Alkermes Announces Statistically Significant Reduction in Heavy Drinking in Alcohol Dependent Patients in Phase III Clinical Trial Of Vivitrex

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Statistically Significant Reduction in Heavy Drinking Shown in Male Patients; No Significant Effect Seen in Female Patients

CAMBRIDGE, Mass., Dec 8, 2003 (BUSINESS WIRE) -- Alkermes, Inc. (Nasdaq: ALKS) today announced preliminary results from its Phase III study of Vivitrex(R) (naltrexone for injectable suspension) in a total of 624 male and female patients with alcohol dependence. Patients received psychosocial therapy and once-monthly injections of Vivitrex 380 mg, Vivitrex 190 mg, or placebo for a six- month period. The primary endpoint of the study was the rate of heavy drinking over the period. In the overall study population, patients treated with Vivitrex 380 mg experienced approximately a 25% reduction in the rate of heavy drinking relative to placebo, which was statistically significant (p less than 0.03). Gender played a dominant role in the study results. Two thirds of the patients enrolled in the study were male, which is representative of the alcohol dependent population.(1) Male patients treated with Vivitrex 380 mg showed approximately a 48% reduction in the rate of heavy drinking relative to placebo, which was highly statistically significant (p less than 0.0001). Female patients treated with Vivitrex 380 mg showed no significant difference from placebo.

In the overall study population, patients treated with Vivitrex 190 mg experienced approximately a 17% reduction in the rate of heavy drinking relative to placebo with a trend toward statistical significance (p less than 0.10). Again, gender played a dominant role in the study results at the 190 mg dose. Male patients treated with Vivitrex 190 mg showed approximately a 25% reduction in the rate of heavy drinking relative to placebo, which was statistically significant (p less than 0.03), suggesting a clear dose response relationship in the male treatment groups in this study. Female patients treated with Vivitrex 190 mg showed no significant difference from placebo.

The study was prospectively designed to control for gender differences and other key factors that were believed to be predictive of drinking behavior. The study subjects were randomized and balanced across each of the 24 treatment centers and within treatment groups with respect to key factors, including gender. The reduction in the rate of heavy drinking observed in the overall treatment group (males and females combined) does not appear to be representative of the average treatment effect across all patients in the study because the entire effect was observed in the male treatment group.

"These data show that the long-acting formulation of Vivitrex results in meaningful clinical benefit for male alcohol-dependent patients and can significantly advance the practice of treating alcoholism," said James Garbutt, M.D., Professor of Psychiatry at University of North Carolina at Chapel Hill and a lead investigator for the Vivitrex Phase III trial. "As one of the largest studies ever conducted for alcohol pharmacotherapy, this landmark Phase III trial shows that treatment with Vivitrex resulted in a reduction in heavy drinking events and highlights the role that drug therapy can play in helping patients break the cycle of alcoholism."

"Based on the results of this successful study, Alkermes intends to move forward with our extensive development plans for Vivitrex," said Richard Pops, Chief Executive Officer of Alkermes. "These Phase III results represent an important milestone in reaching our ultimate goal of developing Vivitrex into an innovative product that offers the potential to improve outcomes for alcohol-dependent patients. We look forward to sharing these data with the U.S. Food and Drug Administration as we proceed on our path towards submission of a New Drug Application."

Alkermes will complete the full analysis of the trial data, including impact of gender. The company plans to submit the data for publication in a peer-reviewed journal.

"The data from this Phase III trial with Vivitrex indicates a potentially significant development in treating people with alcohol problems," said Richard Rosenthal, M.D., immediate past president of the American Academy of Addiction Psychiatry (AAAP). Kathleen Brady, M.D., Ph.D., president of AAAP adds "A new contribution to our tools to treat the major public health problem of alcohol abuse and dependence is welcome."

Vivitrex is a proprietary long-acting formulation of naltrexone based on Alkermes' Medisorb(R) injectable, extended-release technology. By providing an extended-release dose administered once monthly, rather than daily, Vivitrex is designed to facilitate compliance with treatment regimens and improve outcomes for alcohol-dependent patients.

