Alkermes Presented New Data Analysis on Healthcare Resource Use Among Veterans With Alcohol Dependence

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- Retrospective Study of Veterans Health Administration Data Showed an Association Between VIVITROL Treatment and Reduced Emergency Department Visits and Inpatient Hospital Stays -

DUBLIN, June 30, 2021 /PRNewswire/ -- **Alkermes plc** (Nasdaq: ALKS) today announced the presentation of new health economics and outcomes research related to healthcare resource use (HRU) among veterans with alcohol dependence at the 2021 Research Society on Alcoholism (RSA) Scientific Meeting/International Society for Biomedical Research on Alcoholism (ISBRA) Conference, which took place virtually June 19-23, 2021.

The company presented results from a retrospective, observational study using data from the Veterans Health Administration (VHA) database, which includes healthcare encounters, treatments and laboratory tests at VHA facilities. The study assessed treatment patterns and HRU among 3,665 patients diagnosed with alcohol dependence who were treated with VIVITROL® (naltrexone for extended-release injectable suspension (XR-NTX)).

In the study, VIVITROL treatment for alcohol dependence was associated with decreases in inpatient care and increases in outpatient care during the one-year period following initiation of treatment with VIVITROL, compared to the one-year period before VIVITROL treatment initiation. Specifically:

- During the baseline period, defined as the one year before VIVITROL initiation, 61.5 percent of patients had at least one inpatient admission, and 39.8 percent of patients had an emergency department visit.
- During the follow up period, defined as one year after VIVITROL initiation, 37.8 percent of patients had at least one inpatient admission and 35.4 percent of patients had an emergency department visit.

These HRU changes may reflect a possible transition to less resource-intensive care for veterans initiating VIVITROL. The generalizability of these results to the U.S. population may be limited.

"Alkermes is committed to advancing research on substance use disorders and veterans represent an important demographic given the pervasiveness of alcohol dependence and the broad unmet medical need within the veteran community," said Amy O'Sullivan, Vice President, Health Economics & Outcomes Research. "Though more research is needed, the VHA dataset provides insight into how the use of VIVITROL may impact engagement in treatment, healthcare resource utilization, and health outcomes in this patient population."

Details of the poster presentation at RSA are as follows:

- Poster #240: Treatment Patterns and Healthcare Resource Use Among Patients with Alcohol Dependence who Initiated Extended-Release Naltrexone: An Analysis of Veterans Affairs Data, was presented Sunday, June 20.

Alkermes previously presented data from another retrospective, observational study using the same VHA database at the Association of Military Surgeons of the United States (AMSUS), The Society of Federal Health Professionals, Annual Meeting in December 2020. That study was one of the first studies to provide insights into the patient journey among veterans from alcohol dependence diagnosis to VIVITROL initiation and beyond. Patients studied had extensive health care use and carried a high burden of chronic disease, including hypertension (40.5 percent), chronic pain (10.8 percent), and diabetes (9.7 percent). In addition, a majority had diagnoses for mental health comorbidities, such as depression (74.1 percent), non-alcohol/opioid substance use disorder (66.3 percent), and post-traumatic stress syndrome (52.9 percent). Key findings included:

- Although 25 percent of patients initiated VIVITROL within 60 days of diagnosis, the average time from initial diagnosis to VIVITROL initiation was analogous to 13.6 months.
- While many of the patients studied (75.8 percent) received oral naltrexone prior to initiating VIVITROL, 22.0 percent initiated VIVITROL as first-line medication. Additionally, about half of the patients studied (46.6 percent) did not initiate other alcohol dependence medications during the study period following initiation of treatment with VIVITROL.

About Alcohol Dependence

Alcohol dependence is a chronic, relapsing disease that poses serious and potentially fatal health risks.[1] In 2017, it affected nearly 8 million people aged 12 and older in the U.S., with a significant burden on veterans.[2]

About VIVITROL

VIVITROL® (naltrexone for extended-release injectable suspension) is a once-monthly medication for the treatment of alcohol dependence and for the prevention of relapse to opioid dependence, following opioid detoxification. Treatment with VIVITROL should be part of a comprehensive management program that includes psychosocial support. For more information, visit www.vivitrol.com.

