Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to the process and timing of anticipated future development of AcelRx's product candidates, ARX-04 (sufentanil sublingual tablet, 30 mcg) and Zalviso® (sufentanil sublingual tablet system), including the Phase 3 SAP302 and SAP303 studies for ARX-04; AcelRx’s pathway forward towards gaining approval of Zalviso in the U.S.; the anticipated timing, design and results of IAP312 clinical trial for Zalviso; anticipated resubmission of the Zalviso New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA; and the therapeutic and commercial potential of AcelRx’s product candidates, including ARX-04 and Zalviso. These forward-looking statements are based on AcelRx Pharmaceuticals’ current expectations and inherently involve significant risks and uncertainties. AcelRx Pharmaceuticals’ actual results and timing of events could differ materially from those anticipated in such forward-looking statements, and as a result of these risks and uncertainties, which include, without limitations, risks related to AcelRx Pharmaceuticals’ ability to complete Phase 3 clinical development of ARX-04; AcelRx’s ability to successfully execute the pathway towards a resubmission of the Zalviso NDA to the FDA, including the initiation and completion of the IAP312 clinical study for Zalviso; AcelRx’s ability to receive regulatory approval for Zalviso; any delays or inability to obtain and maintain regulatory approval of its product candidates, including ARX-04 in the United States and Europe, and Zalviso in the United States; the uncertain clinical development process, including adverse events; the risk that planned clinical trials may not begin on time, have an effective clinical design, enroll a sufficient number of patients, or be initiated or completed on schedule, if at all; the success, cost and timing of all development activities and clinical trials, including the additional clinical trial for Zalviso, IAP312, and the Phase 3 ARX-04 SAP302 and SAP303 trials; the fact that the FDA may dispute or interpret differently clinical results obtained to date from the Phase 3 SAP301 study of ARX-04; the accuracy of AcelRx’s estimates regarding expenses, capital requirements and the need for financing; and other risks detailed in the “Risk Factors” and elsewhere in AcelRx’s U.S. Securities and Exchange Commission filings and reports, including its Quarterly Report on Form 10-Q filed with the SEC on May 2, 2016. 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.
Sublingual Sufentanil: New Approach in development to treat moderate-to-severe acute pain

**AcelRx Highlights:**
- Over $100 million in cash
- Two US Phase 3 products

**ARX-04**
- Emergencies
- Short-stay Surgeries and Procedures

**Zalviso®**
- Inpatient Surgeries
- Approved in EU
Opioids Remain Important Analgesics

- The Ebers Papyrus (ca. 1500 B.C.) documents many opioid remedies for pain and suffering\(^1\)
- Over 3000 years later, opioids remain an important treatment for moderate-to-severe acute pain\(^2\)
- 2016 American Pain Society Guidelines for managing postoperative pain include the use of opioids\(^3\)
- Following major surgery, non-opioid adjuvants only reduce postoperative opioid use by 0 – 50\%\(^4\)
- Opioid medications remain the mainstay for treatment of severe pain in the ER\(^5\)
- AcelRx products are for short-term use and only to be used in hospitals or administered by trained medical professionals

Patient Satisfaction with Pain Management a Focus for Medical Facilities and Healthcare Professionals

Patients now shopping for hospitals and comparing based on HCAHPS scores

The HCAHPS (Hospital Consumer Assessment of Healthcare Providers and Systems) Survey is the first national, standardized, publicly reported survey of patients' perspectives of hospital care.

4) How often was patients’ pain well controlled? During this hospital stay...
   - How often was your pain well controlled?
   - How often did the hospital staff do everything they could to help you with your pain?

Medicare & Medicaid reimbursement tied directly to HCAHPS scores

December 2015: Centers for Medicare & Medicaid Services (CMS) refreshed the HCAHPS results on the Hospital Compare Web site, www.medicare.gov/hospitalcompare
## Unmet Needs in Treatment of Moderate-to-Severe Acute Pain

<table>
<thead>
<tr>
<th>Route of Delivery</th>
<th>Emergencies</th>
<th>Short-Stay Surgeries/Procedures</th>
<th>Inpatient Surgeries</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM/IV are invasive • Oral = slow onset</td>
<td>IV may prolong stay • Oral = slow onset</td>
<td>IV may limit mobility • PCA pump = potential for programming errors</td>
<td></td>
</tr>
</tbody>
</table>

### Common Opioids
- IV morphine and hydromorphone = delayed CNS uptake/slow off; active metabolites can cause prolonged opioid effects/side effects
- IV fentanyl = rapidly absorbed/short-acting requiring frequent redosing
Commonly used IV opioids have a delayed equilibration time between plasma and brain.

