

# AcelRx Pharmaceuticals Overview

March 2020



*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.; AcelRx's intentions, plans, hopes, beliefs, anticipations, expectations or predictions of the future; the number of REMS-certified facilities and formulary approvals expected by the end of 2020; statements relating to the consummation of the merger or other transactions, including the co-promotion agreement, with Tetrphase and the potential benefits of such transactions; the status of the collaboration and license agreement with Grünenthal or any other future potential collaborations, including potential milestones and royalty payments under the Grünenthal agreement; the therapeutic and commercial potential of AcelRx's products and product candidates, including potential market opportunities for DSUVIA, DZUVEO and ZALVISO; projected cash flows; expected R&D and SG&A expenses; and the Company's expected financial discipline. 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; the inability to maintain compliance with the DSUVIA Risk Evaluation and Mitigation Strategy; the inability to maintain regulatory approval of DSUVIA in the United States; the inability to secure regulatory approval of ZALVISO in the United States; the DSUVIA clinical trial results; the possibility that the FDA may dispute or interpret differently the results from the ZALVISO development program, including the results from the IAP312 clinical trial; 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 Annual Report on Form 10-K filed with the SEC on March 16, 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 most recent annual, quarterly or current report as filed or furnished with the SEC. The Company's SEC reports are available at [www.acelrx.com](http://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.

Presentation intended for investor use.

# Key leadership



**Vincent Angotti**  
Chief Executive Officer



- Chief Executive Officer and a member of the Company's Board of Directors in March 2017
- Over 25 years of experience leading executive and commercial teams at public and private life sciences companies
- Previous positions: CEO of XenoPort, Inc. , SVP Sales & Marketing of Reliant Pharmaceuticals, Inc., Career began at Novartis Pharmaceuticals where he held various roles of increasing responsibility

**Raffi Asadorian**  
Chief Financial Officer



- Chief Financial Officer since August 2017
- Over two decades of finance, strategy and corporate development experience at publicly traded and private equity owned companies
- Previous positions: CFO of Amyris, Unilabs, and PLIVA. Career began at PricewaterhouseCoopers where he was a Partner in its Transaction Services group

**Pamela P. Palmer, MD, PhD**  
Chief Medical Officer



- Co-founded AcelRx in July 2005 and serves as Director and Chief Medical Officer
- Director of the UCSF Pain Center for Advanced Research and Education (PainCARE) from 2005 to 2009; Co-founded Omeros Corporation in 1994
- Dr. Palmer has a medical degree and a doctorate in neuroscience from Stanford University, and continued on to the University of California, San Francisco for her anesthesia residency

AcelRx acquires Tetrphase in a stock for stock deal, agreed March 15, 2020  
and expected to close in Q2 2020



**AcelRx**  
*Pharmaceuticals, Inc.*



**TETRAPHASE**  
PHARMACEUTICALS

**AcelRx**  
*Pharmaceuticals, Inc.*

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**Acute**



**Chronic**



**Medically  
Supervised  
Setting**



**Patient  
Retail  
Script**





# Portfolio of approved and late-stage pipeline of sufentanil sublingual products for moderate-to-severe acute pain



- Single dose sufentanil sublingual 30 mcg tablet in a pre-filled applicator
- HCP administered in a Certified Medically Supervised Setting
- US/EU large potential market opportunity in multiple settings<sup>1</sup>



- Multiple doses sufentanil sublingual 15 mcg tablets in a 40-count cartridge
- Patient administered in a Medically Supervised Setting
- Approved and Marketed in EU
- US: potentially complementary market opportunity with DSUVIA



1. Data on file. In-house commissioned market research. QuintilesIMS, "ARX-04 and ZALVISO US forecast" December 2016 & "ARX-04: Asset forecast for Europe – Emergency medical services and Postoperative pain" May 2016

This presentation is intended for investors, not health care professionals. Zalviso is an unapproved investigational drug in the U.S. See boxed warning, including ISI and full prescribing information at the conclusion of this presentation.

