



## **Alkermes Announces Priority Review by FDA for VIVITROL® for Opioid Dependence**

May 25, 2010

**-- FDA Designation Underscores Need for New Treatment Options --**

**-- Potential First and Only Non-Narcotic, Non-Addictive Medication for Opioid Dependence Available in a Once-Monthly Formulation --**

WALTHAM, Mass., May 25, 2010 (BUSINESS WIRE) --Alkermes, Inc. (NASDAQ: ALKS) today announced that the supplemental New Drug Application (sNDA) for VIVITROL® (naltrexone for extended-release injectable suspension) for opioid dependence has been designated a priority review by the U.S. Food and Drug Administration (FDA). The designation is assigned to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists and accelerates the FDA's target review timeline from ten to six months. The FDA has issued an action date for the sNDA of October 12, 2010 under the Prescription Drug User Fee Act (PDUFA). If approved for opioid dependence, VIVITROL would be the first and only non-narcotic, non-addictive medication for the treatment of opioid dependence available in a once-monthly formulation.

"We are very encouraged by the FDA's decision to grant priority review for VIVITROL for opioid dependence. The designation further supports the existence of a high unmet need for alternative therapies for patients with this chronic disease," said Richard Pops, Chief Executive Officer at Alkermes. "Developing VIVITROL for this indication reinforces our commitment to patients and treatment providers in this field; we remain dedicated to bringing future addiction treatments to this population."

The sNDA was submitted after completion of a six-month, multi-center, randomized phase 3 clinical trial for VIVITROL for opioid dependence which met its primary efficacy endpoint and all secondary efficacy endpoints. Data from the intent-to-treat analysis showed that patients treated once-monthly with VIVITROL demonstrated statistically significant higher rates of opioid-free urine screens, compared to patients treated with placebo ( $p < 0.0002$ ). Furthermore, the median patient taking VIVITROL had 90% opioid-free urine screens during the evaluation phase of the study and patients treated with VIVITROL demonstrated a significant reduction in opioid craving compared to patients treated with placebo as measured by a visual analog scale. VIVITROL was generally well tolerated in the study and no patients on VIVITROL discontinued the study due to adverse events. The most common adverse events experienced by patients receiving VIVITROL during the study were nasopharyngitis and insomnia.

### **About Opioid Dependence**

A chronic brain disease, opioid dependence is characterized by cognitive, behavioral and physiological symptoms in which an individual continues to use opioids despite significant harm to himself and others.<sup>1</sup> The misuse of opioids can create euphoria of such intensity that it reinforces drug taking behavior and may lead to opioid dependence or addiction.<sup>2</sup> In addition to the use of heroin, an illegal opioid drug, opioid abuse and addiction includes the non-medical use of opioid analgesics, including prescription pain relievers, and represents a growing public health problem in the U.S. According to the 2008 U.S. National Survey on Drug Use and Health, an estimated 1.3 million people aged 18 or older were dependent on pain relievers or heroin.<sup>3</sup> The overall cost of prescription opioid abuse in the U.S. has been estimated at \$9.6 billion, including health care, criminal justice and workplace costs,<sup>4</sup> and the overall cost of heroin addiction in the U.S. has been estimated to be approximately \$22 billion, including productivity losses, criminal activity, healthcare and social welfare costs.<sup>5</sup>

### **About VIVITROL**

VIVITROL is the first and only once-monthly, extended-release injectable medication for the treatment of alcohol dependence and was approved by the FDA in April 2006. The proprietary Medisorb® drug delivery technology in VIVITROL enables the medication to be gradually released into the body at a controlled rate over a one-month time period. For a copy of the VIVITROL full prescribing information, including boxed warning, please visit <http://www.vivitrol.com/> or call 1-800-VIVITROL (1-800-848-4876).

### **VIVITROL Important Safety Information in Alcohol Dependence**

VIVITROL is contraindicated in patients receiving opioid analgesics or with current physiologic opioid dependence, patients in acute opiate withdrawal, any individual who has failed the naloxone challenge test or has a positive urine screen for opioids, or in patients who have previously exhibited hypersensitivity to naltrexone PLG, carboxymethylcellulose or any other components of the diluent.

VIVITROL patients must be opioid free for a minimum of 7-10 days before treatment. Attempts to overcome opioid blockade due to VIVITROL may result in a fatal overdose. In prior opioid users, use of opioids after discontinuing VIVITROL may result in a fatal overdose because patients may be more sensitive to lower doses of opioids. Patients requiring reversal of the VIVITROL blockade for pain management should be monitored by appropriately trained personnel in a setting equipped for cardiopulmonary resuscitation.