1. Lotsch et al., Anesthesiol 95:1329-38, 2001
# Sublingual Sufentanil

**Potential for Real-Time Tracking Between Dosing & Effect**

## Sublingual Sufentanil dosing closely matched with effect

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Plasma</th>
<th>Effect Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>8</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

## Brain levels delayed with IV morphine dosing

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Morphine/M6G in plasma*</th>
<th>Morphine/M6G in brain*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>8</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

*Assumes equipotency of morphine and M6G; other potency ratios achieved similar results.

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1. Sublingual sufentanil and IV PCA dosing frequency based on IAP309 study;
2. Plasma and brain concentrations modelled from published plasma and CNS equilibration values by Dr. Dennis Fisher – consultant to AcelRx.
Proprietary Sublingual Sufentanil Tablets Have Unique Properties

**Sufentanil**
- **Lipophilic** so absorbed sublingually
- **Potent** so small tablet possible
- **Wide therapeutic index**\(^1\) to maximize analgesia while minimizing side effects
- **Low GI bioavailability** minimizes delayed effect of swallowed drug

**Tablet**
- **Small size** dissolves in minutes
- **Minimizes saliva production** to limit swallowed drug and avoid delayed drug uptake from GI
- **Bioadhesive** to keep in place under tongue
- **Discrete dosing unit** reduces errors of continuous dosing

\(^1\) as determined by animal models
In Medically Supervised Settings, ~90M Pts Treated Annually in the US for Moderate-to-Severe Acute Pain$^{1,2,3}$

Emergency Departments
Ambulatory Surgery Centers
Short-stay Surgeries
Interventional Procedures

$1.7$ Billion Combined Market Potential

$445.5M^3$

$1.3B^{1,2}$

ARX-04
Zalviso

ARX-04 Overview

Proposed Development
AcelRx Pharmaceuticals is developing ARX-04, sublingual sufentanil 30 mcg tablet pre-filled in a single dose applicator for the management of moderate-to-severe acute pain in a medically supervised setting.

Development Status
- SAP302 ongoing in the emergency room
- SAP303 ongoing in postoperative patients
- NDA submission anticipated in Q4 2016

- EMS (pre-hospital)
- Emergency Departments
- Ambulatory Surgery Centers
- Short-Stay Surgeries
- Interventional Procedures
Department of Defense Provides Support for Treating Pain Associated with Trauma

**Battlefield**

- IM morphine standard of care\(^1\)
- IM dosing often ineffective due to shock and lack of circulation to muscles; death can occur due to oxygen desaturation upon reperfusion\(^2\)
- IV lines time-consuming and challenging to start
- DoD Needs: Rapid onset with predictable offset and minimal cognitive effects

**Civilian Equivalent = EMS/ED**

- Guidelines support opioids for moderate-to-severe acute pain\(^3\)
- IV lines challenging to start in ambulances\(^4\)
- Can take 30 minutes or more to have an IV line inserted in ED\(^5\)

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Surveyed physicians expect fewer than 20% of their ER patients to wait 15 min or less for their first dose of IV opioids

65% of physicians stated that they would use a product like ARX-04 in their institution

Areas for Improvement

- Field Trauma: 2%
- Pre-Hospital: 10%
- ED, waiting: 52%
- ED following eval or during a procedure: 23%
- ED, awaiting admission: 5%
- ED, upon discharge: 8%

Potential ARX-04 Market

Cost of Initial IV Opioid Dose in the ED for the Treatment of Acute Pain Exceeds $140 - ISPOR¹

Title
• Cost of Delivering Intravenous Opioid Analgesia in Emergency Departments (EDs) in the U.S.