# Opioid related medication errors continue to plague the acute care setting



2005



2017



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)*

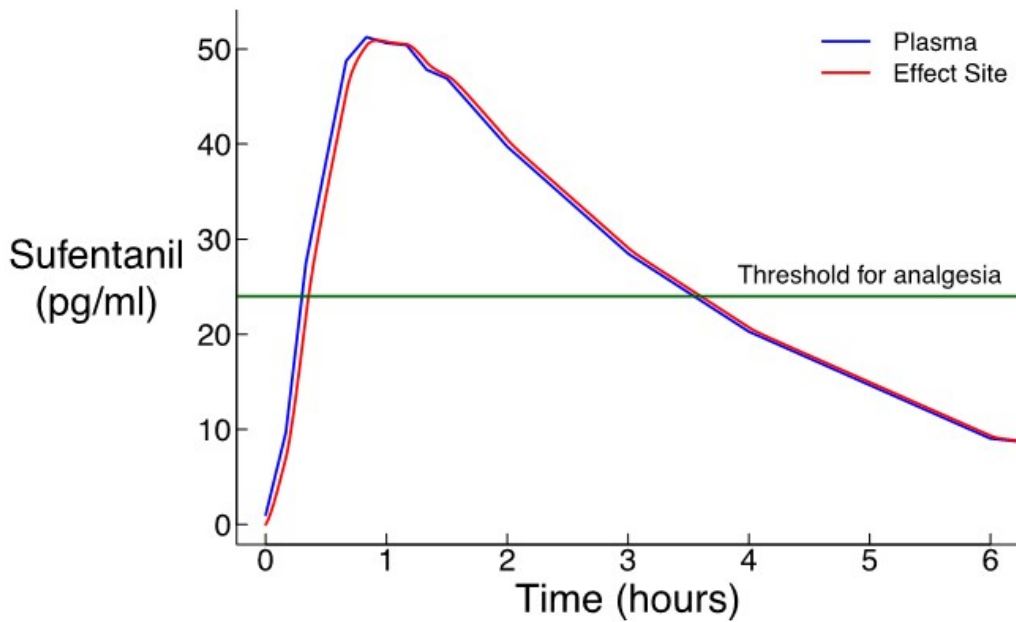




# Sublingual Sufentanil addresses an unmet need in acute pain management



## Sufentanil Sublingual (30 mcg)<sup>1</sup>



***The PK profile shows analgesia as early as 15 minutes and with a duration of ~3 hours<sup>2,3,4</sup>***

1. Fisher DM, et al. Pharmacokinetic Properties of a Sufentanil Sublingual Tablet Intended to Treat Acute Pain. *Anesthesiology* 2018; 128:943-52  
2. Sufentanil effect site concentrations modeled by D. Fisher MD, consultant to AcelRx, based on the work by Scott et al., *Anesth* 1991  
3. Lehmann et al. 1991 *Acta Anaesthesiol Scand* 1991

# Proprietary 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



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



## DSUVIA® sufentanil sublingual tablet (SST) 30 mcg

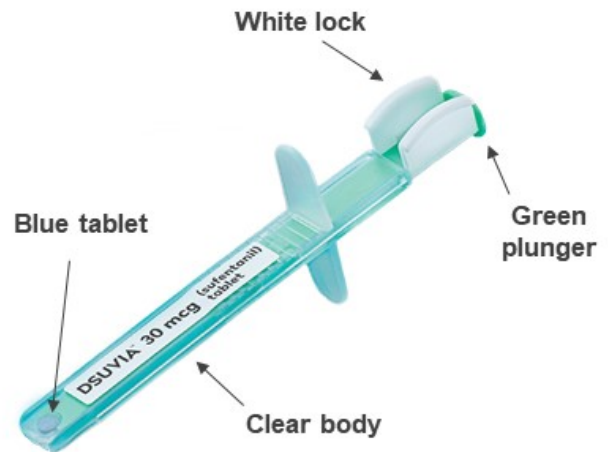
DSUVIA is indicated for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.<sup>1</sup>

### Applicator features

- Blue tablet visible through clear applicator
- White lock prevents accidental dispensing

### Developed with attention to diversion issues

- Unique small solid blue tablet
- 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
- Barcode for automatic dispensing cabinets (ADC)



11 1. DSUVIA [package insert]. Redwood City, CA: AcelRx Pharmaceuticals, Inc; 2019.