Phase III Trial Design

The Phase III clinical trial, a randomized, placebo-controlled, double-blind study, was designed to evaluate the safety and efficacy of Vivitrex in alcohol-dependent patients during a six-month period. The primary endpoint was the event rate of heavy drinking over the six-month period. A heavy drinking event is defined as five or more drinks per day for a man and four or more drinks per day for a woman. The multi-center study enrolled 624 patients, and randomized patients to receive, in addition to psychosocial therapy, Vivitrex 190 mg, Vivitrex 380 mg, or placebo. Vivitrex was administered by injection in a clinical setting once per month for six months. At designated intervals during the study, patients returned to the clinic for study evaluations and psychosocial therapy. Following the six-month treatment period, patients were eligible to enter an extension study designed to collect long-term safety data for an additional 12 months.

Adverse Events

Vivitrex was generally well tolerated by patients in the Phase III trial. In patients receiving Vivitrex, the three most common adverse events reported during the six-month study were nausea, headache, and fatigue. Injection site reactions were more commonly seen in the treatment groups versus the placebo group. Less than 2% of the patients discontinued in the trial due to injection site reaction.

Challenges of Treating Alcohol Dependency

The treatment approach for alcohol dependence includes detoxification, psychosocial therapy, and, more recently, pharmacotherapy. As a pharmacotherapy, naltrexone has been shown to reduce relapse to heavy drinking in alcohol-dependent patients, decrease the number of drinks consumed when relapse does occur, and promote abstinence.(2) Naltrexone is a potent opioid receptor antagonist and has been reported to reduce both the craving and the reinforcing euphoric qualities of alcohol.(3)

Although naltrexone in oral form has been shown to be effective as a maintenance agent in the treatment of alcohol dependence, a major limitation of its utility can be poor adherence to therapy. In the treatment of alcohol dependence, oral naltrexone is indicated for daily administration. In a clinical study led by researchers at the University of Pennsylvania Medical Center comparing oral naltrexone to placebo, it was reported that greater than 40% of patients treated with naltrexone were noncompliant with the daily oral regimen.(4) That study also reported that, for medication-noncompliant patients, relapse to clinically significant drinking was similar to placebo treated patients and significantly higher than the rate observed with medication-compliant patients.

Prevalence of Alcohol Dependency

In the U.S., it is estimated that 18 million people (age 18 years and older) suffer from alcohol dependency or meet diagnostic criteria for alcohol abuse disorder.(5) There are 2.3 million alcohol-dependent persons who seek treatment for their condition each year.(6) More than half of all adult Americans have direct family experience with alcohol problems. Alcohol abuse is the cause of more than 100,000 deaths in America each year.(7) According to a study by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA), in 1998, alcohol dependence and abuse cost Americans - private citizens, corporations, local and state governments and the federal government - a total of $184.6 billion.(8)

About Vivitrex

Vivitrex is a long-acting, injectable form of naltrexone that was developed utilizing Alkermes' proprietary Medisorb drug-delivery technology. Using the Medisorb technology, naltrexone is encapsulated in microspheres made of a biodegradable polymer that dissolves slowly and releases drug at a controlled rate following intramuscular injection. Upon receipt of regulatory approval, Alkermes plans to commercialize Vivitrex using a specialty sales force to call on addiction specialists and substance abuse centers. Alkermes is in discussions with potential partners about broader commercialization of the product in the U.S. and Europe, and for other indications such as opiate dependence. The Vivitrex clinical development program has been funded in part with a Small Business Innovation Research Program grant from the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

Alkermes is developing products using the Medisorb technology on its own and in partnership with pharmaceutical and biotechnology companies. Risperdal Consta(R), which also uses the Medisorb technology, was developed in collaboration with its partner, Janssen-Cilag, S.A., a wholly-owned subsidiary of Johnson & Johnson. Approved for sale in more than 40 countries, including the U.S., Risperdal Consta is the only long-acting injectable atypical antipsychotic available.

About Alkermes

Alkermes, Inc. is an emerging pharmaceutical company developing products based on its sophisticated drug delivery technologies to enhance therapeutic outcomes. Our areas of focus include: controlled, extended-release of injectable drugs utilizing our ProLease(R) and Medisorb(R) delivery systems and the development of inhaled pharmaceutical products based on our proprietary AIR(R) pulmonary delivery system. Our business strategy is twofold. We partner our proprietary technology systems and drug delivery expertise with many of the world's finest pharmaceutical companies and also develop novel, proprietary drug candidates for our own account. In addition to our Cambridge, Massachusetts headquarters and research and manufacturing facilities, we operate research and manufacturing facilities in Ohio.

