that has exceeded our expectations in multiple preclinical studies. The drug candidate demonstrated a fast onset of analgesia, while at the same time showing greatly reduced abuse liability and sedation as compared to standard short-acting opioids. NKTR-192 is an excellent addition to Nektar's pain portfolio, and we look forward to evaluating this new mu-opioid analgesic molecule in the clinic."

Preclinical data for NKTR-192 was highlighted last November at the Society for Neuroscience Annual Meeting: Neuroscience 2011. Data from in vivo and in vitro studies demonstrated that NKTR-192 exhibits onset of analgesic activity within five minutes, as well as a peak effect comparable to current opioids. In preclinical models used to predict the abuse liability of compounds, NKTR-192 shows a marked reduction in self-administration of NKTR-192 as compared to reference opioids. Additionally, NKTR-192 exhibits a significantly reduced rate of entry into the CNS as compared to leading opioid agents.

Nektar is also developing NKTR-181, a long-acting mu-opioid analgesic for the treatment of chronic pain conditions, such as osteoarthritis and low back pain. The company has completed Phase 1 clinical development of NKTR-181 demonstrating sustained and dose-dependent analgesic responses with NKTR-181, a dramatically slower rate of entry into the CNS and an excellent tolerability profile. Nektar plans to advance NKTR-181 into Phase 2 clinical development in chronic pain patients in mid-2012.

About NKTR-192

NKTR-192 is Nektar Therapeutics' drug candidate for the treatment of moderate to severe acute pain. NKTR-192 is a novel mu-opioid analgesic created using Nektar's advanced polymer conjugation technology to slow drug entry into the central nervous system (CNS). By dramatically slowing the rate of drug entry into the CNS, NKTR-192 is intended to maintain opioid-like efficacy without the abuse potential and other CNS side effects associated with rapid-acting opioids. In preclinical testing, NKTR-192 demonstrates a rapid onset of analgesia and relatively short half-life, without exhibiting sedative or abuse potential at analgesic doses.

About Opioids and Pain Management

Approximately 140 million prescriptions are written annually in the U.S. for acute and sub-chronic pain indications, such as muscle injuries, post-operative pain, and kidney stones.(1,2) Although prescription opioids are considered the most effective treatment for moderate-to-severe pain, their abuse has been identified by the U.S. Food and Drug Administration (FDA) and the Centers for Disease Control as a significant public health issue. The abuse properties of opioid drugs are believed to be related to their rapid rate of entry into the brain.(3)

Rapid-acting opioids enter the brain quickly, frequently causing a euphoric effect, or drug-related "high" which results in high potential for substance abuse, addiction and diversion. In addition to the potential to be abused, opioids can also cause drowsiness, impacting a patient's ability to function normally. The pharmaceutical industry has invested heavily in the development of new formulations of these drugs in order to combat the abuse and diversion of these painkillers. However, these

reformulations have been primarily focused on physical means of deterrence, and abusers have found ways to overcome these formulation barriers.

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 is being evaluated in Phase 3 clinical studies 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 in development to treat chronic pain, 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 eight approved products in the U.S. or Europe through partnerships with leading biopharmaceutical companies, including Affymax's OMONTYS® for anemia, 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 1 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" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the therapeutic potential of NKTR-192 including the potential for NKTR-192 to exhibit reduced abuse potential and side effects typically associated with comparable opioid medicines; our future plan to initiate a Phase 2 study for NKTR-181; and the value and potential of certain other drug candidates in our R&D 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 potential of our drug candidates, 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, the following: (i) our statements regarding the potential therapeutic potential of NKTR-192 are based on preclinical data only and clinical study results may not confirm one or more of these potential therapeutic benefits; (ii) NKTR-192 is in the first stage 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 drug development; (iii) the FDA and other regulatory agencies could impose significant risk mitigation requirements that hamper market acceptance of NKTR-192, even if approved by one or more government health authorities; (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 such as NKTR-192, is therefore very uncertain and unpredictable and could unexpectedly fail at any time; (v) patents may not issue from our patent applications for NKTR-192, patents (if issued) may not be enforceable, or additional intellectual property licenses from third parties may be required; and (vi) the outcome of any existing or future intellectual property or other litigation related to Nektar's proprietary drug candidates including without limitation NKTR-192; and (vii) certain other important risks and uncertainties set forth in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 29, 2012 which filing can be accessed at www.sec.gov. 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) 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) and H. Lullmann et. al., 2005, "Color Atlas of Pharmacology".

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