Phase 2 Data From Oral NKTR-118 Presented at American College of Gastroenterology in San Diego

New Approach to Treat Opioid-Induced Constipation

SAN DIEGO, Oct 27, 2009 /PRNewswire-FirstCall via COMTEX News Network/ -- Data from a phase II study demonstrated that oral NKTR-118 improved lower gastrointestinal dysfunction by increasing the frequency of bowel movements in patients with opioid-induced constipation, while simultaneously preserving opioid-mediated analgesia. NKTR-118, an oral peripherally-acting opioid antagonist, is an investigational product candidate in clinical development for the treatment of opioid-induced constipation.

(Logo: *http://www.newscom.com/cgi-bin/prnh/20091027/PH99766LOGO*)

In the phase II double blind, randomized, placebo-controlled study of 208 patients with opioid-induced constipation, NKTR-118 achieved the primary endpoint of change from baseline in spontaneous bowel movements (SBMs). Patients receiving either 25 mg or 50 mg of oral NKTR-118 once daily had a significantly greater change from baseline in SBMs during the first week of treatment than patients receiving placebo. The mean change from baseline in SBMs per week for patients receiving 25 mg NKTR-118 was 3.6 versus 1.9 in the placebo group (p= 0.002). Patients receiving 50 mg NKTR-118 had a mean change from baseline in SBMs per week of 4.4 versus 1.9 in the placebo group (p=0.0001). The increase from baseline in SBMs versus placebo averaged over the four-week treatment period was significant for both the 25 mg (p=0.002) and 50 mg (p<0.0001) dose groups. Results for the 5 mg dose of NKTR-118 were not significant.

The study also showed that there was a statistically significant difference in median time to first SBM for patients in the 25 mg and 50 mg dose cohorts as compared to placebo. Median time to first SBM for patients in the 25 mg dose cohort was 6.6 hours as compared to placebo which was 48.6 hours (p=0.001), and for patients in the 50 mg dose cohort, median time to first SBM was 2.9 hours as compared to placebo, which was 44.9 hours (p<0.002). Results for the 5 mg dose of NKTR-118 were not significant.

"Patients who take opioids are at risk of experiencing the painful and potentially serious side effect of opioid-induced constipation (OIC) -- which can require patients to seek remedies only available in a hospital or in-office setting," said Dr. Lynn Webster, Medical Director of Lifetree Clinical Research and lead clinical investigator of the phase II trial. "The results of the NKTR-118 phase II trial presented today indicate that, if approved, this product may have the potential to offer patients suffering from OIC a simple and non-invasive oral treatment that may improve their gastrointestinal function."

The study also showed there was no apparent reversal of opioid-mediated analgesia with any of the NKTR-118 dose groups, as measured by no change in Numeric Rating Scale (NRS) pain scores and no increase in mean daily opiate use.

The most commonly reported side effects from this Phase II study of NKTR-118 were dose dependent gastrointestinal-related effects. The majority of side effects for both the 5 and 25 mg dose cohorts were graded as mild by the investigators. Side effects included diarrhea (13% at 25 mg and 31% at 50 mg, versus 4% and 5% for the placebo arms), nausea (13% for 25 mg and 20% for 50 mg, versus 19% and 8% for the placebo arms) and abdominal pain (30% for 25 mg and 17% for 50 mg, versus 7% and 0% for the placebo arm). No treatment-related serious adverse events (SAE) for the 5 or 25 mg cohorts were observed. Only one patient experienced an SAE of hospitalization due to abdominal cramping in the 50 mg cohort.

These data from the Phase II clinical trial of NKTR-118 were presented today during the oral plenary session of the American College of Gastroenterology (ACG) 2009 Annual Clinical Meeting.

About NKTR-118

On September 21, 2009, AstraZeneca and Nektar Therapeutics announced that they entered into an exclusive worldwide license agreement for NKTR-118 and NKTR-119.

NKTR-118 is an investigational drug candidate that combines Nektar's advanced small molecule polymer conjugate technology platform with naloxol, a derivative of the opioid-antagonist drug, naloxone.

Top line results of the phase II study were presented at the American Academy of Pain Management in early October, 2009.

About Opioid-Induced Constipation

It is estimated that for those patients who take opiates chronically for pain management, anywhere from 40-90% of such patients will develop constipation. Less than half of those patients find effective relief from current treatment options that include prescription and over-the-counter laxatives and stool softeners. These symptoms of bowel dysfunction are a result of the drug binding to the mu-opioid receptor in the gut (1). Opioid-induced bowel dysfunction encompasses symptoms such as constipation, bloating, abdominal cramping, and gastroesophageal reflux. Constipation is the hallmark of this syndrome and is generally its most prominent component.

According to IMS Health, about 230 million prescriptions were written for opioids in 2007 in the United States alone. This is estimated to represent about 65-75% of the worldwide opioid market. Currently, there are no oral drugs approved that are indicated to treat opioid-induced constipation. Opioid bowel dysfunction and opioid-induced constipation can significantly impact quality of life and increase healthcare utilization.

About AstraZeneca

AstraZeneca is a major international healthcare business engaged in the research, development, manufacturing and marketing of meaningful prescription medicines and supplier for healthcare services. AstraZeneca is one of the world's leading pharmaceutical companies with healthcare sales of US$ 31.6 billion and is a leader in gastrointestinal, cardiovascular, neuroscience, respiratory, oncology and infectious disease medicines. For more information about AstraZeneca, please visit: *www.astrazeneca.com*.

About Nektar

Nektar Therapeutics (Nasdaq: NKTR) 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 in the U.S. or Europe for partners, which include leading biopharmaceutical companies, including UCB's Cimzia(R), Roche's PEGASYS(R) for hepatitis C and Amgen's Neulasta(R) for neutropenia. Nektar has created a robust pipeline of potentially high-value therapeutics to address unmet medical needs by leveraging and expanding its technology platforms to improve and enable molecules. Nektar is currently conducting clinical and preclinical programs in oncology, pain and other therapeutic areas. NKTR-102, PEGylated irinotecan, is currently in Phase 2 clinical studies in ovarian, breast and colorectal cancer. NKTR-105, PEGylated docetaxel, is currently in a Phase 1 clinical study in patients with refractory solid tumors.

Nektar is headquartered in San Carlos, California, with additional R&D 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*.

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.

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