NKTR-192, A New Short-Acting Mu-Opioid Analgesic Molecule, Achieves Desired Pharmacokinetic Profile in First Phase 1a Clinical Study

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SAN FRANCISCO, Sept. 18, 2012 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) announced today that positive data from the first single-ascending dose Phase 1a clinical study of NKTR-192, the company's novel short-acting mu-opioid analgesic candidate, demonstrate that the drug candidate achieved its target pharmacokinetic profile. These data support its continued development as a new analgesic for the treatment of acute pain. The company also announced that dosing has commenced in a second single-ascending dose Phase 1a clinical study of NKTR-192, which will explore the pharmacodynamic profile of this new drug candidate in healthy subjects.

NKTR-192 is a new mu-opioid agonist molecule designed to have a short-acting profile and onset of pain relief suitable for the treatment of acute pain, but with a reduced rate of entry into the CNS as compared to other fast-acting opioids used to treat acute pain, such as Vicodin® and Percocet®.

"With prescription opioid abuse at epidemic levels in the United States, we need new thinking, new approaches and new molecules to address this serious problem," said Robert Medve, M.D., Chief Medical Officer of Nektar Therapeutics. "With NKTR-192, we set out to build a new molecule that behaves differently than other opioids, preserving the powerful pain relief but changing the way it enters the brain and how it targets receptors throughout the body. The way we have engineered NKTR-192 may allow us to reduce the euphoria, or rush, that can drive opioid abuse and dependence, while at the same time reducing other unwanted CNS side effects, such as sedation. These potential unique characteristics of NKTR-192 are built into the molecular design — this is designed to be different."

The second Phase 1a clinical study will assess the pharmacodynamic profile and tolerability of single ascending doses of NKTR-192 in up to 48 healthy subjects. The Phase 1 clinical development program is being conducted in the United States at Lifetree Clinical Research.

"Results from our first clinical study of NKTR-192 demonstrated that this new mu-opioid molecule achieved a short-acting pharmacokinetic profile which is ideal for the treatment of acute pain," continued Dr. Medve. "In our second clinical study, we will measure multiple pharmacodynamic endpoints, including indicators of CNS entry and models of analgesia in healthy volunteers. NKTR-192 is an excellent addition to Nektar's pain portfolio and we look forward to the continued development of this new mu-opioid analgesic molecule in the clinic."

In preclinical studies, NKTR-192 has demonstrated a reduced rate of entry into the central nervous system, demonstrating 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 physically engineered into its new molecular design so its potential differentiating properties are inherent to the molecule.

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 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.

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 mu-opioid medicines 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 and early Phase 1 data only and future clinical study results may not confirm one or more of these potential therapeutic benefits; (ii) NKTR-192 is in the very early 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 drug development; (iii) while we have conducted numerous experiments using laboratory and home-based chemistry techniques that have not been able to convert NKTR-192 into a rapid-acting and more abusable opioid, there is a risk that in the future a technique could be discovered to convert NKTR-192 into a rapid-acting and more abusable opioid which would significantly diminish the value of this drug candidate; (iv) 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; (v) 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; (vi) 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 (vii) the outcome of any existing or future intellectual property or other litigation related to Nektar's proprietary drug candidates including NKTR-192; 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, 2012 which filing can be accesssed 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.

Nektar Investor Inquiries:
Jennifer Ruddock/Nektar Therapeutics (415) 482-5585
Susan Noonan/SA Noonan Communications, LLC (212) 966-3650

Nektar Media Inquiries:
Mary Cunney (917) 208-2162
Mike Huckman (646) 500-7631

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[2] IMS, NSP, NPA and Defined Health 2010 Estimates.

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