# FDA Approves Risperdal Consta for Treating Schizophrenia; First Long-Acting, Newer-Generation Antipsychotic Addresses Major Challenge of Schizophrenia Treatment

October 29, 2003

Alkermes Will Host an Investor Conference Call on October 30, 2003 at 8:00am EST

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 29, 2003-- Alkermes, Inc. (NASDAQ: ALKS) today announced the U.S. Food and Drug Administration (FDA) approved RISPERDAL(R) CONSTA(TM) ((risperidone) long-acting injection) for the treatment of schizophrenia. It is the first long-acting, newer-generation (atypical) antipsychotic to be approved by the FDA. The treatment uses advanced technology to deliver and maintain therapeutic medication levels in the body through just one injection every two weeks.

Risperdal Consta addresses a major challenge in the treatment of schizophrenia(1) and helps patients, clinicians and families/caregivers know with certainty that patients receive needed medication for this serious brain disorder. As many as 75 percent of patients with schizophrenia have difficulty taking their oral medication on a regular basis.(2) This may lead to worsening of symptoms.(3)

Johnson & Johnson Pharmaceutical Research & Development, L.L.C. (J&JPRD) and Alkermes developed Risperdal Consta. The product will be marketed by Janssen Pharmaceutica Products, L.P.

"By providing consistent levels of medication during a two-week period, Risperdal Consta eliminates many of the peaks and valleys that you get with medication that you have to take daily. Patients also don't have to remember to take a pill every single day, which is difficult for anyone with a chronic disease," said John Kane, M.D., Executive Director of The Zucker Hillside Hospital and professor of psychiatry at the Albert Einstein College of Medicine in New York. "It gives patients a new choice and helps them change their lives."

"We are extremely gratified that Alkermes' Medisorb(R) technology has made possible the development of Risperdal Consta, with its hope of helping the millions of persons afflicted with schizophrenia in the United States and around the world," commented Richard Pops, Chief Executive Officer of Alkermes. "We are committed to supporting Janssen's efforts to implement a rapid United States product launch."

Schizophrenia is a brain disorder that impairs a person's ability to think clearly, relate to others and distinguish between reality and imagination. It is estimated that more than 2 million Americans suffer from the condition.(4) Atypical antipsychotic medications have become the most commonly prescribed treatments for schizophrenia, and many experts believe these medications have advantages over older medications.(5),(6) However, until now, these treatments have been available only in short-acting formulations.

Clinical Trial Findings

The effectiveness of Risperdal Consta was established in a 12-week, placebo-controlled study in 400 adults with schizophrenia(7) both in inpatient and outpatient settings.(8) Efficacy was assessed using the Positive and Negative Syndrome Scale (PANSS), a common measure of the total severity of positive symptoms (psychological disturbances "added" as a result of the disorder, such as hallucinations, delusions, suspiciousness and paranoia) and negative symptoms (normal functioning the patient has "lost," resulting in lack of initiative and loss of normal enjoyment).

Patients who received Risperdal Consta experienced significantly greater improvements in both positive and negative symptoms than did those who were administered placebo:

- Forty-seven percent of patients treated with a 25 mg dosage of Risperdal Consta experienced clinical improvement compared to 17 percent of those who received placebo. Clinical improvement is defined as 20 percent or more reduction in PANSS total score.(9)

"Symptoms of schizophrenia such as hallucinations, paranoid thoughts and social withdrawal greatly interfere with a person's ability to live a normal life," said Dr. Kane. "Treatment options such as Risperdal Consta that reduce symptoms and help to ensure the continuity of therapy offer hope to patients and family members who have the same dreams for the future as everyone else."