INDICATIONS

VIVITROL is indicated for:

- Treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation

of treatment with VIVITROL. Patients should not be actively drinking at the time of initial VIVITROL administration.
- Prevention of relapse to opioid dependence, following opioid detoxification.
- VIVITROL should be part of a comprehensive management program that includes psychosocial support.

CONTRAINDICATIONS
VIVITROL is contraindicated in patients:

- Receiving opioid analgesics
- With current physiologic opioid dependence
- In acute opioid withdrawal
- Who have failed the naloxone challenge test or have a positive urine screen for opioids
- Who have exhibited hypersensitivity to naltrexone, polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other components of the diluent

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS
Vulnerability to Opioid Overdose:

- After opioid detoxification, patients are likely to have a reduced tolerance to opioids. VIVITROL blocks the effects of exogenous opioids for approximately 28 days after administration. As the blockade wanes and eventually dissipates completely, use of previously tolerated doses of opioids could result in potentially life-threatening opioid intoxication (respiratory compromise or arrest, circulatory collapse, etc.).
- Cases of opioid overdose with fatal outcomes have been reported in patients who used opioids at the end of a dosing interval, after missing a scheduled dose, or after discontinuing treatment. Patients and caregivers should be told of this increased sensitivity to opioids and the risk of overdose. Discuss the availability of naloxone for the emergency treatment of opioid overdose with the patient and caregiver, at the initial VIVITROL injection and with each subsequent injection. Strongly consider prescribing naloxone for the emergency treatment of opioid overdose.
- Although VIVITROL is a potent antagonist with a prolonged pharmacological effect, the blockade produced by VIVITROL is surmountable. The plasma concentration of exogenous opioids attained immediately following their acute administration may be sufficient to overcome the competitive receptor blockade. This poses a potential risk to individuals who attempt, on their own, to overcome the blockade by administering large amounts of exogenous opioids.
- Any attempt by a patient to overcome the VIVITROL blockade by taking opioids may lead to fatal overdose. Patients should be told of the serious consequences of trying to overcome the opioid blockade.

Injection Site Reactions:

- VIVITROL must be prepared and administered by a healthcare provider.
- VIVITROL injections may be followed by pain, tenderness, induration, swelling, erythema, bruising, or pruritus; however, in some cases injection site reactions may be very severe.
- In the clinical trials, one patient developed an area of induration that continued to enlarge after 4 weeks, with subsequent development of necrotic tissue that required surgical excision.
- Injection site reactions not improving may require prompt medical attention, including, in some cases, surgical intervention.
- Inadvertent subcutaneous/adipose layer injection of VIVITROL may increase the likelihood of severe injection site reactions.
- Select proper needle size for patient body habitus, and use only the needles provided in the carton.
- Patients should be informed that any concerning injection site reactions should be brought to the attention of their healthcare provider.

Precipitation of Opioid Withdrawal:

- When withdrawal is precipitated abruptly by administration of an opioid antagonist to an opioid-dependent patient, the resulting withdrawal syndrome can be severe. Some cases of withdrawal symptoms have been severe enough to require hospitalization, and in some cases, management in the ICU.
- To prevent occurrence of precipitated withdrawal, opioid-dependent patients, including those being treated for alcohol dependence, should be opioid-free (including tramadol) before starting VIVITROL treatment:
    - An opioid-free interval of a minimum of 7–10 days is recommended for patients previously dependent on short-acting opioids.
    - Patients transitioning from buprenorphine or methadone may be vulnerable to precipitated withdrawal for as long as two weeks.

- If a more rapid transition from agonist to antagonist therapy is deemed necessary and appropriate by the healthcare provider, monitor the patient closely in an appropriate medical setting where precipitated withdrawal can be managed.
- Patients should be made aware of the risk associated with precipitated withdrawal and be encouraged to give an accurate

account of last opioid use.
- Precipitated opioid withdrawal has been observed in alcohol-dependent patients in circumstances where the prescriber had been unaware of the additional use of opioids or co-dependence on opioids.

