AcelRx Pharmaceuticals Overview
January 2021

Investor materials
Cautionary statements

This presentation contains forward-looking statements, including, but not limited to, statements related to the safety, efficacy and therapeutic value of DSUVIA® (sufentanil sublingual tablet, 30 mcg) and ZALVISO® (the sufentanil sublingual tablet system); the commercial potential of DSUVIA and ZALVISO, including potential market opportunities; the commercial launch of DSUVIA in the U.S.; the expected commencement and continuation of investigator-initiated studies; revenues and cash, cash equivalents and short-term investments AcelRx expects to report for fiscal year 2020; the timing and size of the procurement of DSUVIA by the military; and the expected benefits of the agreement with Zimmer Biomet Dental, including the scope of its sales force, the estimated addressable market, and the timing of when distribution activities can begin. These and any other forward-looking statements are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking terminology such as "believes," "expects," "anticipates," "may," "will," "should," "seeks," "approximately," "intends," "plans," "estimates," or the negative of these words or other comparable terminology. These forward-looking statements involve risks and uncertainties that could cause actual results to differ materially from those projected, anticipated or implied by such statements, including, without limitation: any issues with the commercial launch of DSUVIA; that the military and hospital systems delay, or fail to place, orders; that AcelRx may not experience the expected benefits from the Zimmer Biomet arrangement; the uncertainties inherent in the initiation and execution of investigator-initiated studies; and other risks as detailed in the "Risk Factors" section and elsewhere in AcelRx's U.S. Securities and Exchange Commission (SEC) filings and reports, including its Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 filed with the SEC on November 5, 2020. You are cautioned not to place undue reliance on any such forward-looking statements, which speak only as of the date such statements were made. To the degree financial information is included in this presentation, it is in summary form only and must be considered in the context of the full details provided in the Company’s filings with the SEC. The Company’s SEC reports are available at www.acelrx.com under the “Investors” tab. AcelRx undertakes no duty or obligation to update any forward-looking statements contained in this presentation as a result of new information, future events or changes in its expectations, except as required by law.

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Focused on the management of acute pain in medically supervised settings

Acute ≠ Chronic

Medically Supervised Setting ≠ Patient Retail Script
## Portfolio of commercial and late-stage development products

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA submitted</th>
<th>Post-approval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ARX-02</strong>*</td>
<td>Sublingual sufentanil tablet for cancer breakthrough pain</td>
<td>Approved in U.S.</td>
<td>Approved in E.U.</td>
<td>UHS/Tvetenstrand, Cleveland Clinic, Brigham &amp; Women’s, Other IITs/studies</td>
</tr>
<tr>
<td><strong>ARX-03</strong>*</td>
<td>Combination sublingual sufentanil tablet and triazolam in a single dose applicator for mild sedation</td>
<td>NDA-ready in the U.S.</td>
<td>Approved in E.U.</td>
<td>Various EU studies</td>
</tr>
</tbody>
</table>

| 30 mcg sublingual sufentanil tablet in a single-dose applicator; HCP administered | Approved in U.S. | Approved in E.U. | UHS/Tvetenstrand, Cleveland Clinic, Brigham & Women’s, Other IITs/studies |
| 15 mcg sublingual sufentanil tablet in a pre-programmed handheld PCA device | NDA-ready in the U.S. | Approved in E.U. | Various EU studies |

* AcelRx is not currently investing resources in these development stage products; these are investigational products and are not approved by the FDA or any other regulatory agency.
Opioid related medication errors continue to plague the acute care setting

Opioids are the second most frequent drug class of medication errors within the acute hospital setting

References: Hahn 2007; ISMP Medication Safety Update for 2018 (ASHP midyear 2017)
Current IV opioids on the market do not fully address the patient or healthcare professional needs

**Slower acting opioids**
(IV morphine)

**Fast acting, but fast offset opioids**
(IV fentanyl/sufentanil)

3 hrs
blood:brain equilibration

6 min
blood:brain equilibration
Sublingual Sufentanil addresses an unmet need in acute pain management

**Sufentanil Sublingual (30 mcg)**

- All effect site and IV plasma concentrations modeled by D. Fisher MD, consultant to AcelRx
- Minkowitz, et al, Sufentanil Sublingual Tablet 30 mcg for the management of pain following abdominal surgery, Pain Practice 2017

**PK profile demonstrates analgesia as early as 15 minutes with a duration of ~3 hours.**

* Max amount of sufentanil that can be administered via IV bolus to avoid respiratory issues
Sufentanil sublingual tablets have unique properties