The most common side effects experienced by patients taking Risperdal Consta during the 12-week study were headache, agitation, psychosis, insomnia, dizziness, rhinitis and pain.(10) Overall, similar proportions of patients reported adverse events in the placebo and Risperdal Consta groups (80 percent vs. 83 percent), and serious adverse events were more common in the placebo group (23.5 percent) than in the Risperdal Consta groups (13 percent in the 25 mg group and 14 percent in the 50 mg group). The incidence of spontaneously reported adverse events related to extrapyramidal symptoms (reversible movement disorders or muscle disturbances such as restlessness, tremors and muscle stiffness) in the 25 mg Risperdal Consta group was similar to placebo (10 percent vs. 13 percent). The rate of adverse events related to extrapyramidal symptoms in the 50 mg group was 24 percent.(11) Treatment was discontinued due to side effects by 12 percent of patients receiving Risperdal Consta (37/302) and 12 percent of patients (12/98) receiving placebo.(12)

As with oral Risperdal,(a) patients taking Risperdal Consta experienced low weight gain over 12 weeks (0.5 kg (1.1 lbs.) in the 25 mg group and 1.2 kg (2.6 lbs.) in the 50 mg group.)(13) In addition, patients reported that injection-site pain was low at the first injection and decreased further as the study progressed. On a 100-point rating scale, where 0 represented no pain and 100 represented unbearable pain, patients receiving the 25 mg dose reported pain at a level of nine following their sixth dose. Further, in all groups, less then 5 percent of patients experienced redness, swelling or indurations following injection.(14)

Delivery Technology

Risperdal Consta uses the proprietary Medisorb(R) drug-delivery technology developed by Cambridge, MA based Alkermes. The technology encapsulates active medication into polymer-based microspheres that are injected into the body, where they degrade slowly - gradually releasing the drug at a carefully controlled rate.

To date, Risperdal Consta has been approved in more than 40 countries around the world. In the United States, Risperdal Consta will be manufactured by Alkermes and marketed by Janssen Pharmaceutica Products, L.P. Available in 25 mg, 37.5 mg and 50 mg dose units, it is approved for the treatment of schizophrenia. In clinical trials, Risperdal Consta was generally well tolerated. However, as with all other psychotropic medications, it was associated with certain side effects. Treatment-emergent adverse events with an incidence of 5% or greater in at least one of the Risperdal(R) Consta(TM) groups (25 mg or 50 mg) and at least twice that of placebo were: somnolence, akathisia, parkinsonism, dyspepsia, constipation, dry mouth, fatigue, weight increase. As with all antipsychotic medications, prescribing should be consistent with the need to minimize the risk of tardive dyskinesia, a neurological side effect that can include repetitive twitching; if its signs and symptoms appear, discontinuation of Risperdal(R) Consta(TM) should be considered. In the integrated database of multiple-dose studies the incidence of tardive dyskinesia was 0.6% (9/1499 patients). For more information in the near future visit Risperdalconsta.com.

Johnson & Johnson Pharmaceutical Research & Development, L.L.C. (J&JPRD) and Alkermes, Inc. developed Risperdal Consta to combine the advantages of long-acting delivery with the established benefits of oral risperidone. Risperdal has been marketed in tablet form in the United States by Janssen Pharmaceutica Products, L.P., since 1994, and also is available in oral solution and quick dissolving tablet forms. Approved for marketing in more than 100 countries, Risperdal is the most widely prescribed atypical antipsychotic in the world. In a study published in the January 2002 issue of The New England Journal of Medicine, Risperdal was found to be significantly more effective in reducing the risk of relapse than haloperidol, a conventional antipsychotic long considered the "gold standard" in treatment of psychosis.(15)

About Alkermes

Alkermes is an emerging pharmaceutical company developing products based on our 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 Advanced Inhalation Research, Inc. ("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 Massachusetts headquarters, research and manufacturing facilities, we operate research and manufacturing facilities in Ohio. For more information, please visit www.alkermes.com.

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act about the commercialization of Risperdal Consta and anticipated demand following launch in the United States. These statements reflect Alkermes' current beliefs; however, as with any pharmaceutical product, there remain substantial risks and uncertainties related to launch, pricing and market acceptance. There are no guarantees regarding how quickly Janssen Pharmaceutica Products, L.P. will launch in the United States, what the demand for the product may be in the United States, nor whether Alkermes can manufacture Risperdal Consta on a commercial scale or economically. For additional information about the factors that affect Alkermes' business and product candidates, please see Alkermes' filings with the Securities and Exchange Commission under the Securities Exchange Act of 1934, including its Form 10-K filed in June 2003 and Form 10-Q filed in August 2003.