# An alternative to IV opioids for moderate-to-severe acute pain in hospitals, surgical centers and ED's

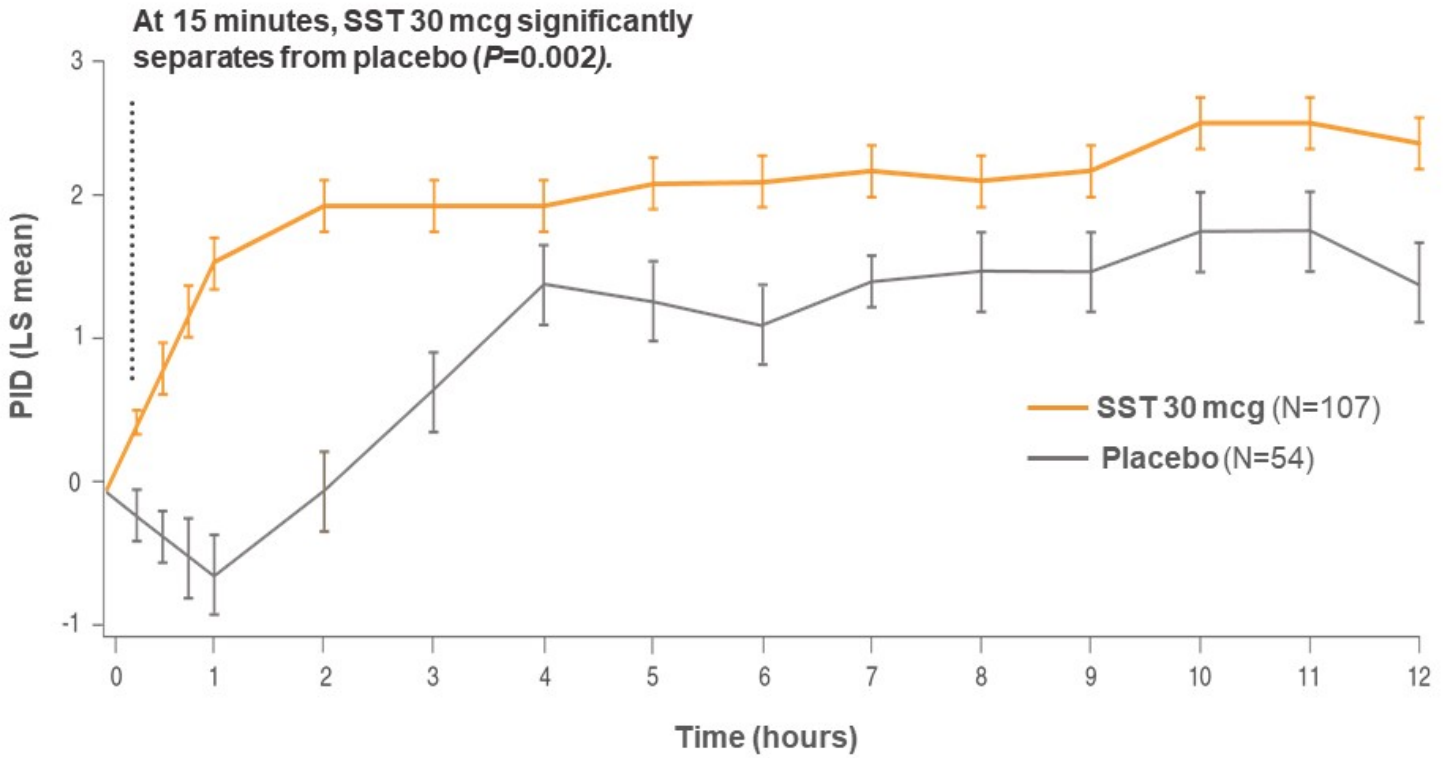


Approximately  
equivalent to a  
standard dose of  
5mg IV  
morphine



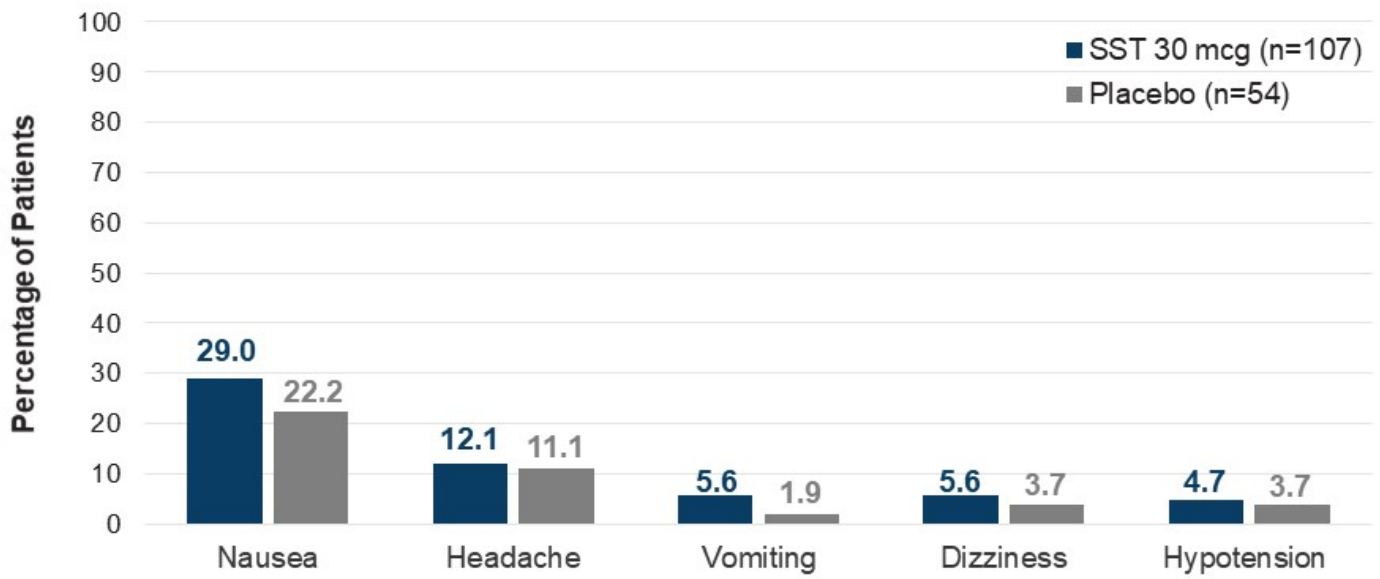
**DSUVIA**  
(sufentanil)  
sublingual tablet 30 mcg

# Postoperative Abdominal Pivotal Study: Pain Intensity Difference (PID) Over the First 12 Hours<sup>1,2</sup>



1. Minkowitz HS, et al. *Pain Pract.* 2017;17(7):848-858.
2. DSUVIA [package insert]. Redwood City, CA: AcelRx Pharmaceuticals, Inc; 2019.

# DSUVIA most common adverse reactions<sup>1,2,\*</sup>



\*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**

1. DSUVIA [package insert]. Redwood City, CA: AcelRx Pharmaceuticals, Inc; 2019.

14 2. Minkowitz HS, et al. *Pain Pract.* 2017;17(7):848-858.





## REMS Goal

*To mitigate the risk of respiratory depression resulting from accidental exposure*