Study Design
• Descriptive analyses, sponsored by AcelRx and using Premier database (2013-2014) of > 600 US hospital EDs for cost of starting an IV and delivering an initial dose of IV opioid
• Average costs of each component were aggregated for total costs; direct acquisition and indirect cost (labor, pharmacy, etc.) were also included

Results
• Based on an analysis of over 7 million patients, the cost ranges from $143 for morphine to $145 for fentanyl

Conclusion
• The cost of materials and labor to establish an IV line to administer an opioid is almost 95% of the total cost, which is a substantial considering the number of ED visits annually

¹Oral presentation at the International Society for Pharmacoeconomic and Outcomes Research Meeting, May 21-25, 2016 in Washington, DC.
ARX-04 Pivotal Efficacy Studies Completed
Remaining Trials are Open-Label Safety Studies

Pivotal Studies - Completed
- Positive Phase 2: SAP202 Bunionectomy Study
- Positive Phase 3: SAP301 Abdominal Surgery Study

Safety Studies - Ongoing
- SAP302: Emergency Room Study
- SAP303: Postoperative Elderly Patients and Patients with Comorbidities
ARX-04 Abdominal Surgery Study: SAP301
Postoperative Ambulatory Surgery Patients

<table>
<thead>
<tr>
<th>Surgery Types</th>
<th>Study Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Open Hernioplasty</td>
<td>- Randomized 163 patients</td>
</tr>
<tr>
<td>- Abdominoplasty</td>
<td>- Randomized 2:1 active to placebo</td>
</tr>
<tr>
<td>- Laparoscopic Abdominal Surgery</td>
<td>- Completers = 24 hours in the study, extension to 48 hours if needed</td>
</tr>
<tr>
<td></td>
<td>- Primary endpoint: Sum of the pain intensity difference to baseline over the first 12 hours (SPID12)</td>
</tr>
</tbody>
</table>
Significantly greater SPID12 compared to placebo

ARX-04 also positive on secondary endpoints

No difference in AE’s between ARX-04 and placebo

AE’s typical of opioid therapy (nausea, headache, vomiting)
ARX-04 Abdominal Surgery Study: SAP301
SPID1 Statistically Better than Placebo after 15 Minutes

SPID Over First Hour of Treatment

Statistical separation at 15 minutes

ARX-04

* p<0.01
** p<.001

Placebo

Minutes

Sum of Pain Intensity Difference

0 15 30 45 60
ARX-04 Emergency Room Study: SAP302
Emergency Room Patients

**ER Patient Types**
- Patients presenting to the Emergency Room with trauma or injury associated with moderate-to-severe pain
- Exclusions: Pregnant, opioid tolerant, oxygen dependent

**Study Details**
- Single arm open label
- 40 patients single dose
- 60 patients multiple dose
- Primary endpoint: Sum of the pain intensity difference to baseline over the first hour (SPID1)
- Six-item screener (cognition)
1.3 has been identified as the minimum clinically significant difference in pain when administering 0-10 point numerical rating scale (NRS) to measure pain

---

### ARX-04 ER Study: SAP302 – Interim Results

**Single-Arm, Open-Label: Adverse Events**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Total n=40 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Adverse Event</td>
<td>34 (85%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Feeling Hot</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Disorientation</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Facial Hypoesthesia</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
### ARX-04 Postoperative Study: SAP303  
*Short-stay Postoperative Patients*

#### Patient Types
- Post surgical patients moderate-to-severe pain
- Age 40 or older
- Encourage enrollment of patients with comorbidities (renal impairment, liver impairment, etc.)

#### Study Details
- Single arm, multi-center open label
- ARX-04 dosed once every 60 minutes as needed for up to 12 hours
- Targeting to enroll 100 patients
- Primary endpoint: Sum of the pain intensity difference to baseline over the first 12 hours (SPID12)
Zalviso® Overview

Proposed Development

AcelRx Pharmaceuticals is developing Zalviso sufentanil sublingual tablet system for the management of moderate-to-severe acute pain in adult patients in a hospital setting.