- **Small size** dissolves in minutes

- **Sublingual absorption** potentially maintains therapeutic levels for 3 hours

- **Minimizes saliva production** to limit swallowed drug and maintain sublingual bioavailability

- **Bioadhesive** to keep in place under tongue

- **Sufentanil for drug safety:** sufentanil used because of its high therapeutic index\(^{(a)}\) with no active metabolites

- **Discrete dosing unit** designed to reduce dosing errors and mitigate risk of diversion associated with clear liquids

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Department of Defense provided $22M supporting the development of DSUVIA®

- **Milestone C review completed April 2020** concluding that DSUVIA was approved for ALL Army sets, kits and outfits for deployed troops moving forward (forecasted $30M in initial stocking orders over three years, which have begun)

- **Joint Deployment Formulary** approval received in September 2020

- **Additional Federal/State government opportunities** (e.g., Strategic National Stockpile)

Developed with attention to diversion issues

- Circumvents potential for clear liquid substitution or diversion of unused dose
- Non-retractable plunger mitigates against refilling with “substitute” tablet
- Tamper-evident packaging
- No controlled substance wastage

![DSUVIA® Image](image-url)
At 15 minutes, SST 30 mcg significantly separates from placebo ($P=0.002$).
SAP 301 Post-operative Abdominal study: DSUVIA most common adverse reactions$^{1,2,*}$

<table>
<thead>
<tr>
<th>Condition</th>
<th>SST 30 mcg (n=107)</th>
<th>Placebo (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>29.0</td>
<td>22.2</td>
</tr>
<tr>
<td>Headache</td>
<td>12.1</td>
<td>11.1</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5.6</td>
<td>1.9</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5.6</td>
<td>3.7</td>
</tr>
<tr>
<td>Hypotension</td>
<td>4.7</td>
<td>3.7</td>
</tr>
</tbody>
</table>

$^*$IV morphine 1 mg/hour was allowed as a rescue medication for the placebo treatment arm.

- Safety database included 646 patients exposed to $\geq 30$ mcg sufentanil in first hour of treatment
- 20% aged 65-74 years of age
- 11% aged $\geq 75$ years

All events were considered to be mild in severity with the exception of nausea (n=1, unrelated) that was considered moderate in severity.

*2 patients experienced transient room air O₂ desaturations below 95%, which immediately improved with nasal cannula O₂

Cognitive impairment assessment demonstrated 97% of patients had no cognitive impairment

Six-Item Screener (SIS) Score
From Baseline to 1 Hour

<table>
<thead>
<tr>
<th>SIS Score Change</th>
<th>Baseline to 1 Hour, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>0</td>
<td>64 (85.3)</td>
</tr>
<tr>
<td>1</td>
<td>7 (9.3)</td>
</tr>
<tr>
<td>2</td>
<td>2 (2.7)</td>
</tr>
</tbody>
</table>

Six-Item Screener (SIS) Scores (0-6 scale)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Baseline</th>
<th>60 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50 years</td>
<td>(n=51)</td>
<td>(n=12)</td>
</tr>
<tr>
<td>50-59 years</td>
<td>(n=8)</td>
<td>(n=4)</td>
</tr>
</tbody>
</table>

Mean ± standard deviation; 60-minute SIS scores assessed at Cmax for SST 30 mcg

August 2020 publication demonstrated reduced opioid use and time in the PACU when administering DSUVIA

50%+ Reduction in opioids administered (includes intra- and post-operative opioids)

34% reduction in phase 1 PACU time when using DSUVIA

This study compared a prospective group of patients with preoperative dosing of a single sublingual DSUVIA tablet to a historical control group receiving standard intravenous (IV) opioid administration for same-day general surgery procedures. A total of 127 patients were evaluated in the study. Study limitations include that it was an open-label study, the retrospective nature of the control group, and the focus on only general surgery patients. AcelRx did not provide funding for the conduct of the study but did fund medical writing support. Dr. Tvetenstrand is a paid consultant of AcelRx.
August 2020 publication demonstrated reduced other medication use when using DSUVIA

Significant reduction in supplemental IV medications when using DSUVIA

(a) ephedrine, norepinephrine, or phenylephrine;
(b) \( p = 0.015 \) via Chi Square Test;
(c) \( p < 0.001 \) via Chi Square Test

