New Data for NKTR-181, a First-in-Class Investigational Opioid to Treat Chronic Low Back Pain in Adult Patients New to Opioid Therapy, Presented at College on Problems of Drug Dependence 80th Annual Scientific Meeting

June 14, 2018

SAN FRANCISCO, June 14, 2018 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced that new clinical and preclinical data for NKTR-181 were presented this week at the 80th Annual Scientific Meeting of the College on Problems of Drug Dependence (CPDD) in San Diego, California. NKTR-181 is a new molecular entity (NME) and the first analgesic opioid molecule to exhibit a reduced incidence of specific CNS-mediated side effects, such as euphoria, through the targeted alteration of brain-entry kinetics.

"We are privileged that these meaningful new data from our clinical trials, as well as our translational research, were recognized for oral presentation at the prestigious CPDD meeting," said Steve Doberstein, Ph.D., Senior Vice President and Chief Research and Development Officer of Nektar Therapeutics. "The data presented show that NKTR-181 demonstrates consistently low abuse potential when we look at a range of measurements used to understand potential abuse liability of investigational medicines including the MADDERS assessment. In addition, we demonstrated in our preclinical research that NKTR-181 has a unique neuropharmacodynamic profile with slow brain uptake and a blunted dopamine response as compared to oxycodone."

The full presentations made at CPDD can be found at the links below:

College on Problems of Drug Dependence 80th Annual Scientific Meeting (2018), San Diego, CA

- **Oral Presentation:** *"Assessment of Drug Abuse-Related Events with MADDERS in SUMMIT-07: A Phase-3 Study of NKTR-181 in Patients with Moderate to Severe Chronic Low-Back Pain"*
  - **Abstract #76**
  - **Presenter:** Ryan Lanier, Ph.D., Analgesic Solutions
  - **Session:** The Pain and the Strain Comes Mainly from the Brain
  - **Date/Time:**Wednesday, June 13 at 1:30 pm-1:45 pm Pacific Time
- **Oral Presentation:***"Neuropharmacodynamic Profile of NKTR-181: Correlation to Low Abuse Potential"*
  - **Abstract #335**
  - **Presenter:** Laurie Vanderveen, Ph.D., Nektar Therapeutics
  - **Session:** Basically Opioids
  - **Date/Time:**Tuesday, June 12 at 10:15 am-10:30 am Pacific Time
- **Poster Presentation**: *"NKTR-181 demonstrates low abuse potential in recreational opioid users in two double-blind, randomized crossover human abuse potential studies"*, Henningfield, J., et al.
  - **Abstract #168**
  - **Session:** Abuse Liability
  - **Date/Time:** Thursday, June 14 at 12:00 pm- 2:00 pm Pacific Time

There is wide variation across opioids with respect to nonmedical use, abuse, and associated overdose deaths, with the highest rates of nonmedical use and overdose occurring with those that produce euphoric effects. In 2014, nearly 2 million Americans either abused or were dependent on prescription opioid pain relievers.[1]

Nektar recently submitted a New Drug Application for NKTR-181 for the treatment of chronic low back pain in adult patients new to opioid therapy. The NDA is supported by an extensive clinical and nonclinical data package. The clinical data submitted in the NDA comprised 15 studies in 2,234 subjects and includes: a 600-patient efficacy study in patients with chronic low back pain who are new to opioid therapy; a 630-patient long-term 52-week safety study in patients with noncancer pain, who are new to opioid therapy, as well as those who are experienced with opioid therapy; pharmacokinetic/pharmacodynamic studies in over 450 subjects; and two human abuse potential studies evaluating both therapeutic and supratherapeutic doses of NKTR-181 versus an oxycodone control in recreational drug users.

About Chronic Low Back Pain

Low back pain is the second most common cause of disability for adults in the U.S.[2] Approximately 149 million work days are lost every year because of low back pain, with total costs estimated to be $100 to 200 billion a year (of which two-thirds is due to lost wages and lower productivity).[3]

About NKTR-181

NKTR-181 is the first long-acting, selective full mu-opioid agonist designed to provide potent pain relief, without the inherent high levels of euphoria, which lead to abuse and addiction with standard opioids. The novel molecular structure of NKTR-181 is designed to have low permeability across the blood-brain barrier in order to slow its rate of entry into the brain and attenuate the

dopamine release that underlies euphoria. In addition, NKTR-181 has a 14-hour elimination half-life to enable twice-daily dosing for pain control.

Current and past strategies of abuse deterrence to address the addictive properties of standard opioids rely on formulations alone. However, all abuse-deterrent formulations are precursors to highly euphorigenic rapid-acting opioids, which can be liberated through tampering.

NKTR-181 is not a prodrug, a reformulation, or a drug product formulated for sustained release of an existing opioid. Nonclinical and clinical data show that the inherent properties of NKTR-181 reduce its rate of entry into the brain compared to standard mu opioids, regardless of route of administration.[4] NKTR-181 is an investigational medicine and has not been approved by the FDA or any other regulatory agencies.

About Nektar Therapeutics
Nektar Therapeutics is a research-based development stage biopharmaceutical company whose mission is to discover and develop innovative medicines to address the unmet medical needs of patients. Our R&D pipeline of new investigational medicines includes treatments for cancer, auto-immune disease and chronic pain. We leverage Nektar's proprietary and proven chemistry platform in the discovery and design of our new therapeutic candidates. 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 which can be identified by words such as: "design," "exhibit," "address," "can" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the potential therapeutic benefit of NKTR-181 for treating patients with pain, the potential importance of NKTR-181 in addressing opioid abuse, the risks of opioid abuse resulting from use of NKTR-181, and certain other statements regarding the prospects and potential of NKTR-181. 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) challenges and uncertainties inherent in pharmaceutical research and development, including the uncertainty of regulatory success, where the risk of failure remains high and failure can unexpectedly occur prior to regulatory approval due to lack of sufficient efficacy, safety considerations or other factors; (ii) the regulatory pathway to review and approve NKTR-181 for use in patients, even with a Fast Track designation by the FDA, is subject to substantial uncertainty both in the United States and in equivalent foreign regulatory agencies; (iii) regulations concerning and controlling the access to opioid-based pharmaceuticals are strict and there is no guarantee which scheduling category will apply to NKTR-181 if regulatory approval is achieved; (iv) drug manufacturing challenges which can delay or render unavailable sufficient supplies of NKTR-181; (v) changing standards of care and new regulations (including, but not limited to, standards and regulations related to health care cost containment) can affect the use NKTR-181 and commercial success following a regulatory approval; (vi) Nektar's patent applications for NKTR-181 may not issue in one or more jurisdictions, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required in the future; (vii) the outcome of any existing or future intellectual property or other litigation related to NKTR-181 is unpredictable and could have a material adverse effect on our business; and (viii) certain other important risks and uncertainties set forth in Nektar's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 10, 2018. 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]. Substance Abuse and Mental Health Services Administration, National Survey on Drug Use and Health, 2014.

[2]. Arch Intern Med 2009 February 9; 169(3): 251-258.

[3]. World Health Organization: Priority Medicines for Europe and the World Update Report, 2013; Background Paper 6.24, Low Back Pain.

[4]. 2010 Society of Neuroscience Annual Meeting (Nov 13-17, #HHH11)

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