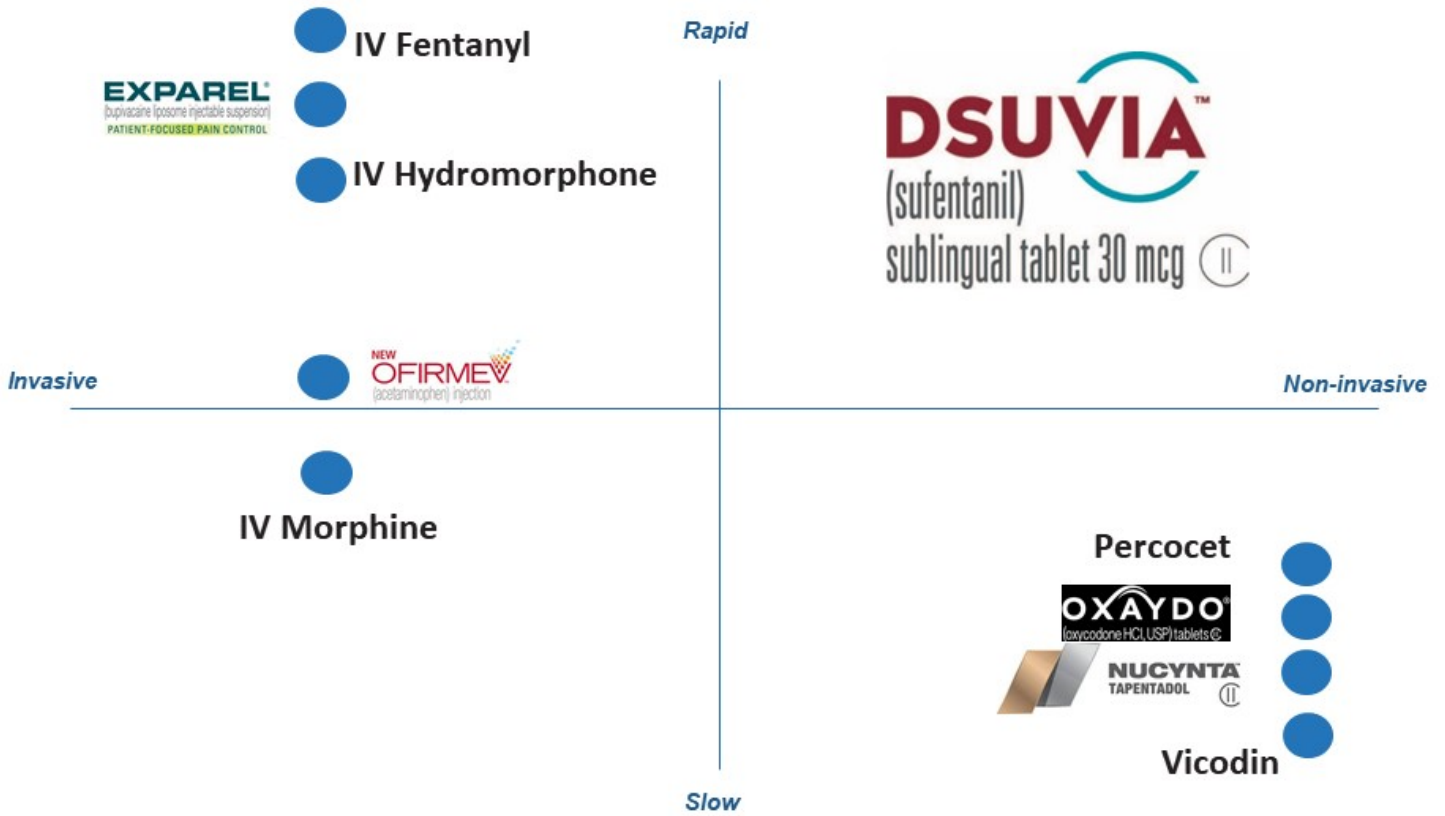
### Healthcare settings must:

- Be able to manage acute opioid overdose
- Establish processes and procedures so that DSUVIA is not dispensed outside of certified healthcare setting
- Train relevant staff that DSUVIA is not to be dispensed outside of certified setting and to refer to the Directions for Use prior to administration

### Wholesalers must:

- Establish processes and procedures and ensure that DSUVIA is distributed only to certified healthcare settings

