



## **Nektar Announces Positive Results from Phase 2 Study of Oral NKTR-118 in Patients with Opioid-Induced Constipation (OIC)**

### **--Highly Statistically Significant Results Achieved at Two Dose Levels with No Reversal of Analgesia**

SAN CARLOS, Calif., March 2, 2009 /PRNewswire-FirstCall via COMTEX News Network/ -- Nektar Therapeutics (Nasdaq: NKTR) announced positive topline results today from a Phase 2 double-blind, randomized, placebo-controlled study of NKTR-118 in patients with opioid-induced constipation (OIC). NKTR-118, a peripheral opioid antagonist, is an oral once-a-day investigational drug to treat OIC, the most common and debilitating manifestation of opioid-bowel dysfunction (OBD). The Phase 2 study of NKTR-118 is terminating early on the basis of overwhelming evidence of efficacy at two different dose levels of 25 mg once daily and 50 mg once daily. The study achieved a clinically meaningful and highly statistically significant, dose-dependent increase in spontaneous bowel movements (SBMs) from baseline after the first week of NKTR-118 treatment with the 25 mg dose and the 50 mg dose versus placebo ( $p < 0.01$  for all comparisons). Patients receiving the 25 mg dose of NKTR-118 had an average of 5.1 SBMs during the first week of treatment as compared to 1.5 SBMs per week during the baseline period. Patients receiving the 50 mg dose of NKTR-118 had an average of 5.7 SBMs during the first week of treatment versus 1.6 SBMs per week during the baseline period. The increase in SBMs versus placebo was maintained over the 28-day treatment period ( $p < 0.01$ ). More importantly, in the 25 mg and 50 mg dose cohorts, there was no reversal of analgesia as measured by a change in pain Numerical Rating Scale (NRS) and no increase in opiate use.

"These data show that NKTR-118 taken orally once-daily at the 25 mg and 50 mg dose levels dramatically increased bowel movements within the first week of treatment for patients with OIC," said Lynn R. Webster, M.D., Medical Director, Lifetree Clinical Research and Pain Clinic, member of the board of directors of the American Academy of Pain Management and lead clinical investigator for the Phase 2 Study of NKTR-118. "Further, these effects were sustained over the entire 28-day treatment period without opiate withdrawal or reversal of analgesia. There are no oral therapies to date that have demonstrated as much promise as NKTR-118 to help this heterogeneous population of patients."

Oral NKTR-118 combines Nektar's advanced small molecule polymer conjugate technology platform with naloxol, a derivative of the opioid-antagonist drug, naloxone. Nektar's technology has been shown to increase oral bioavailability and reduce penetration across the blood-brain barrier, an important potential advance for many other small molecule therapies.

"NKTR-118 demonstrates that our advanced polymer conjugate technology can potentially create new small molecule drugs with optimal physicochemical and pharmacological properties," said Howard W. Robin, President and CEO of Nektar. "Nektar is well-recognized as the industry leader in large molecule PEGylation. This validation of our platform with small molecules is a major achievement for Nektar and sets the stage for the future growth of our pipeline."

#### About the Phase 2 Study for NKTR-118

The Phase 2 study for NKTR-118, in 208 pain patients experiencing OIC, was an international, multicenter, randomized, double-blind, dose-escalation, placebo-controlled trial.

The primary endpoint of the study was a change in SBMs from a two-week baseline period during which the patient had to demonstrate significant constipation in the absence of laxatives, to the change in SBMs at the end of the first week of randomized study drug. Patients in the study were being treated for moderate to severe pain with 30 to 1,000 morphine equivalent units. Under the study protocol, patients were randomly assigned to placebo or one of three different dose cohorts (5 mg, 25 mg, and 50 mg given as a single daily oral dose) for a treatment period of four weeks. In addition to measures of SBMs, patients also recorded daily use of opiates and pain NRS scores.

Secondary endpoints included reversal of analgesia as measured by a change in pain NRS or increase in opiate use during the 28-day treatment period. NKTR-118 did not result in an increase in pain and was not associated with an increase in opiate use at any time during the 28-day treatment period at any dose. NKTR-118 was also not associated with opiate withdrawal as assessed by a change in the Clinical Opiate Withdrawal Scale. The most frequent side effects observed in the study that led to discontinuation of medication were diarrhea, nausea and abdominal cramping. These side effects were most frequent in the 50 mg dose group.