This study compared a prospective group of patients with preoperative dosing of a single sublingual DSUVIA tablet to a historical control group receiving standard intravenous (IV) opioid administration for same-day general surgery procedures. A total of 127 patients were evaluated in the study. Study limitations include that it was an open-label study, the retrospective nature of the control group, and the focus on only general surgery patients. AcelRx did not provide funding for the conduct of the study but did fund medical writing support. Dr. Tvetenstrand is a paid consultant of AcelRx.
Pharmacoeconomic analysis of published study results

Intraoperative fentanyl
- 9.1mg more MME in control group; 2ml vial of fentanyl cost is $2

Postoperative fentanyl
- 52% greater use of fentanyl in post-op n control group; $2/vial x 52%

IV Acetaminophen
- 52% greater use of IV acetaminophen in control group; $47/vial x 52%

IV Ephedrine
- 21% greater use of IV ephedrine in control group; $29/vial x 21%

PACU time
- 18.6 minutes longer in PACU in control; $7/min in PACU if not limiting operating room cases; 18.6 x $7/min

PACU Time +
- IF PACU availability limits number of surgeries; $15 minute in surgical revenue lost; $15/min x 18.6

Total Costs
- $163
- $442
- $58 for DSUVIA

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1-Symphony Health Wholesale Acquisition Cost database, 2020 for fentanyl 100 mcg/2mL (Acorn)
2-Symphony Health Wholesale Acquisition Cost database, 2020 for Ofirmev 1000 mg/100 mL (Mallinckrodt)
3-Symphony Health Wholesale Acquisition Cost database, 2020 for ephedrine 50 mg/mL (Par Pharma)
4-https://www.beckershospitalreview.com/november-ceo-roundtable-conference/docs/Wednesday,%20November%2018/Track%20D/2_Wed_945am_OR_Efficiency_&_Cost_Effectiveness.pdf

Note: The intent of presenting this economic information is to portray the experience one site had when they added DSUVIA to their treatment armamentarium - results may vary.
**DSUVIA® use across subspecialties – December publication**

Reduced Intraoperative Use of IV Opioids Associated with SST 30 mcg

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Control (N=158)</th>
<th>SST-treated (N=140)</th>
<th>*** p &lt; 0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>OVERALL</td>
<td>15.7</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td>Abdominal</td>
<td>17</td>
<td>11.4</td>
<td></td>
</tr>
<tr>
<td>Ortho</td>
<td>15</td>
<td>8.6</td>
<td></td>
</tr>
<tr>
<td>GYN</td>
<td>14.9</td>
<td>7.9</td>
<td></td>
</tr>
<tr>
<td>GU</td>
<td>13.4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>ENT</td>
<td>14</td>
<td>8.8</td>
<td></td>
</tr>
</tbody>
</table>

The evaluation focused on 140 patients who were dosed with DSUVIA compared to 158 patients who had been dosed with traditional IV opioids during the same time period undergoing the same surgical procedures. Study limitations included that it was a single-center, retrospective study of DSUVIA dosing in a surgical patient population and both inpatient and outpatient surgery data was combined. The study did not control for whether patients were opiate naïve or opiate tolerant in the treatment groups. AcelRx did not provide funding for the conduct of the evaluation but did fund medical writing support. Dr. Cassavaugh is a paid consultant of AcelRx.
Sufentanil molecule and sublingual administration combine to create DSUVIA’s unique pharmacokinetics and pharmacodynamics.

**Characteristics**
- **Sufentanil**
  - Lipophilic (fat-loving)
  - High therapeutic index (Lethal Dose/Effective Dose)
- **Sublingual Administration**
  - Low peak plasma concentration

**Effect**
- Onset
- Duration
- AE profile
- Cognition
- Lower MME (morphine milligram equivalents)

**Result**
- Enhanced recovery for patient
- Reduced patient discharge time
A clear unmet need in acute pain management

- **Invasive**
  - IV Fentanyl
  - IV Hydromorphone
  - IV Morphine

- **Non-invasive**
  - Rapid
    - DSUVIA (sufentanil) sublingual tablet 30 mcg
  - Slow
    - Percocet
    - Vicodin

Source: Competitive landscape review—see full report for details (indicative only), Greater Than One primary market research, Greater Than One analysis 2017; All names, logos, and brands are property of their respective owners.
DSUVIA has an opportunity to address unmet needs for patients and healthcare providers

- Patient experience
- Ease of use
- No risk of IV infection
- Hospital/ER/ASC efficiency
- Lower total cost
IV administration is resource and cost intensive

Component cost of IV opioid dose

- Drug: $62
- Catheter: $15
- Lidocaine: $15
- Tubing: $5
- Saline Bag: $4
- IV Pump: $37
- IV Start & Infusion: $15

91.9M adult moderate-to-severe acute pain patient visits in medically supervised settings

- Emergency department
- Outpatient surgery
- Other procedures
- Inpatient/other surgery

Increasingly performed in ambulatory surgery centers and procedural suites, and include cosmetic surgery, burn and wound care, oral surgery and other painful procedures.

