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Positive Results for NKTR-118 (oral PEG-naloxol) Presented at American Academy of Pain Management Meeting

NKTR-118 Currently in Phase 1 Clinical Development for the Treatment of Opioid Bowel Dysfunction

SAN CARLOS, Calif., Sept 26, 2007 /PRNewswire-FirstCall via COMTEX News Network/ -- Nektar Therapeutics (Nasdaq: NKTR) presented positive results this week from Phase 1 and preclinical studies of NKTR-118 (oral PEG-naloxol) at the American Academy of Pain Management (AAPM) meeting in Las Vegas, Nevada. NKTR-118 is Nektar's proprietary oral therapy being studied for its potential to treat patients suffering from opioid-bowel dysfunction (OBD), including opioid-induced constipation (OIC).

Data from a single-dose, proof-of-principle Phase 1 trial on NKTR-118 demonstrate that the drug antagonized the morphine-induced delay in gastrointestinal (GI) transit time without reversing the central opioid effect as measured by pupillometry. Further, the study shows that the drug was well-tolerated at single, oral doses up to 1,000 mg. Data from this study were also presented earlier this month at the American College of Clinical Pharmacology meeting in San Francisco, California.

In preclinical studies presented at AAPM this week, oral NKTR-118 improved GI transit time in an animal model of morphine-induced constipation, while maintaining a substantial analgesic effect. In addition, NKTR-118 demonstrated significantly lower brain permeation than naloxone.

"These positive study results for NKTR-118 show that the drug offers potential for treating opioid-induced constipation, a serious and debilitating side effect of opioid therapy," said Tim Riley, Ph.D. Vice President of PEGylation Research at Nektar. "This application of Nektar's PEGylation technology to reduce blood-brain barrier penetration of a small molecule drug is ground-breaking. Going forward, we will leverage the ability to use PEGylation technology to manage penetration of the blood-brain barrier with additional, innovative CNS product opportunities."

Phase 1 Clinical Study Design and Results

This single-dose, double-blind, placebo-controlled study was conducted to evaluate the safety, tolerability, pharmacokinetic, and pharmacodynamic profile of NKTR-118 in healthy male subjects. The trial measured the morphine-induced delay in GI transit time, a peripheral effect, using the lactulose hydrogen GI motility test. Pupillometry, a measurement of the diameter of the pupil of the eye, was used to monitor antagonism of morphine-induced pupil constriction, a central nervous system (CNS) effect. Escalating single oral doses of NKTR-118 up to 1,000 mg were studied. A total of 48 subjects received active NKTR-118 as compared to placebo.

Single oral doses of NKTR-118 antagonized morphine-induced delay in GI transit time demonstrating the potential of the drug to relieve constipation. Further, no diminution of morphine-induced construction of the pupil, a CNS effect, was observed at single oral doses of NKTR-118 of 125 mg or less. NKTR-118 was well-tolerated at single doses up to 1,000 mg. Further, NKTR-118 was rapidly absorbed with dose-proportional pharmacokinetics over the 8-1,000 mg dose range.

Preclinical Results for NKTR-118

Preclinical studies conducted in animals investigated the permeation rate of NKTR-118 administered as compared to naloxone, antipyrine (a high brain permeation standard) and atenolol (a low brain permeation standard with no appreciable blood brain barrier penetration). NKTR-118 showed brain permeation similar to atenolol. PEGylation of naloxol greatly reduced, by 15-fold, the permeation of the drug into the brain, as compared to naloxone.

Oral NKTR-118, administered at a dose of 30 mg/kg, demonstrated the ability to improve GI transit time in an animal model of morphine-induced constipation, while maintaining substantial central analgesic effect. In addition, orally-administered NKTR-118 had a favorable safety and pharmacokinetic profile in an animal model.

About NKTR-118

NKTR-118 is an oral drug that combines Nektar's advanced small molecule PEGylation technology platform with naloxol, a

derivative of the opioid-antagonist drug, naloxone. In preclinical studies, Nektar's PEGylation technology has been shown to prevent oral NKTR-118 from crossing 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. NKTR-118 is currently in a second Phase 1 trial to evaluate the safety and tolerability of repeated dose administration.

According to IMS Health, more than 200 million prescriptions were written for opioids in 2006 in the United States, alone. Many studies indicate that a high percentage of patients receiving opioids are likely to experience significant constipation and other symptoms of OBD. Currently, there are no specific drugs approved that are indicated to treat OBD or OIC. Stool softeners or laxatives may be ineffective for many patients with OIC and they are often associated with side effects like diarrhea and cramping.

Data Presentations for NKTR-118

The NKTR-118 poster presentations from this week's American Academy of Pain Management's Annual Clinical Meeting in Las Vegas, Nevada from September 27-30, 2007 can be found on Nektar's website at http://www.nektar.com/wt/page/nktr118_media:

Poster #27: "Clinical Investigation of NKTR-118 as a Selective Oral Peripheral Opioid Antagonist"

Poster #28: "NKTR-118 (oral PEG-naloxol), a PEGylated Derivative of Naloxone; Demonstration of Selective Peripheral Opioid Antagonism After Oral Administration in Preclinical Models"

Nektar PEGylation Platform

Nektar PEGylation technology can enhance the properties of therapeutic agents by increasing drug circulation time in the bloodstream, decreasing immunogenicity and dosing frequency, increasing bioavailability and improving drug solubility and stability. It can also be used to modify pharmaceutical agents to preferentially target certain systems within the body. It is a technique in which non-toxic polyethylene glycol (PEG) polymers are attached to therapeutic agents, and it is applicable to most major drug classes, including proteins, peptides, antibody fragments, small molecules, and other drugs.

Nektar PEGylation technology is also used in eight additional approved partnered products in the U.S. or Europe today, including Roche's PEGASYS(R) for hepatitis C and Amgen's Neulasta(R) for neutropenia.

About Nektar

Nektar Therapeutics is a biopharmaceutical company that develops and enables differentiated therapeutics with its industry-leading PEGylation and pulmonary drug development technology platforms. Nektar PEGylation and pulmonary technology, expertise, and manufacturing capabilities have enabled nine approved products for partners, which include the world's leading pharmaceutical and biotechnology companies. Nektar is also developing its own product candidates by applying its PEGylation and pulmonary technology platforms to existing medicines with the objective to enhance performance, such as improving efficacy, safety and compliance.

This press release contains forward-looking statements regarding the potential of the company's PEGylation technology platform and NKTR-118. These forward-looking statements involve important risks and uncertainties, including but not limited to: (i) clinical trials for NKTR-118 are long, expensive and uncertain processes, (ii) because the NKTR-118 product development program is in the early phases of clinical development, the risk of failure is high and can occur at any stage of development, (iii) the company may fail to obtain regulatory approval of NKTR-118, (iv) potential competition from approved drugs or drugs under development that may be safe and effective for the same indication as that targeted by NKTR-118, and (v) the company's patent applications for NKTR-118 may fail to issue; patents that have issued may not be enforceable; or unanticipated intellectual property licenses from third parties may be required in the future. Other important risks and uncertainties are detailed in the company's reports and other filings with the SEC; including its most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q. 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.

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