# A clear unmet need in acute pain management



# DSUVIA has an opportunity to address unmet needs for patients and healthcare providers



**Patient  
experience**



**Ease of use**



**Hospital/ER  
efficiency**



**No risk of IV  
infection**

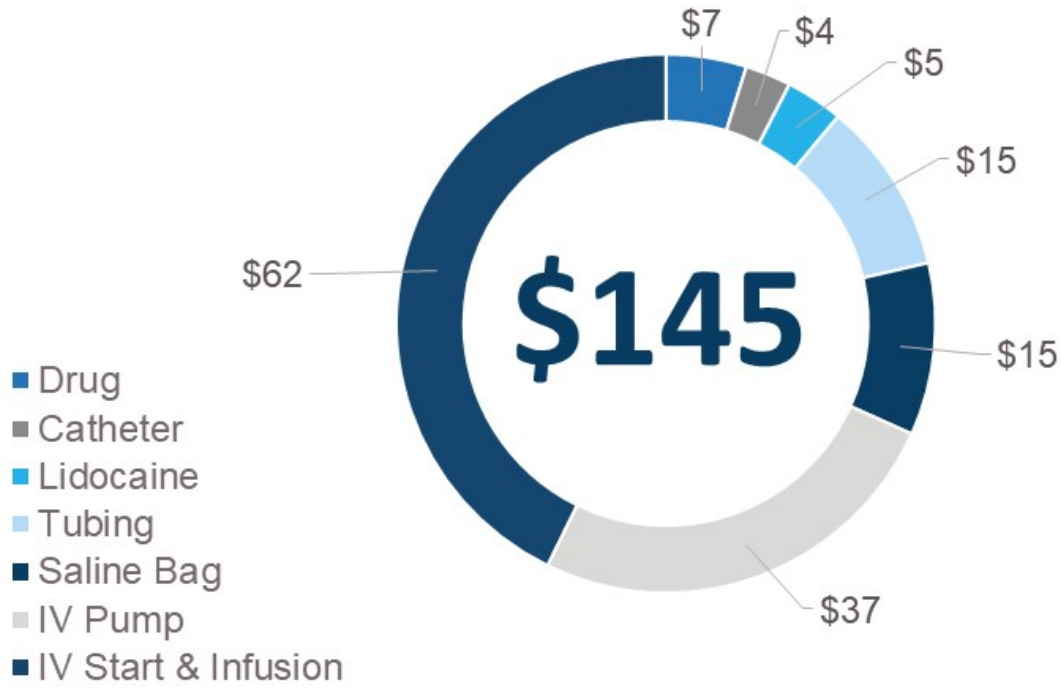


**Lower total  
cost**

# IV administration is resource and cost intensive



## Component cost of IV opioid dose<sup>1</sup>

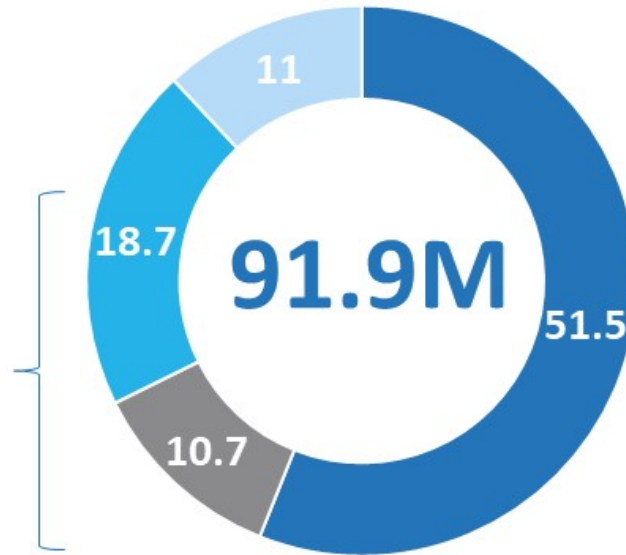


# 91.9M adult moderate-to-severe acute pain patient visits in medically supervised settings

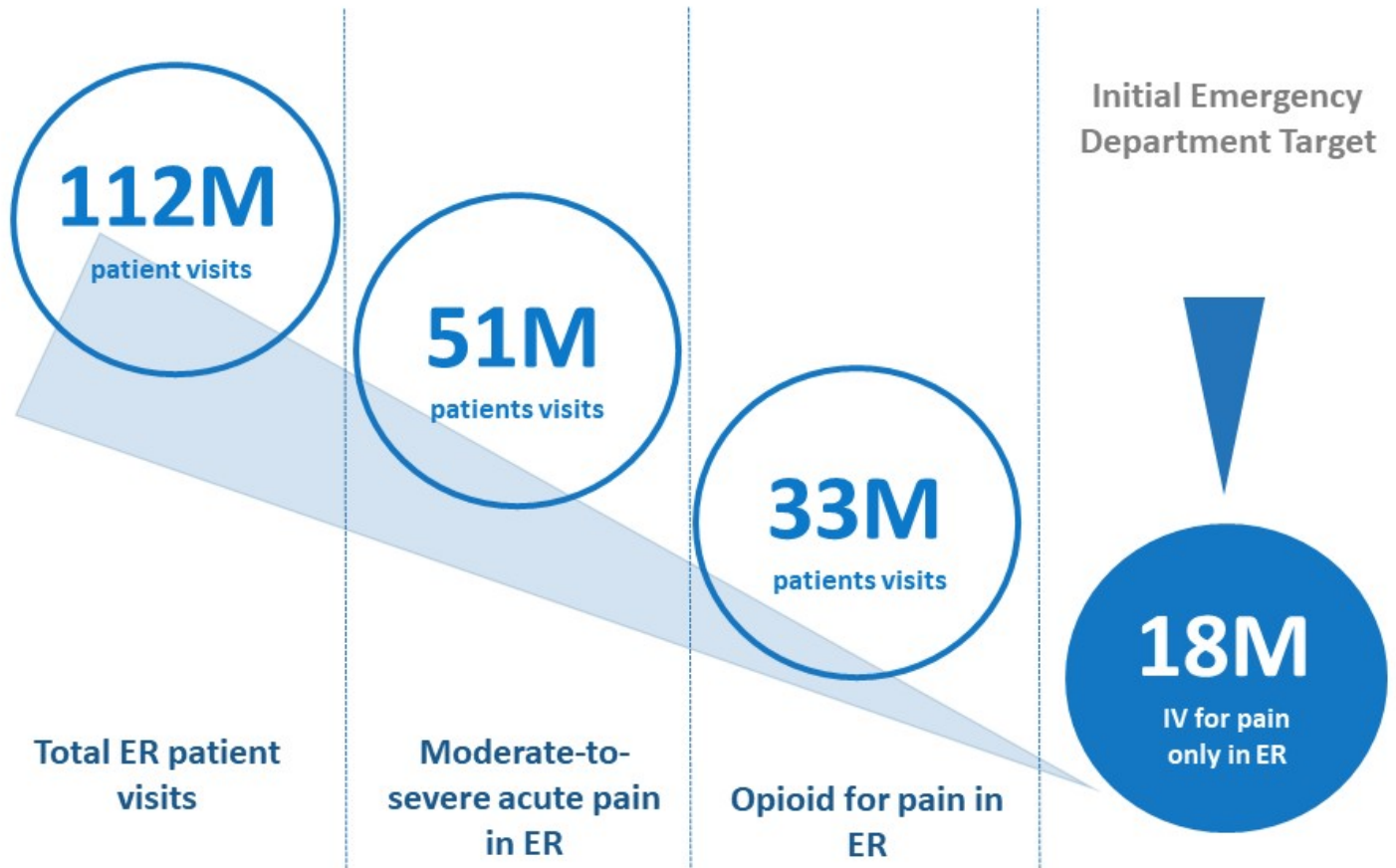


- Emergency department
- Outpatient surgery
- Other procedures
- Inpatient/other surgery

