# Positive Data for Nektar's New Mu-Opioid Analgesic Molecule to Treat Acute Pain Highlighted at Neuroscience 2011

## NKTR-192 Demonstrates Rapid Onset of Analgesia, Slow Uptake into the Brain, Reduced Abuse Liability and Less Sedation Compared to Standard Opioid Therapies

SAN FRANCISCO and WASHINGTON, Nov. 14, 2011 /PRNewswire/ -- Nektar Therapeutics (NASDAQ: NKTR) announced today that positive preclinical data for NKTR-192, a novel mu-opioid agonist, was presented at the 41st Annual Meeting of the Society for Neuroscience being held November 12-16, 2011 in Washington, DC. NKTR-192 is a new oral analgesic candidate being developed for the treatment of acute pain. It is designed to minimize the unwanted central nervous system (CNS) side effects observed with standard opioid therapies and to reduce abuse liability by slowing the rate of drug entry into the brain. NKTR-192 is a novel mu-opioid analgesic molecule that was created using Nektar's proprietary polymer conjugate technology and its differentiating properties are inherent to the design of its new molecular structure.

Approximately 140 million prescriptions are written annually in the U.S. for acute 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 (CDC) 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)

"NKTR-192 is an exciting new opioid molecule that builds on Nektar's pain platform, which includes NKTR-181, our novel opioid for chronic pain, currently in Phase 1 development," said Rob Medve, M.D., Chief Medical Officer of Nektar Therapeutics. "NKTR-192 has the potential to offer highly effective short-acting pain relief with a wide therapeutic window, including reduced abuse liability and sedation. A new opioid analgesic with this compelling profile would be a major advance in the treatment of acute pain, such as post-operative pain and other painful conditions like muscle or bone injuries. We look forward to advancing this compound into the clinic in the first half of 2012."

Data from multiple *in vivo* and *in vitro* preclinical studies were presented at Neuroscience 2011. NKTR-192 exhibits a relatively fast onset of analgesia, within 5-15 minutes, in multiple preclinical *in vivo* models of pain. Analgesia with NKTR-192 is comparable to oxycodone. In preclinical *in vivo* models of self-administration used to predict the abuse liability of compounds, NKTR-192 shows a marked reduction in self-administration of drug as compared to both oxycodone and cocaine. Additionally, in a series of *in situ* brain perfusion studies, NKTR-192 exhibits a significantly reduced rate of entry into the CNS as compared to fentanyl, oxycodone and hydrocodone. The preclinical data presented also demonstrated that NKTR-192 is a mu-opioid agonist, binding to receptors in the CNS and in the periphery, believed to be the primary mechanism of pain relief for opioid therapies.

These data will be highlighted during today's Neuroscience 2011 press conference to be held at 1:30 pm eastern time in the Walter E. Washington Convention Center in the Press Room. The poster presentation entitled Harrison et al. "*Pharmacological characterization of an orally active opioid analgesic with rapid onset of activity and low abuse liability (NKTR-192: An Orally Active Opioid Analgesic with Rapid Onset of Activity and Low Abuse Liability)"* can be found on Nektar's website at http://www.nektar.com/product_pipeline/cns_pain_nktr-192.html .

**About NKTR-192**

NKTR-192 is Nektar Therapeutics' product candidate for the treatment of moderate to severe acute pain. NKTR-192 is a novel mu-opioid analgesic created using Nektar's advanced polymer conjugate technology designed to slow drug entry into the 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 demonstrated a rapid onset of analgesia and relatively short half-life, without exhibiting sedative or abuse potential at analgesic doses. Nektar intends to file an IND for NKTR-192 in the first quarter of next year and expects to advance NKTR-192 into clinical trials in the first half 2012.

**About Opioids and Pain Management**

Opioid drugs are widely prescribed in pain management and are highly effective for treatment of moderate-to-severe pain.

Each year, there are over 250 million prescriptions written for these opioid painkillers in the U.S. alone.(1) However, the FDA has identified prescription opioid abuse as a significant public health issue. The abuse of these drugs has led to extremely high societal costs estimated in the tens of billions of dollars annually in the U.S.(4) Rapid-acting opioids enter the brain quickly, frequently causing a euphoric effect, or "high" which results in high potential for drug abuse, addiction and diversion. In addition to their 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 NKTR-118, an investigational drug candidate, being evaluated in Phase 3 clinical studies as a once-daily, oral tablet for the treatment of opioid-induced constipation. The agreement also includes NKTR-119, an earlier stage development program that is a co-formulation of NKTR-118 and an opioid. NKTR-181, a novel mu-opioid analgesic molecule wholly-owned by Nektar, is being evaluated in Phase 1 clinical studies. In oncology, NKTR-102, a novel proprietary topoisomerase I-inhibitor, is being evaluated in Phase 2 clinical studies for the treatment of breast, ovarian and colorectal cancers.

Nektar's technology has enabled seven 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 peginesatide, for which Affymax and partner Takeda submitted an NDA to the FDA in May 2011, and Baxter's BAX 855, a long-acting PEGylated rFVIII program planned to enter Phase 1 clinical development in 2011.

Nektar is headquartered in San Francisco, California, with additional R&D 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.


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This press release contains forward-looking statements that reflect Nektar's current views as to the therapeutic potential of NKTR-192 to effectively treat acute pain while reducing abuse liability and certain serious side effects associated with traditional opioid therapies, preclinical observations regarding the biological effect of NKTR-192, the timing of the planned start of clinical studies for NKTR-192, the potential of Nektar's polymer conjugate technology platform, and the potential for certain of Nektar's other drug candidates and those of its collaboration partners. These forward-looking statements involve substantial risks and uncertainties including but not limited to one or more of the following: (i) the preclinical data for NKTR-192 described in this press release and presented at the 41st Annual Meeting of the Society for Neuroscience may not be predictive of future success in clinical trials; (ii) the commencement of a Phase 1 clinical study for NKTR-192 in the first half of 2012 could be delayed due to regulatory delays, the need to successfully complete certain toxicology studies, drug manufacturing challenges, and other important factors that can impact clinical development efforts; (iii) 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-192 is therefore very uncertain and unpredictable and one or more research and development programs could unexpectedly fail; (iv) Nektar's patent applications for its proprietary or partner drug candidates may not issue, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required; and (v) the outcome of any existing or future intellectual property or other litigation related to Nektar's proprietary drug candidates including without limitation NKTR-191. Other important risks and uncertainties are detailed in Nektar's filings with the Securities and Exchange Commission, including without limitation, those risks and uncertainties set forth in Nektar's Quarterly Report on Form 10-Q for the quarter ended September 30, 2011 filed with the SEC on November 4, 2011. Nektar undertakes no obligation to update forward-looking statements, whether as a result of new information, future events or otherwise.

*References:*


1. IMS Health 2010.

2. Defined Health Research

3. Winger et al. (2002), JPET, 301, 690-697; Marsch et al., (2001). JPET, 299, 1056-1065. Webster and Dove (2007). *Avoiding Opioid Abuse*.

4. Birnbaum, et al. (2011) Pain Medicine 12(4): 657-667.

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