Reference: Aggregated Medical Literature review, QuintilesIMS primary market research, QuintilesIMS analysis 2016. ARX-04 and Zalviso US data-December 2016.
AcelRx four pillars building a foundation for revenue growth

1. Department of Defense
2. Commercial partnership in specialty markets (dental, fertility, EMS, etc.)
3. Hospital and ASC penetration
4. Product acquisition and in-licensing

Multiple opportunities for revenue growth outside hospital
Pillar 1: Milestone C Approval achieved in April 2020

- Milestone C review completed April 2020 concluding that DSUVIA was approved for ALL Army sets, kits and outfits for deployed troops moving forward (forecasted $30M in initial stocking orders over three years, which have begun)
- $3.6 million, four-year contract awarded in September 2020 for a DSUVIA comparative study
- Joint Deployment Formulary approval received in September 2020
- Seven US based Military Treatment Facilities (MTFs) already formulary approved
- Supply chain US sourced with production capacity
- Additional Federal/State government opportunities (e.g., Strategic National Stockpile)
Pillar 2: Exclusive distribution and promotion agreement for DSUVIA for dental and oral surgery agreed in July 2020

- Nationwide sales representatives focused on dental and oral surgery
- Estimated addressable market of over 7 million surgeries
- Distribution to begin after satisfaction of applicable licensing requirements; promotion expected to begin earlier
Pillar 3: Approximately 300 hospitals and 600 ASCs are our current priority target customers

Hospital Target Criteria
- Outpatient surgery volume
- Emergency Dept. volume
- Early adopters
- Access

ASC Target Criteria
- Relevant ASC specialty
- Geographical proximity to hospital targets
- Procedural volume
Pillar 3: Staged commercial launch plan with 25 sales representatives including a restructured co-promotion with LaJolla Pharmaceuticals in October 2020
Business development remains a key priority

- **Partner DSUVIA** in large market, non-core specialty areas outside the hospital and ambulatory surgery centers (oral surgery, plastic surgery, EMS, etc.) to leverage commercial scale of a larger or specialty partner

- Identify, evaluate and execute transactions to bring in **additional products** for healthcare institutions to leverage our commercial infrastructure

- **Outlicense** DSUVIA/DZUVEO in other geographies with potential partners; active discussions for Europe
$5.4M
Preliminary unaudited 2020 revenues\(^{(1)}\)

$8.6M
Q3 ‘20 operating expense\(^{(2)}\)

$42.9M
December 31, 2020 cash and ST investments\(^{(1)}\)

348
Formulary approvals

\(^{(1)}\) The information above related to the Company’s expected operating results for the year ended and as of December 31, 2020, including revenue and cash, cash equivalents and short-term investments, is preliminary, has not been audited and is subject to change upon completion of the audit of the Company’s financial statements as of and for the year ended December 31, 2020.

\(^{(2)}\) Combined R&D and SG&A including $1.3M non-cash stock-based comp and depreciation.
AcelRx investment highlights

- **DSUVIA commercial launch** with full 25 sales reps including the restructured LaJolla Pharmaceuticals co-promote

- **US Army Milestone C approval** in April 2020 for all SKO’s; expect initial stocking orders of $30M over three years, which have begun; addition to joint deployment formulary in September; $3.6M, four-year contract awarded in Sept.

- **Strategic partnership with Zimmer Biomet Dental agreed in July 2020** to promote and distribute DSUVIA for use during oral and dental surgery to reach a 7.5 million annual procedure addressable market

- **August publication of new data** demonstrating substantial reductions in PACU opioid use and significant decrease in PACU time when dosing DSUVIA

- Active business development: (a) continuing focus on **distribution partners** for large opportunity, specialty areas, (b) evaluating **new hospital products** and (c) out-licensing DZUVEO

- **Zalviso FDA resubmission** timing awaiting FDA opioid approval policy finalization

- **81 issued patents** (26 in US); 17 Orange Book listed patents expiring by 2031

- **$42.9 million** of cash/short-term investments at December 31, 2020\(^{(1)}\)

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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.

IMPORTANT SAFETY INFORMATION
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.

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