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

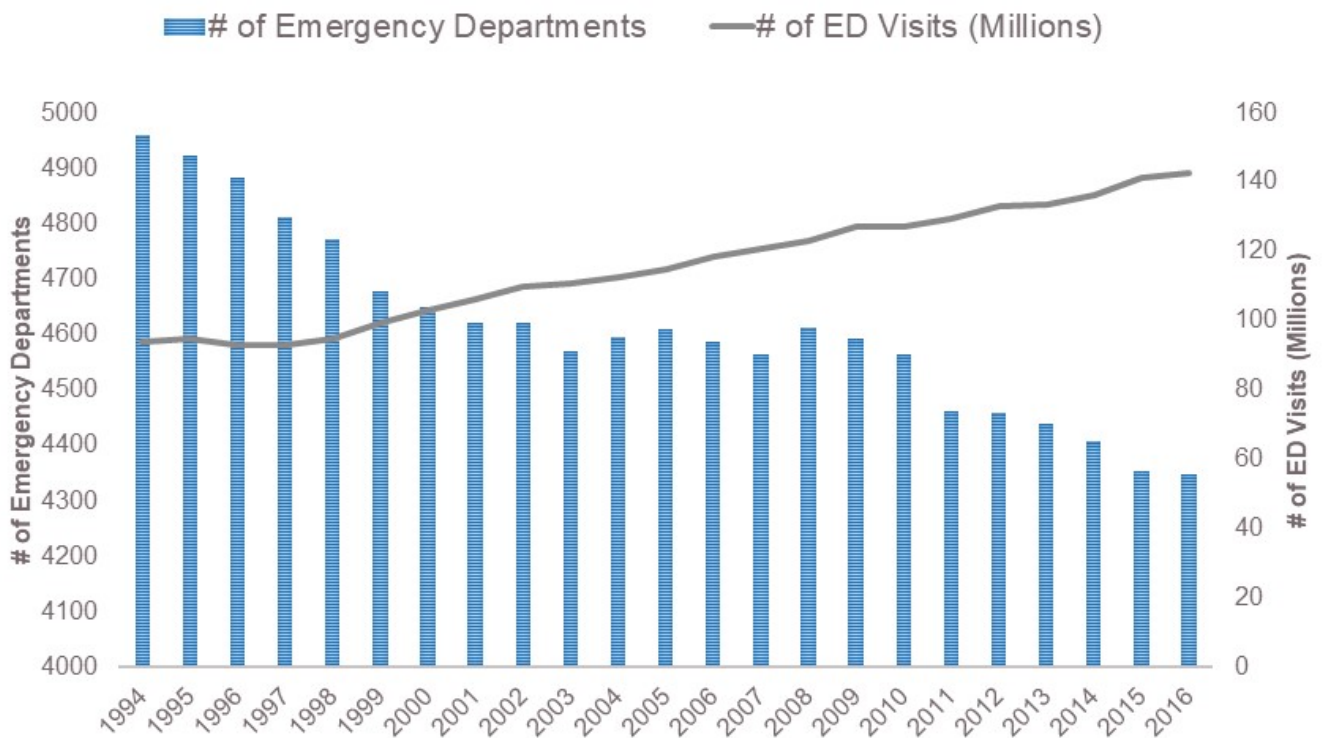


# Initial emergency department target of 18M adult patient visits annually receiving IVs exclusively for pain meds





# Overcrowding of emergency departments driving need to find ways to improve patient throughput

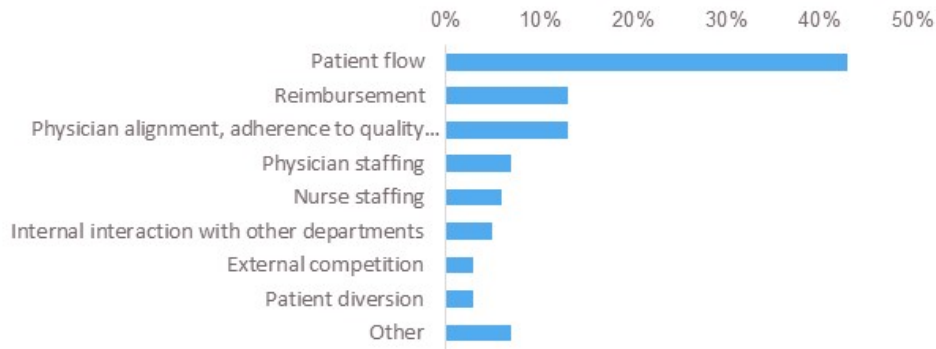


Reference: Aha.org [Internet] Trend Watch Chartbook 2018. Available from <https://www.aha.org/system/files/2018-07/2018-chartbook-table-3-3.pdf>

# IV access delays treatment in the Emergency Department



250 hospital administrators asked to rank ED challenges<sup>1</sup>



**64**

Minutes

(n=144)

Median time from triage to IV access for patients not requiring advanced IV techniques (IQR 30 to 146 minutes)<sup>1</sup>