Note: Alkermes will host a conference call at 8:00am EST on October 30, 2003. The conference call may be accessed by dialing 1-800-297-9150 for domestic callers and 1-703-871-3025 for international callers. The conference call ID number is 310390. Additionally, the call will be webcast on the investor relations section of Alkermes' website at www.alkermes.com and archived on the site until Friday, November 7, 2003 at 5:00pm EST.

A replay of the conference call will be available from 11:00am EST on October 30, 2003 through 5:00pm EST on November 6, 2003, and may be accessed by visiting Alkermes' website or by dialing 1-888-266-2081 for domestic callers and 1-703-925-2533 for international callers. The replay access code is 310390.

(a) The FDA initially approved Risperdal, marketed by Janssen Pharmaceutica Products, L.P., in 1993 as a treatment for schizophrenia. Risperdal is available in 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg and 4 mg doses. Risperdal is also available as a quick dissolving tablet (Risperdal(R) M-Tab(TM)) in 0.5 mg, 1 mg and 2 mg doses, and as an oral solution. In clinical trials, Risperdal was generally well tolerated. However, as with all other antipsychotic medications, Risperdal can cause some side effects. In two controlled trials involving individuals with schizophrenia and schizoaffective disorder, adverse events that occurred in at least 5 percent of patients receiving Risperdal and were experienced at least twice as often as those taking placebo were anxiety, drowsiness, extrapyramidal symptoms, dizziness, constipation, nausea, dyspepsia (upset stomach), rhinitis (runny nose), rash and tachycardia (rapid heart beat). While dose dependent, extrapyramidal symptoms typically occur at a rate that is comparable to that seen with placebo at doses less than or equal to 6 mg/day. For more information, refer to the full prescribing information for Risperdal or visit www.janssen.com.

(1)Weiden, PJ, Zygmunt, A. J. Prac Psych Behavior Health. 1997, March: 106-110.

(2)Weiden, PJ, Zygmunt, A. J. Prac Psych Behavior Health. 1997, March: 106-110.

(3)Kane, JM., "Schizophrenia," The New England Journal of Medicine, 1996, pg. 39.

(4)NIH Publication No. 02-3517.

(5)Csernansky, JG. "A Comparison of Risperidone and Haloperidol for the Prevention of Relapse in Patients with Schizophrenia," The New England Journal of Medicine, January 3, 2002, Vol 346: 16-22.

(6)IMS Data.

(7)Kane, JM., "Long-Acting Injectable Risperidone: Efficacy and Safety of the First Long-Acting Atypical Antipsychotic," American Journal of Psychiatry, 2003, 160:6, pg. 1125.

(8)Kane, JM., "Long-Acting Injectable Risperidone: Efficacy and Safety of the First Long-Acting Atypical Antipsychotic," American Journal of Psychiatry, 2003, 160:6, pg. 1126.

(9)Kane, JM., "Long-Acting Injectable Risperidone: Efficacy and Safety of the First Long-Acting Atypical Antipsychotic," American Journal of Psychiatry, 2003, 160:6 pg. 1128.

(10)Kane, JM., "Long-Acting Injectable Risperidone: Efficacy and Safety of the First Long-Acting Atypical Antipsychotic," American Journal of Psychiatry, 2003, 160:6 pg. 1130.

(11)Kane, JM., "Long-Acting Injectable Risperidone: Efficacy and Safety of the First Long-Acting Atypical Antipsychotic," American Journal of Psychiatry, 2003, 160:6 pg. 1128.

(12)Kane, JM., "Long-Acting Injectable Risperidone: Efficacy and Safety of the First Long-Acting Atypical Antipsychotic," American Journal of Psychiatry, 2003, 160:6 pg. 1127.

(13)Kane, JM., "Long-Acting Injectable Risperidone: Efficacy and Safety of the First Long-Acting Atypical Antipsychotic," American Journal of Psychiatry, 2003, 160:6 pg. 1129.

(14)Data on file, Janssen Pharmaceutica Products, L.P.

(15)Csernansky, JG. "A Comparison of Risperidone and Haloperidol for the Prevention of Relapse in Patients with Schizophrenia," The New England Journal of Medicine, January 3, 2002, Vol 346: 16-22.

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