Certain statements set forth above may constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Although we believe that such statements are based on reasonable assumptions within the bounds of our knowledge of our business and operations, various factors may cause our actual results to differ materially from our expectations. These include whether and when a new drug application will be submitted to the FDA and whether such submission will be accepted; whether the FDA will interpret clinical and preclinical data, if and when such data is submitted, in a manner consistent with our interpretations of such data; whether the FDA will approve the NDA submission on a timely basis or at all; whether Vivitrex, if approved, would be accepted by the market; whether Alkermes can successfully assemble a specialty sales force and how effective such a sales force may be at marketing Vivitrex, if approved; whether we enter into any collaboration with a third party to market or fund the development and/or commercialization of Vivitrex and whether the terms of such a collaboration meet our expectations; and whether we can complete manufacturing scale up successfully and in a timely manner or manufacture Vivitrex in the quantities demanded. For further information with respect to factors that could cause actual results to differ from expectations, reference is made to the reports filed by us with the Securities and Exchange Commission under the Securities Exchange Act of 1934, as amended.

Note: Alkermes will host a conference call at 8:30am EST on Monday, December 8, 2003. The conference call may be accessed by dialing 1-888-792-1079 for domestic callers and 1-703-871-3092 for international callers. The conference call ID number is 343576. Additionally, the call will be webcast on the investor relations section of Alkermes' website at www.alkermes.com and archived on the site until Monday, December 15, 2003 at 5:00pm EST.

A replay of the conference call will be available from 11:30am EST on December 8, 2003 through 12:00pm EST on December 10, 2003, and may be accessed by dialing 1-888-266-2081 for domestic callers and 1-703-925-2533 for international callers. The replay access code is 343576.

1. Grant, B., et al. Epidemiologic Bulletin No. 35: Prevalence of DSM-IV alcohol abuse and dependence, United States 1992. Alcohol Health & Research World 18(3):243-248, 1994. Available at: http://www.niaaa.nih.gov/databases/abdep4.htm.

2. Anton, R., Moak, D., Waid, R., Latham, P., Malcolm, R., Dias, J. (1999) Naltrexone and Cognitive Behavioral Therapy for the Treatment of Outpatient Alcoholics: Results of a Placebo-Controlled Trial. Am J Psychiatry 156(11): 1758-1763; O'Brien, C., Volpicelli, L., Volpicelli, J. (1996) Naltrexone in the Treatment of Alcoholism: A Clinical Review. Alcohol 13(1):35-9.; Volpicelli, J., Alterman, A., Hayashida, M., O'Brien, C. (1992) Naltrexone in the Treatment of Alcohol Dependence. Arch Gen Psychiatry 49: 876-880.; O'Malley, S., Jaffe, A., Chang, G., Schottenfeld, R., Meyer, R., Rounsaville, B. (1992) Naltrexone and Coping Skills Therapy for Alcohol Dependence. Arch Gen Psychiatry 49: 881-887.

3. Volpicelli, J., Alterman, A., Hayashida, M., O'Brien, C. (1992) Naltrexone in the Treatment of Alcohol Dependence. Arch Gen Psychiatry 49: 876-880.

4. Volpicelli, J. (1997) Naltrexone and Alcohol Dependence, Role of Subject Compliance, Arch Gen Psych 54: 737.

5. Grant, B., et al. Epidemiologic Bulletin No. 35: Prevalence of DSM-IV alcohol abuse and dependence, United States 1992. Alcohol Health & Research World 18(3):243-248, 1994. Available at: http://www.niaaa.nih.gov/databases/abdep4.htm.

6. Alkermes Forecasting Data 2003.

7. National Institute on Alcohol Abuse and Alcoholism, epidemiology data on file.

8. Harwood, H. The Economic Costs of Alcohol and Drug Abuse in the United States: Estimates, Update Methods, and Data. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute on Drug Abuse and National Institute on Alcohol Abuse and Alcoholism. December 2000.

SOURCE: Alkermes, Inc.

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