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## **Nektar Presents Positive Preclinical Data on Oral, Peripherally-Acting Kappa Agonist Molecules at 2014 American Academy of Pain Management Meeting**

SAN FRANCISCO, Sept. 19, 2014 /PRNewswire/ -- Nektar Therapeutics (NASDAQ:NKTR) today announced results from preclinical studies characterizing the analgesic profiles of a series of the company's internally-discovered oral, peripherally-acting kappa opioid receptor agonist molecules. The preclinical research candidates were created using Nektar's small molecule polymer medicinal chemistry platform.

The analgesic properties of kappa receptor agonism are well described in the medical literature.<sup>1,2</sup> Kappa opioid receptors are expressed in the peripheral nervous system as well as in the central nervous system (CNS), and activation of these receptors at both sites has been shown to result in a reduction in pain and inflammation in a wide range of preclinical models.<sup>1,4</sup> However, the therapeutic use of kappa receptor agonists has been limited because activation of these receptors in the CNS is associated with significant dysphoria and other unwanted side effects (i.e., anxiety, restlessness and fidgeting).<sup>3</sup>

"We are encouraged by the results of our research, which shows that we can achieve efficacy through the peripheral activation of the kappa opioid receptor, while at the same time reducing the side effects observed with centrally-acting kappa agonist molecules," said Stephen K. Doberstein, Ph.D., senior vice president and chief scientific officer of Nektar Therapeutics. "With this research, we are continuing to capitalize on the ability of our small molecule polymer medicinal chemistry platform to create new peripherally-acting molecules that could address different pain conditions."

Results presented showed that a series of novel, oral, peripherally-acting kappa agonist molecules demonstrated a 15-fold improved therapeutic index (separation between efficacy and CNS-mediated side effects) compared with kappa agonist molecules that were not peripherally selective. The preclinical data is being presented today at the American Academy of Pain Management Annual Meeting (Choi IY, et al. Characterization of novel, oral peripherally-acting kappa agonists in preclinical models).

### **About Nektar**

Nektar Therapeutics has a robust R&D pipeline of potentially high-value therapeutics in pain, oncology, hemophilia and other therapeutic areas. In the area of pain, Nektar has an exclusive worldwide license agreement with AstraZeneca for MOVANTIK™, 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 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, has completed Phase 2 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, etirinotecan pegol (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.

### **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 regarding the potential of our polymer medicinal chemistry platform and drug candidates such as our proprietary kappa opioid receptor agonist molecules. 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) positive preclinical findings, such as those for our proprietary kappa opioid receptor agonist molecules, are subject to inherent scientific and medical uncertainties typical for this early stage of drug development and may not be confirmed in subsequent preclinical studies or in clinical trials; (ii) 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; (iii) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future success of applying our technology platform to potential new drug candidates (such as our kappa opioid receptor agonist molecules) is therefore highly uncertain and unpredictable and one or more research and development programs could fail; (iv) patents may not issue from our patent applications, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required; and (v) 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 1, 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.

1. Machelska H, et al. Peripheral effects of the kappa-opioid agonist EMD 61753 on pain and inflammation in rats and humans. *J Pharmacol Exp Ther.* 1999;290(1): 354-61.
2. Hope PJ, Fleetwood-Walker SM, Mitchell R. Distinct antinociceptive actions mediated by different opioid receptors in the region of lamina I and laminae III-V of the dorsal horn of the rat. *Br J Pharmacol.* 1990;101(2): 477-83.
3. Vanderah TW, et al. Novel D-amino acid tetrapeptides produce potent antinociception by selectively acting at peripheral kappa-opioid receptors. *Eur J Pharmacol.* 2008. 583(1):62-72.
4. Millan MJ, et al. Inflammation of the hind limb as a model of unilateral, localized pain: influence on multiple opioid systems in the spinal cord of the rat. *Pain.* 1988;35(3):299-312.

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