Final patients in the 50 mg dose cohort are completing treatment. Final results from the Phase 2 study are expected to be presented at scientific and medical conferences in 2009. The results of the Phase 2 study will enable Nektar to evaluate the

drug in Phase 3 pivotal trials in order to submit a New Drug Application (NDA) to the Food and Drug Administration (FDA).

#### About NKTR-118

Oral NKTR-118 combines Nektar's advanced small molecule polymer conjugate technology platform with naloxol, a derivative of the opioid-antagonist drug, naloxone. Nektar's technology has been shown to increase oral bioavailability and reduce penetration of oral NKTR-118 across the blood-brain barrier, an important potential advance for this and possibly many other small molecule therapies.

The antagonist NKTR-118 targets mu-opioid receptors within the enteric nervous system, which mediate OBD, a symptom complex resulting from opioid use that encompasses constipation, bloating, abdominal cramping, and gastroesophageal reflux. Constipation is the hallmark of this syndrome and is generally its most prominent component. In patients who take opiates chronically for pain management, anywhere from 45-90% of patients will develop debilitating constipation associated with other symptoms of opiate-induced bowel dysfunction as a result of the opiate binding to the mu-opioid receptor in the gut(1).

According to IMS Health, about 230 million prescriptions were written for opioids in 2007 in the United States alone. Currently, there are no oral drugs approved that are indicated to treat OIC. OBD and OIC can significantly impact quality of life and increase healthcare utilization.

1. Panchal SJ, Muller-Schwefe P, Wurzelmann JI. Opioid-induced bowel dysfunction: prevalence, pathophysiology and burden. *Int J Clin Pract.* 2007;61(7):1181-1187.

Conference Call to be Held at 2 PM Pacific time, Monday, March 2, 2009

Howard Robin, president and chief executive officer, and John Nicholson, chief financial officer, will host a conference call to discuss today's announcement and the company's fourth quarter and year-end 2008 financial results.

The call will be held today, March 2, 2009, at 5:00 p.m. Eastern Time (ET)/2:00 p.m. Pacific Time (PT). A live audio-only Webcast of the conference call can be accessed through a link that is posted on the home page and Investor Relations section of the Nektar website: <http://www.nektar.com>.

To access the conference call by telephone, please follow these instructions:

Dial: 800.561.2718 (U.S.); 617.614.3525 (international)  
Participant Passcode: 32041145 (Howard Robin is the host)

An audio replay will also be available shortly after the call and will remain so through March 16, 2009.

To access the replay, follow these instructions:  
Dial: 888-286-8010 (U.S.); 617-801-6888 (international)  
Participant Passcode: 44161634

#### About Nektar

Nektar Therapeutics is a biopharmaceutical company developing novel therapeutics based on its PEGylation and advanced polymer conjugation technology platforms. Nektar's technology and drug development expertise have enabled nine approved products for partners, which include leading biopharmaceutical companies. Nektar is also developing a robust pipeline of its own potentially high-value therapeutics that addresses unmet medical needs by leveraging and expanding its technology platforms to improve and enable molecules.

This press release contains forward-looking statements that reflect the company's current views regarding the potential of the company's technology platforms and the potential of NKTR-118 and the results of the Phase 2 study for that drug candidate. These forward-looking statements involve risks and uncertainties, including but not limited to: (i) NKTR-118 is in mid-stage clinical development and the risk of failure remains high and failure can unexpectedly occur at any stage prior to regulatory approval due to efficacy, safety or other factors; (ii) the timing or success of the commencement or end of clinical trials and commercial launch of new drugs may be delayed or unsuccessful due to regulatory delays, clinical trial design, slower than anticipated patient enrollment, drug manufacturing challenges, changing standards of care, clinical outcomes, or delay or failure in obtaining regulatory approval in one or more important markets; (iii) the company's patent applications for its

proprietary or partner product candidates may not issue, patents that have issued may not be enforceable, or intellectual property licenses from third parties may be required in the future; (iv) the outcome of any existing or future intellectual property or other litigation related to the company's proprietary product candidates; and (v) the preliminary Phase 2 results for NKTR-118 described in this press release remain subject to completion of final data gathering and analysis and therefore this data remains subject to change. Other important risks and uncertainties are detailed in the company's reports and other filings with the Securities and Exchange Commission, including its most recent Quarterly Report on Form 10-Q and Annual Report on Form 10-K.

Actual results could differ materially from the forward-looking statements contained in this press release. The company undertakes no obligation to update forward-looking statements, whether as a result of new information, future events or otherwise. For more information on Nektar Therapeutics, please visit <http://www.nektar.com>.

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