AcelRx announces FDA approval of DSUVIA™

November 2, 2018

- DSUVIA (sufentanil sublingual tablet 30 mcg) is indicated for the management of acute pain severe enough to require an opioid analgesic for adult patients in certified medically supervised healthcare settings

- First and only sufentanil sublingual tablet approved for acute pain in healthcare settings

- DSUVIA U.S. launch expected in the first quarter of 2019

- Conference-call scheduled for Monday, November 5th at 8:30 a.m. ET

REDWOOD CITY, Calif., Nov. 2, 2018 /PRNewswire/ -- AcelRx Pharmaceuticals, Inc. (AcelRx) (Nasdaq: ACRX), a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in a medically supervised setting, announced today the approval of DSUVIA™ by the U.S. Food and Drug Administration (FDA). DSUVIA is indicated for the management of acute pain in adults that is severe enough to require an opioid analgesic in certified medically supervised healthcare settings, such as hospitals, surgical centers, and emergency departments.

"The FDA approval of DSUVIA is the culmination of nearly 15 years of research to improve the standard of care for managing acute pain in medically supervised settings," said Dr. Pamela Palmer, Co-Founder and Chief Medical Officer, AcelRx. "As an anesthesiologist, I've seen the challenges that IV opioids pose to patients and providers, such as logistical delays in initiating IV lines, difficulty in accessing veins, and medication errors with injectable opioids. AcelRx was founded to develop a simple, effective, non-invasive analgesic option to enable healthcare professionals to rapidly manage their patients' acute pain."

DSUVIA is a 30 microgram (mcg) sufentanil tablet in a single-dose, pre-filled applicator for under the tongue (sublingual) administration by a healthcare professional only in certified medically supervised settings. In a randomized, double-blind, placebo-controlled clinical study, DSUVIA demonstrated a statistically greater summed pain intensity difference from baseline over the first 12 hours of the study (SPID12) compared to placebo. The pain intensity difference from baseline was superior to that of the placebo group within 15 minutes and median meaningful pain relief occurred following a single dose. The single-strength tablet and single-unit packaging are designed to mitigate the possibility of dosing errors, misuse and diversion. The sublingual administration makes DSUVIA an option for patients with nothing by mouth (NPO) status and patients with difficult IV access (obese, elderly, burn or needle-phobic patients). Avoiding an IV has the potential to offer efficiency improvements in healthcare settings and improve patient experience. There are an estimated 92 million annual adult patient visits to medically supervised settings for moderate-to-severe acute pain. An estimated 51 million of these visits are to emergency departments (ED), with an estimated 18 million of these ED patients receiving an IV only for pain management.[1]

"Managing acute pain is critical to a patient's recovery process, especially in the postoperative setting, but current oral and IV opioid analgesics can be slow-acting and challenging to dose and administer, which in turn can limit optimal pain relief and even be dangerous to patients," said Dr. David Leiman, Clinical Assistant Professor of Surgery, University of Texas at Houston and Director of HD Research. "As a single-dose, non-invasive medication with a rapid reduction in pain intensity, DSUVIA represents an important alternative for healthcare providers to offer patients for acute pain management."

"The approval of DSUVIA, which was developed in collaboration with the Department of Defense, underscores our commitment to provide innovative therapies for use in medically supervised settings," said Vince Angotti, Chief Executive Officer, AcelRx. "We believe the unique features of DSUVIA are an important leap forward in the management of acute pain and patient care in these settings. We are committed to the safe and effective administration of DSUVIA through diligent adherence to our FDA-approved Risk Evaluation and Mitigation Strategies program."

The DSUVIA commercial launch is expected in the first quarter of 2019.

DSUVIA efficacy and safety information

The efficacy and safety of DSUVIA were evaluated in one randomized, double-blind, placebo-controlled trial which enrolled 161 patients (age 18 to 69 years) with acute postoperative pain (pain intensity of ≥ 4 on a 0-10 numeric rating scale) after abdominal surgery (studied up to 48 hours). Patients were dosed with DSUVIA 30 mcg or placebo as needed with a minimum of 60 minutes between doses. Morphine sulfate 1 mg IV was available as rescue medication.