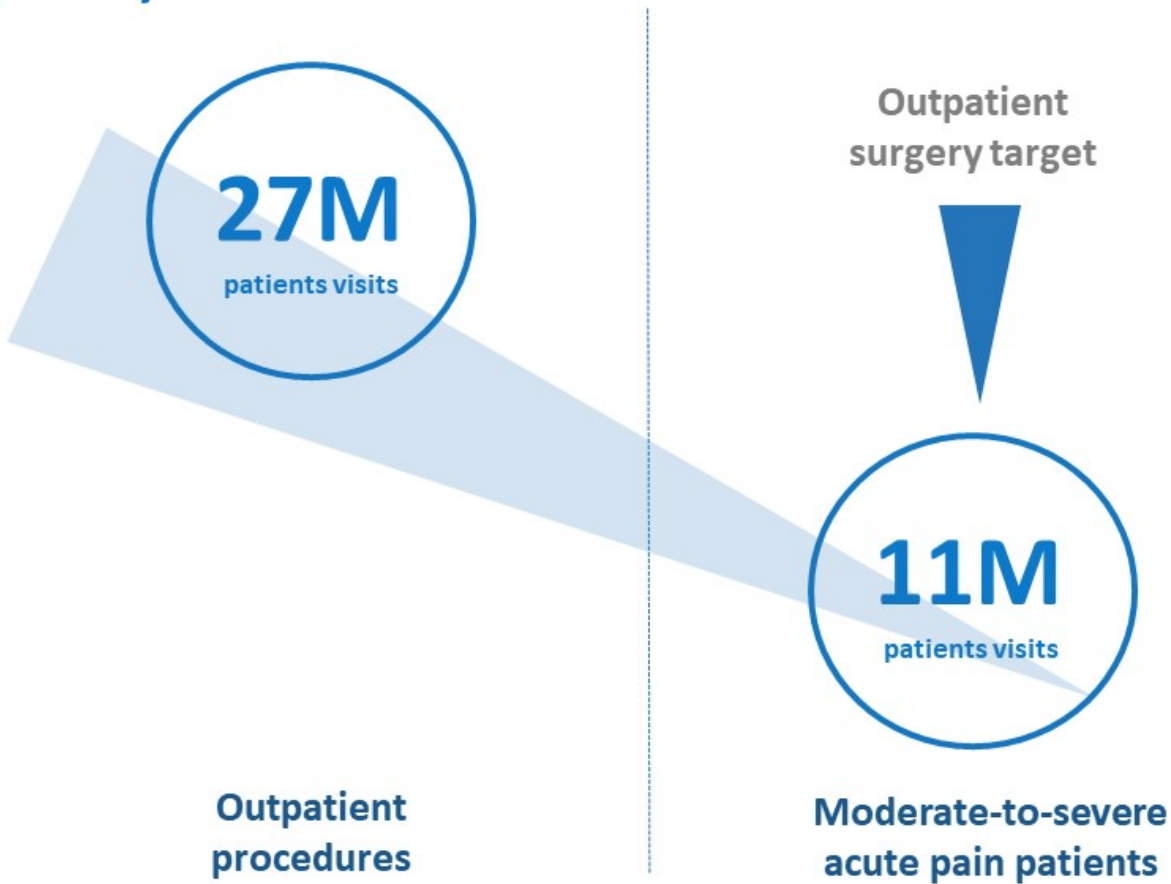
**199**

Minutes

(n=91)

Median time from triage to IV access for patients requiring advanced IV techniques (IQR 131 to 350 minutes)<sup>2\*</sup>

# DSUVIA outpatient surgery opportunity is estimated at 11M adult patient visits annually, where patient throughput is a priority



# Approximately 1,200 hospitals will be a core focus for the launch



**5,530**  
Hospitals

Meet our target criteria

**3,000**  
Hospitals

## Hospital Target Criteria

- Emergency Dept. volume
- Outpatient surgery volume
- Early adopters
- Access

## Initial Focus

**1,200**  
Hospitals

*70% of  
potential  
opportunity*



# Approximately 1,100 ASCs will be our initial non-hospital launch targets



## ASC Target Criteria

- Relevant ASC specialty
- Geographical proximity to hospital targets
- Procedural volume

**11,300**  
ASCs

Relevant ASC specialty

**6,800**  
ASCs

Relevant ASC specialty in existing territory

**5,700**  
ASCs

**Initial Focus**

**1,100**  
ASCs

*60% of potential opportunity*





# Staged commercial launch plan with Q3 being the first quarter with 40 hospital account managers; beginning March 16, co-promoting with Tetraphase



**AceIRx**  
Pharmaceuticals, Inc.

Co-promotion

Q1 2019

15

Account  
Managers

Q3 2019

40

Account  
Managers

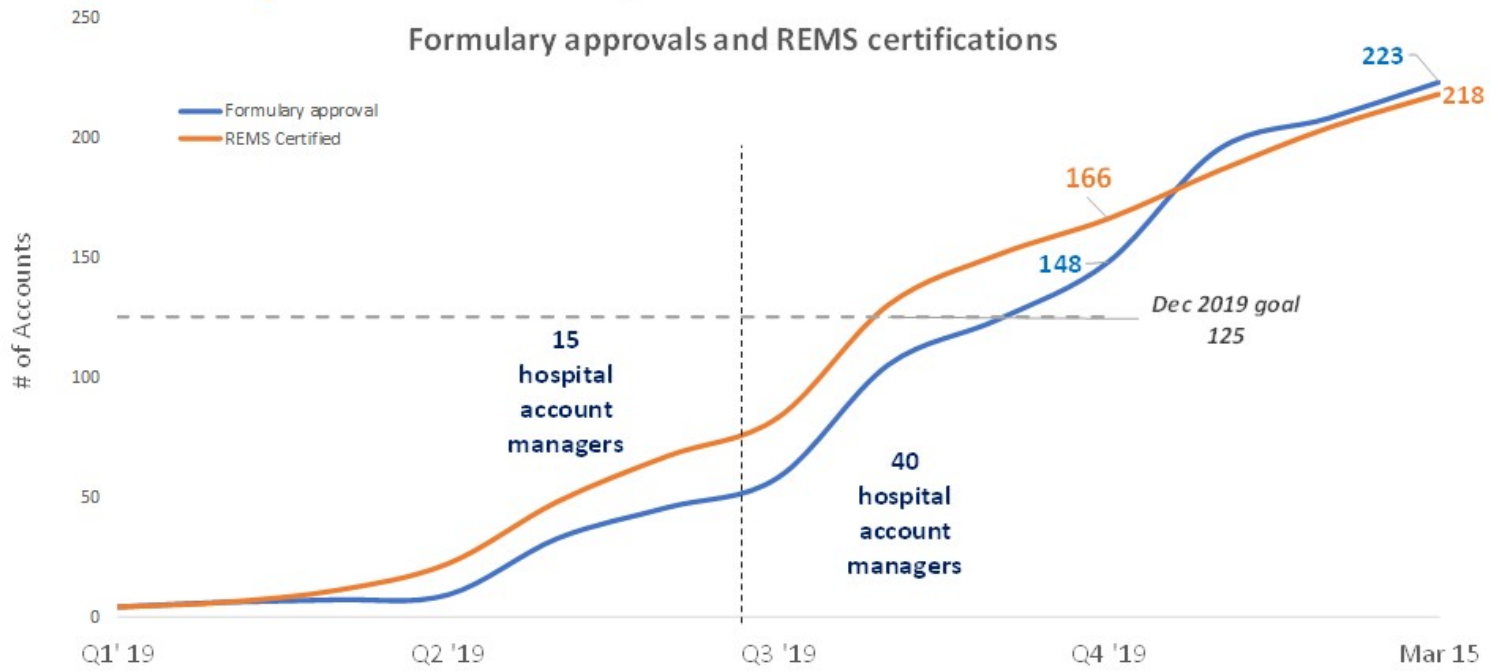
March 16  
2020

35

Combined  
Account  
Managers



# 166 REMS-certified facilities and 148 formulary approvals exceeded year-end goal of 125 for each; 218 and 223, respectively as of March 15, 2020