Hepatotoxicity:

- Cases of hepatitis and clinically significant liver dysfunction have been observed in association with VIVITROL. Warn patients of the risk of hepatic injury; advise them to seek help if experiencing symptoms of acute hepatitis. Discontinue use of VIVITROL in patients who exhibit acute hepatitis symptoms.

Depression and Suicidality:

- Alcohol- and opioid-dependent patients taking VIVITROL should be monitored for depression or suicidal thoughts. Alert families and caregivers to monitor and report the emergence of symptoms of depression or suicidality.

When Reversal of VIVITROL Blockade Is Required for Pain Management:

- For VIVITROL patients in emergency situations, suggestions for pain management include regional analgesia or use of non-opioid analgesics. If opioid therapy is required to reverse the VIVITROL blockade, patients should be closely monitored by trained personnel in a setting staffed and equipped for CPR.

Eosinophilic Pneumonia:

- Patients who develop dyspnea and hypoxemia should seek medical attention immediately. Consider the possibility of eosinophilic pneumonia in patients who do not respond to antibiotics.

Hypersensitivity Reactions including Anaphylaxis:

- Cases of urticaria, angioedema, and anaphylaxis have been observed with the use of VIVITROL.
- Patients should be warned of the risk of hypersensitivity reactions, including anaphylaxis.
- In the event of a hypersensitivity reaction, patients should be advised to seek immediate medical attention in a healthcare setting prepared to treat anaphylaxis. The patient should not receive any further treatment with VIVITROL.

Intramuscular Injections:

- As with any intramuscular injection, VIVITROL should be administered with caution to patients with thrombocytopenia or any coagulation disorder.

Alcohol Withdrawal:

- Use of VIVITROL does not eliminate nor diminish alcohol withdrawal symptoms.

Interference with Laboratory Tests

- VIVITROL may be cross-reactive with certain immunoassay methods for the detection of drugs of abuse (specifically opioids) in urine.
- For further information, reference to the specific immunoassay instructions is recommended.

ADVERSE REACTIONS

- The adverse events seen most frequently in association with VIVITROL therapy for alcohol dependence (ie, those occurring in ≥5% and at least twice as frequently with VIVITROL than placebo) include nausea, vomiting, injection site reactions (including induration, pruritus, nodules, and swelling), arthralgia, arthritis, or joint stiffness, muscle cramps, dizziness or syncope, somnolence or sedation, anorexia, decreased appetite or other appetite disorders.
- The adverse events seen most frequently in association with VIVITROL in opioid-dependent patients (ie, those occurring in ≥2% and at least twice as frequently with VIVITROL than placebo) were hepatic enzyme abnormalities, injection site pain, nasopharyngitis, insomnia, and toothache.

You are encouraged to report side effects to the FDA.
Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

About Alkermes plc
Alkermes plc is a fully-integrated, global biopharmaceutical company developing innovative medicines in the fields of neuroscience and oncology. The company has a portfolio of proprietary commercial products focused on addiction, schizophrenia and bipolar I disorder, and a pipeline of product candidates in development for neurodegenerative disorders and cancer. Headquartered in Dublin, Ireland, Alkermes plc has an R&D center in Waltham, Massachusetts; a research and manufacturing facility in Athlone, Ireland; and a manufacturing facility in Wilmington, Ohio. For more information, please visit Alkermes' website at www.alkermes.com.

Note Regarding Forward-Looking Statements

Certain statements set forth in this press release constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the potential therapeutic value of VIVITROL and the potential impacts of the treatment of alcohol dependence with VIVITROL on healthcare resource utilization and health outcomes. You are cautioned that forward-looking statements are inherently uncertain. 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 they are necessarily subject to a high degree of uncertainty and risk. Actual results may differ materially from those expressed or implied in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others, whether the results of these retrospective, observational studies will be predictive of future results and those risks and uncertainties described under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the year ended Dec. 31, 2020 and in subsequent filings made by the company with the U.S. Securities and Exchange Commission (SEC), which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release.

[1] Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for Management of Substance Use Disorders (SUD). 2015. Available from: https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPGrevised22216.pdf.

[2] GBD 2016 Alcohol and Drug Use Collaborators. The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Psychiatry. 2018 Dec;5(12):987-1012. doi: 10.1016/S2215-0366(18)30337-7.

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