**Naltrexone has the capacity to cause hepatocellular injury when given in excessive doses.**

**Naltrexone is contraindicated in acute hepatitis or liver failure, and its use in patients with active liver disease must be carefully considered in light of its hepatotoxic effects.**

**The margin of separation between the apparently safe dose of naltrexone and the dose causing hepatic injury appears to be only five-fold or less. VIVITROL does not appear to be a hepatotoxin at the recommended doses.**

**Patients should be warned of the risk of hepatic injury and advised to seek medical attention if they experience symptoms of acute**

**hepatitis. Use of VIVITROL should be discontinued in the event of symptoms and/or signs of acute hepatitis.**

VIVITROL is administered as a gluteal intramuscular injection. Inadvertent subcutaneous injection of VIVITROL may increase the likelihood of severe injection site reactions. VIVITROL must be injected using the customized needle provided in the carton. Because needle length may not be adequate due to body habitus, each patient should be assessed prior to each injection to assure that needle length is adequate for intramuscular administration. VIVITROL injection site reactions may be followed by pain, tenderness, induration, swelling, erythema, bruising or pruritus; however, in some cases injection site reactions may be very severe. Injection site reactions not improving may require prompt medical attention, including in some cases surgical intervention.

Consider the diagnosis of eosinophilic pneumonia if patients develop progressive dyspnea and hypoxemia. In an emergency situation in patients receiving VIVITROL, suggestions for pain management include regional analgesia or use of non-opioid analgesics. Alcohol dependent patients, including those taking VIVITROL, should be monitored for the development of depression or suicidal thoughts. Caution is recommended in administering VIVITROL to patients with moderate to severe renal impairment.

The most common adverse events associated with VIVITROL in clinical trials were nausea, vomiting, headache, dizziness, asthenic conditions and injection site reactions.

**About Alkermes**

Alkermes, Inc. is a fully integrated biotechnology company committed to developing innovative medicines to improve patients' lives. Alkermes developed, manufactures and commercializes VIVITROL® for alcohol dependence and manufactures RISPERDAL® CONSTA® for schizophrenia and bipolar I disorder. Alkermes' robust pipeline includes extended-release injectable and oral products for the treatment of prevalent, chronic diseases, such as central nervous system disorders, addiction and diabetes. Headquartered in Waltham, Massachusetts, Alkermes has a research facility in Massachusetts and a commercial manufacturing facility in Ohio.

Certain statements set forth above may constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, the company's expectations and timeline for regulatory action by the FDA relating to the sNDA submission for VIVITROL for the treatment of opioid dependence, and the company's expectations concerning the potential therapeutic and commercial value of VIVITROL for the treatment of opioid dependence. Although the company believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and the company's business is subject to significant risk and uncertainties and there can be no assurance that its actual results will not differ materially from its expectations. These risks and uncertainties include, among others: whether VIVITROL will be approved by regulatory authorities for the treatment of opioid dependence by October 12, 2010 or at all; and, if approved, whether VIVITROL will be commercialized successfully. For further information with respect to factors that could cause the company's actual results to differ materially from expectations, reference is made to the reports the company filed with the Securities and Exchange Commission under the Securities Exchange Act of 1934, as amended. The forward-looking statements made in this release are made only as of the date hereof and the company disclaims any intention or responsibility for updating predictions or financial expectations contained in this release.

VIVITROL® and Medisorb® are trademarks of Alkermes, Inc.; RISPERDAL® CONSTA® is a trademark of Janssen-Cilag group of companies.

<sup>1</sup>DSM-IV-TR, American Psychiatric Association

<sup>2</sup>Tomkins DM, Sellers EM. Addiction and the brain: the role of neurotransmitters in the cause and treatment of drug dependence. *CMAJ*. 2001 March; 164 (6)

<sup>3</sup>SAMHSA, Office of Applied Studies, National Survey on Drug Use and Health, 2008. Accessed from <http://www.oas.samhsa.gov/NSDUH/2k8NSDUH/tabs/Sect5peTabs1to56.htm#Tab5.14A> on March 11, 2010.

<sup>4</sup>Birnbaum HG, White AG, Reynolds JL, Greenberg PE, Zhang M, Vallow S, Schein JR, Katz NP. Estimated costs of prescription opioid analgesic abuse in the United States in 2001: A societal perspective. *Clin J Pain*. 2006 Oct;22(8):667-76.

<sup>5</sup>Mark TL, Woody GE, Juday T, Kleber HD. The economic costs of heroin addiction in the United States. *Drug Alcohol Depend*. 2001;61:195-206.



SOURCE: Alkermes

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