Patients using DSUVIA had a statistically significantly greater SPID12 than patients using placebo. Approximately 22% of patients in the DSUVIA group and 65% of patients in the placebo group took rescue medication within the first 12 hours of the treatment phase.

In controlled and uncontrolled studies, the safety of DSUVIA was evaluated in a total of 646 patients with moderate-to-severe postoperative pain or pain due to trauma which required opioid analgesia. The most frequently reported adverse reactions ≥ 2% in the randomized, placebo-controlled trial were nausea, headache, vomiting, dizziness, and hypotension. The DSUVIA clinical program builds upon the established safety and efficacy of the reference product, sufentanil citrate injection, which has been in commercial use for over three decades.

DSUVIA will not be available in retail pharmacies or for outpatient use. DSUVIA will only be distributed to health care settings certified in the DSUVIA Risk Evaluation and Mitigation Strategy (REMS) program following attestation by an authorized representative that the healthcare setting will comply with appropriate dispensing and use restrictions of DSUVIA. As part of the REMS program, AcelRx will monitor distribution and audit wholesalers' data, evaluate proper usage within the healthcare settings and monitor for any diversion and abuse. Additionally, AcelRx will de-certify healthcare settings that are non-compliant with the REMS program.

Conference-call information
AcelRx will host a conference call Monday, November 5th at 8:30 a.m. Eastern Time to discuss the FDA approval of DSUVIA. The call can be accessed by dialing (866) 361-2335 for domestic callers, (855) 669-9657 for Canadian callers or (412) 902-4204 for international callers. The call will also be webcast live on the Company's website at www.acelrx.com.

About DSUVIA™(sufentanil sublingual tablet, 30 mcg)
DSUVIA™, known as DZUVEO™ outside the United States, approved by the FDA in November 2018, is indicated for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. DSUVIA was designed to provide rapid analgesia via a non-invasive route and to eliminate dosing errors associated with IV administration. DSUVIA is a single-strength solid dosage form administered sublingually via a single-dose applicator (SDA) by healthcare professionals. Sufentanil is an opioid analgesic currently marketed for intravenous (IV) and epidural anesthesia and analgesia. The sufentanil pharmacokinetic profile when delivered sublingually avoids the high peak plasma levels and short duration of action observed with IV administration. The European Medicines Agency (EMA) approved DZUVEO for marketing in Europe in June 2018. For more information, please visit www.DSUVIA.com.

LIMITATIONS OF USE
Not for home use or for use in children. Discontinue treatment with DSUVIA before patients leave the certified medically supervised healthcare setting. Not for use for more than 72 hours. The use of DSUVIA beyond 72 hours has not been studied. Only to be administered by a healthcare provider.

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve DSUVIA for use in patients for whom alternative treatment options [e.g., non-opioid analgesics or opioid combination products]: have not been tolerated, or are not expected to be tolerated, have not provided adequate analgesia, or are not expected to provide adequate analgesia.

The Full Prescribing Information for DSUVIA contains the following Boxed Warning:

WARNING: ACCIDENTAL EXPOSURE AND DSUVIA REMS PROGRAM: LIFE-THREATENING RESPIRATORY DEPRESSION; ADDICTION, ABUSE AND MISUSE; CYTOCHROME P450 3A4 INTERACTION; AND RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Accidental Exposure and DSUVIA REMS Program:
Accidental exposure to or ingestion of DSUVIA, especially in children, can result in respiratory depression and death. Because of the potential for life-threatening respiratory depression due to accidental exposure, DSUVIA is available only through a restricted program called the DSUVIA REMS Program. DSUVIA must only be dispensed to patients in a certified medically supervised healthcare setting. Discontinue use of DSUVIA prior to discharge or transfer from the certified medically supervised setting.

Life-Threatening Respiratory Depression:
Serious, life-threatening, or fatal respiratory depression may occur with the use of DSUVIA. Monitor for respiratory depression, especially during initiation of DSUVIA.

Addiction, Abuse, and Misuse:
DSUVIA exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk before prescribing DSUVIA, and monitor all patients regularly for the development of these behaviors or conditions.

