

September 10, 2007

Nektar Presents Positive Results from Phase 1 Clinical Trial of NKTR-118 (oral PEG-naloxol) at American College of Clinical Pharmacology Meeting

Results Demonstrate that NKTR-118 Shows Promise for the Treatment of Opioid Bowel Dysfunction

SAN CARLOS, Calif., Sept 10, 2007 /PRNewswire-FirstCall via COMTEX News Network/ --

Nektar Therapeutics (Nasdaq: NKTR) presented results today at the American College of Clinical Pharmacology conference in San Francisco, California from a Phase 1 trial of NKTR-118 (oral PEG-naloxol). NKTR-118 is Nektar's proprietary investigational treatment for opioid bowel dysfunction (OBD), including opioid-induced constipation (OIC). Today's presentation highlights the safety profile and activity of NKTR-118 in healthy male subjects.

"This proof-of-principle study in combination with our preclinical work shows that our proprietary PEGylation technology can prevent an oral drug from penetrating the blood-brain barrier, opening the door for future applications of our technology with other small molecules," said Hoyoung Huh, M.D., Ph.D., Nektar's Chief Operating Officer and Head of the PEGylation Business Unit. "These findings for NKTR-118 merit further clinical evaluation of the drug. We look forward to unveiling the results of our multi-dose Phase 1 safety trial on NKTR-118 later this year and advancing this important program into Phase 2 clinical development."

The NKTR-118 Phase 1 results demonstrate that single oral doses of NKTR-118 reverse the effects of morphine on gastrointestinal transit time at doses that do not reverse a central opiate effect as measured by pupillometry.

Phase 1 Clinical Study Design

This single-dose, double-blind, placebo-controlled study was conducted to evaluate safety, tolerability, pharmacokinetic, and pharmacodynamic profile of NKTR-118 in healthy male subjects. The trial measured the morphine-induced delay in gastrointestinal transit time, a peripheral effect, using the lactulose hydrogen gastrointestinal 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.

Phase 1 Clinical Study Results

Single oral doses of NKTR-118 antagonized morphine-induced delay in gastrointestinal transit time demonstrating the potential of the drug to relieve constipation. Further, no dimunition of morphine-induced miosis, 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.

"Debilitating constipation is the most frequent side effect associated with opioid therapy. It can have a serious negative impact on the quality of life for patients," said Russell K. Portenoy, M.D., chairman of the Department of Pain Medicine and Palliative Care at Beth Israel Medical Center and Professor of Neurology and Anesthesiology at the Albert Einstein College of Medicine in New York. "In some cases, it can even be treatment-limiting in managing their pain. Current therapeutic options for managing this side-effect are not optimal and better treatments are needed."

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.

Additional Data Presentations for NKTR-118

Another peer-reviewed presentation of this Phase 1 study, and also a preclinical study for NKTR-118, are scheduled to be presented at the American Academy of Pain Management's Annual Clinical Meeting in Las Vegas, Nevada from September 27-30, 2007.

More information about the 2007 Annual Clinical Meeting of the American Academy of Pain Management is available at: <u>http://www.aapainmanage.org/conference/Conference.php</u>

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 industryleading 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. No information regarding or presented at the scientific meetings referred to above (or contained at the Internet links provided herein) is intended to be incorporated by reference in this press release.

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