Development Status

- Approved in Europe
- Additional US study planned
- NDA resubmission planning in process

- Inpatient Surgeries requiring overnight stays
Current Problems with IV PCA Devices and Delivery

Documented Problems with IV PCA\(^1,2,3\)

- User programming errors resulting in adverse events including death
- Proxy dosing can cause injury and death
- Infection risk
- Can limit ambulation
- Clear liquid syringe can facilitate drug diversion

1. Meissner, Hospital Pharmacy 44:312, 2009
2. ISMP: http://www.ismp.org/Newsletters/acute/acute/articles/20070222.asp
Zalviso:  
*Noninvasive Patient-Controlled Analgesia (PCA)*  
*Designed to Mitigate Issues with IV PCA*

- **Decrease Medication Errors Associated with IV PCA:** Pre-programmed delivery/single-strength tablet
- **Reduce Proxy Dosing:** Patient RFID thumb tag required for dosing
- **Reduces IV-Related Infection Risk:** Noninvasive sublingual delivery
- **Less Hampering of Ambulation:** Patient not tethered to IV pole with Zalviso
- **20 minute Dose Lockout**

- **Multiple Anti-Diversion Features**
  - RFID on cartridge provides full inventory tracking of tablets
  - HCP-controlled access, device tethered to bed, anti-diversion alarms

*Investigational drug and delivery system not FDA approved for commercial use

*http://globalrph.com/pca.htm*
Zalviso Pivotal Studies: 
*Positive versus Placebo and Active Comparator*

**Placebo-Controlled Studies**

- Study IAP310: postoperative pain after abdominal surgery
- Study IAP311: postoperative pain after total hip or knee replacement surgery

**Zalviso vs. IV PCA morphine (IAP309)**

- Zalviso superior as measured by Patient Global Assessment (PGA) and onset of analgesia
- Easier to use as rated by patients and healthcare professionals
Zalviso: Studied for Ability to Treat Moderate to Severe Acute Pain

Pain Intensity Difference to Baseline for Phase 3 Studies

- Statistical separation between Zalviso and IV PCA within 1st hour (P=0.001)

Presentation at the 2014 American Pain Society Annual Meeting, April 30 – May 3, Tampa, FL.
Final Phase 3 Study IAP312:
Open-Label, Single-Arm
Designed to Evaluate Device Performance

IAP312 Multicenter Study

- Study designed specifically to address remaining FDA questions
- Protocol reviewed by FDA and revised based on FDA comments
- Plan to enroll ~315 patients
- 24- to 72-hour duration
- Single-arm, open-label, various postsurgical settings
- Study will collect device failure rate
- Nurses will actively look for dropped tablets
- Multimodal analgesia allowed
- Clinical supplies being prepared and tested
Approved in Europe: First commercial sale by Grunenthal in April 2016

Collaboration Details

- $50M received to date
- R&D and sales milestones remain
- Royalties from mid teens to mid twenties
- EU royalties and milestones partly sold
- Peak Revenues in EU expected to be $150M*
- Launched in Germany, France, UK
- Next launch countries: Belgium, Netherlands, Ireland, Italy (Summer); Portugal (Fall)

* Per market forecast study commissioned by ACRX performed by LEK
Issued Patents on Both Device and Drug Formulations

**IP Strategy**

- Drug-device combination allows for broad patent coverage
- Integrated IP and regulatory strategy designed to minimize ANDA exposure

**IP Portfolio**

- 12 US patents issued on NanoTab
  7 US patents issued on Devices
  Coverage through 2027 - 2031
- 3 EU patents issued on NanoTab
  2 EU patents issued on Device
  Coverage through 2027 - 2029
- 20 issued patents in other territories
- 11 US applications plus 30+ foreign applications in late stage prosecution
Cash on hand at March 31, 2016 > $100M

- Cash on hand at March 31, 2016: $107 million
- Projected cash balance Dec 31, 2016: $70-75 million
- Outstanding Loan Amount: $21 million
- Shares Outstanding: 45 million
- Headcount at March 31, 2016: 41
Significant number of data readouts and regulatory milestones anticipated over the next 18 months

<table>
<thead>
<tr>
<th>Milestone</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ARX-04</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAP-302 ER study results</td>
<td>3Q16</td>
<td></td>
</tr>
<tr>
<td>SAP303 Post-op results</td>
<td>3Q16</td>
<td></td>
</tr>
<tr>
<td>NDA</td>
<td>4Q16 submission</td>
<td>FDA Review</td>
</tr>
<tr>
<td>MAA</td>
<td>1Q17 submission</td>
<td>EMA Review</td>
</tr>
<tr>
<td><strong>Zalviso</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EU launch</td>
<td>3Q16</td>
<td>4Q16</td>
</tr>
<tr>
<td>IAP312 Initiation (TBD)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Thank you for listening

For more information, visit:
www.acelrx.com