Cytochrome P450 3A4 Interaction:
The concomitant use of DSUVIA with cytochrome P450 3A4 inhibitors may result in an increase in sufentanil plasma concentrations, which could increase or prolong adverse drug reactions and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in sufentanil plasma concentration. Monitor patients receiving DSUVIA and any CYP3A4 inhibitor or inducer.

Risks From Concomitant Use With Benzodiazepines or Other CNS Depressants:
"Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

IMPORTANT SAFETY INFORMATION
DSUVIA is contraindicated in patients with significant respiratory depression; acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment; known or suspected gastrointestinal obstruction, including paralytic ileus; and known hypersensitivity to sufentanil or components of DSUVIA.

DSUVIA contains sufentanil, a Schedule II controlled substance. As an opioid, DSUVIA exposes users to the risks of addiction, abuse, and misuse. Potential serious adverse events caused by opioids include addiction, abuse, and misuse, life-threatening respiratory depression, neonatal withdrawal syndrome, risks of concomitant use or discontinuation of cytochrome P450 3A4 inhibitors and inducers, risks from concomitant use with benzodiazepines or other CNS depressants, risk of life threatening respiratory depression in patients with chronic pulmonary disease or in elderly, cachectic, or debilitated patients, adrenal insufficiency, severe hypotension, risks of use in patients with increased intracranial pressure or impaired consciousness, gastrointestinal disorders and seizure disorders. DSUVIA should be used with caution in patients with severe liver or kidney impairment.

For Important Safety Information including full prescribing information, visit: www.DSUVIA.com.

Clinical and Rehabilitative Medicine Research Program (CRMRP)
DSUVIA is funded in part by the Clinical and Rehabilitative Medicine Research Program (CRMRP) of the U.S. Army Medical Research and Materiel Command (USAMRMC) under contract No. W81XWH-15-C-0046. The CRMRP was established in 2008 to foster research and technology advances for regeneration, restoration, and rehabilitation of traumatic injuries. In accordance with USAMRMC guidelines, in the conduct of clinical research, AcelRx has adhered to the policies regarding the protection of human subjects as prescribed by Code of Federal Regulations (CFR) Title 45, Volume 1, Part 46; Title 32, Chapter 1, Part 219; and Title 21, Chapter 1, Part 50 (Protection of Human Subjects).

About AcelRx Pharmaceuticals, Inc.
AcelRx Pharmaceuticals, Inc. is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings. AcelRx's proprietary, non-invasive sublingual formulation technology delivers sufentanil with consistent pharmacokinetic profiles. The Company has one approved product in the U.S., DSUVIA (sufentanil sublingual tablet, 30 mcg), known as DZUVEO in Europe, indicated for the management of acute pain severe enough to require an opioid analgesic for adult patients in certified medically supervised healthcare settings, and one product candidate, Zalviso® (sufentanil sublingual tablet system, SST system, 15 mcg) being developed as an innovatively designed patient-controlled analgesia (PCA) system for reduction of moderate-to-severe acute pain in medically supervised settings. DZUVEO and Zalviso are both approved products in Europe.

For additional information about AcelRx, please visit www.acelrx.com.

Forward-Looking Statements
This press release contains forward-looking statements, including, without limitation, statements related to the safety, efficacy and tolerance of DSUVIA and the planned timing for the commercial launch of DSUVIA. These forward-looking statements are based on AcelRx's current expectations and involve significant risks and uncertainties. AcelRx's actual results and timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, including, without limitation: any delays in the commercial launch of DSUVIA or the Company's other approved products or the inability to maintain regulatory approval of DSUVIA in the United States, and other risks detailed in the "Risk Factors" and elsewhere in AcelRx's U.S. Securities and Exchange Commission filings and reports, including its Annual Report on Form 10-K filed with the SEC on March 9, 2018 and Quarterly Report on Form 10-Q filed with the SEC on August 2, 2018. AcelRx undertakes no duty or obligation to update any forward-looking statements contained in this release as a result of new information, future events or changes in its expectations, except as required by law.

[1] Source: Aggregated Medical Literature review, QuintilesIMS primary market research, QuintilesIMS analysis 2016. ARX-04 and Zalviso US data-December 2016.

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