**465**  
Target 2020  
formulary  
approvals

**465**  
Target 2020  
REMS-  
certified  
facilities



# Zalviso

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# Zalviso®: Sufentanil Sublingual 15 mcg in a patient-controlled analgesia (PCA) system



reddot award  
product design



## Proposed Indication

Management of moderate-to-severe acute pain in adult patients in an in-patient hospital setting

## Dosing

40 count - 15 mcg tablets / cartridge

## Development Status

- Clinical Study in life portion completed
- NDA resubmission timing being evaluated
- Type II resubmission – 6 month review
- Launched in Europe April 2016 by our partner

*Zalviso is an investigational drug in the U.S. and not FDA-approved for commercial use*

**AcelRx**  
Pharmaceuticals, Inc.

# Zalviso IAP312 trial results achieved study objectives



**2.2%**

**7 patients out of 320 experienced a device error (2.2%)**

4 of 7 pts. experienced analgesic gap due to tablet not dispensed

Standard of care (IV PCA) device error ~ 12%<sup>1</sup>

**<0.1%**

**7 tablets discovered by HCP out of 7,293 dispensed (<0.1%)**

The 7 misplaced tablets occurred with 6 patients

No repeat dropped tablets following re-training

Patient Global Assessment	% Success
PGA 24 hrs	86
PGA 48 hrs	89
PGA 72 hrs	100

HCP Global Assessment	% Success
HPGA 24 hrs	91
HPGA 48 hrs	95
HPGA 72 hrs	100

# Zalviso is being commercialized in Europe with our partner, Grünenthal



ZALVISO®



**Welcome to the ZALVISO® Resource Centre**

A free, simple way to learn more about ZALVISO® and how to implement it in your clinical setting. Please proceed to the appropriate website

**I AM A HEALTHCARE PROFESSIONAL**

This site has been designed specifically for healthcare professionals who would like more in-depth information about ZALVISO®. By entering the HCP ZALVISO® Website, you are declaring and confirming that you are a healthcare professional.

**I AM A PATIENT OR A MEMBER OF THE PUBLIC**

This site has been designed specifically for patients and members of the public. It contains general educational information about ZALVISO®. By entering the Patients and Public ZALVISO® Website, you understand that this site is intended to provide educational information.

## XERAVA: Launched in the U.S.

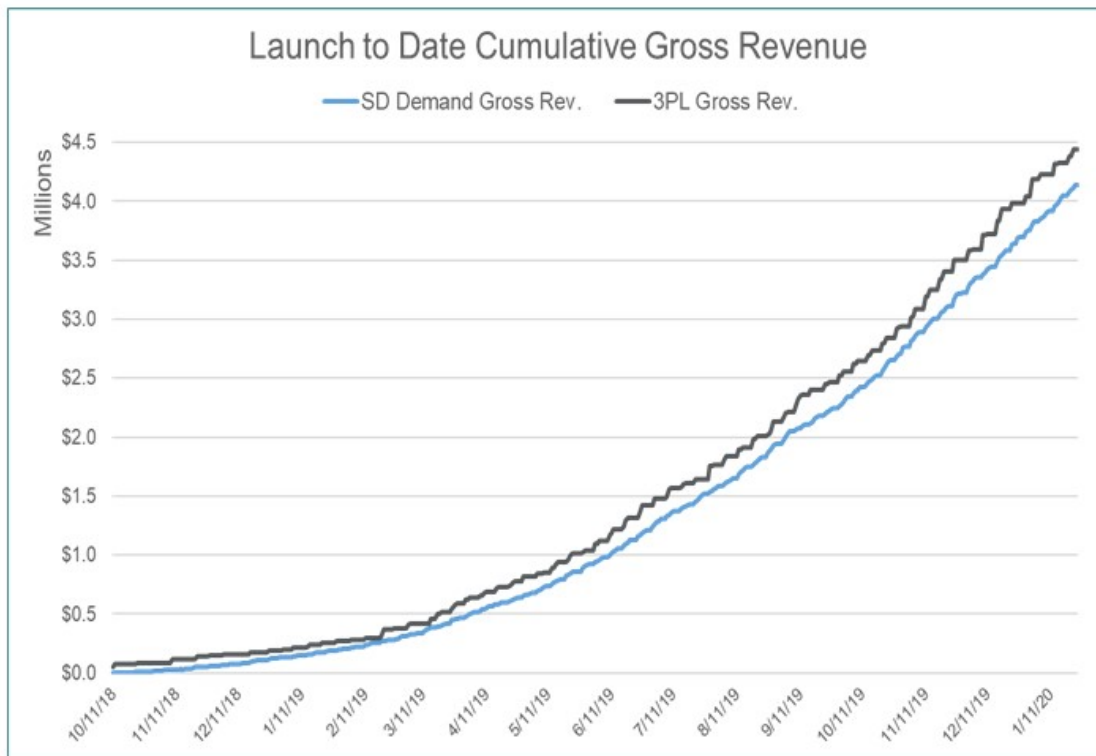


XERAVA (eravacycline) for the treatment of complicated intra-abdominal infections in patients 18 years of age and older

- FDA approved on August 27, 2018
- EMA approved on September 20, 2018
- Launched in the U.S. in mid-October 2018
- Label supports broad use

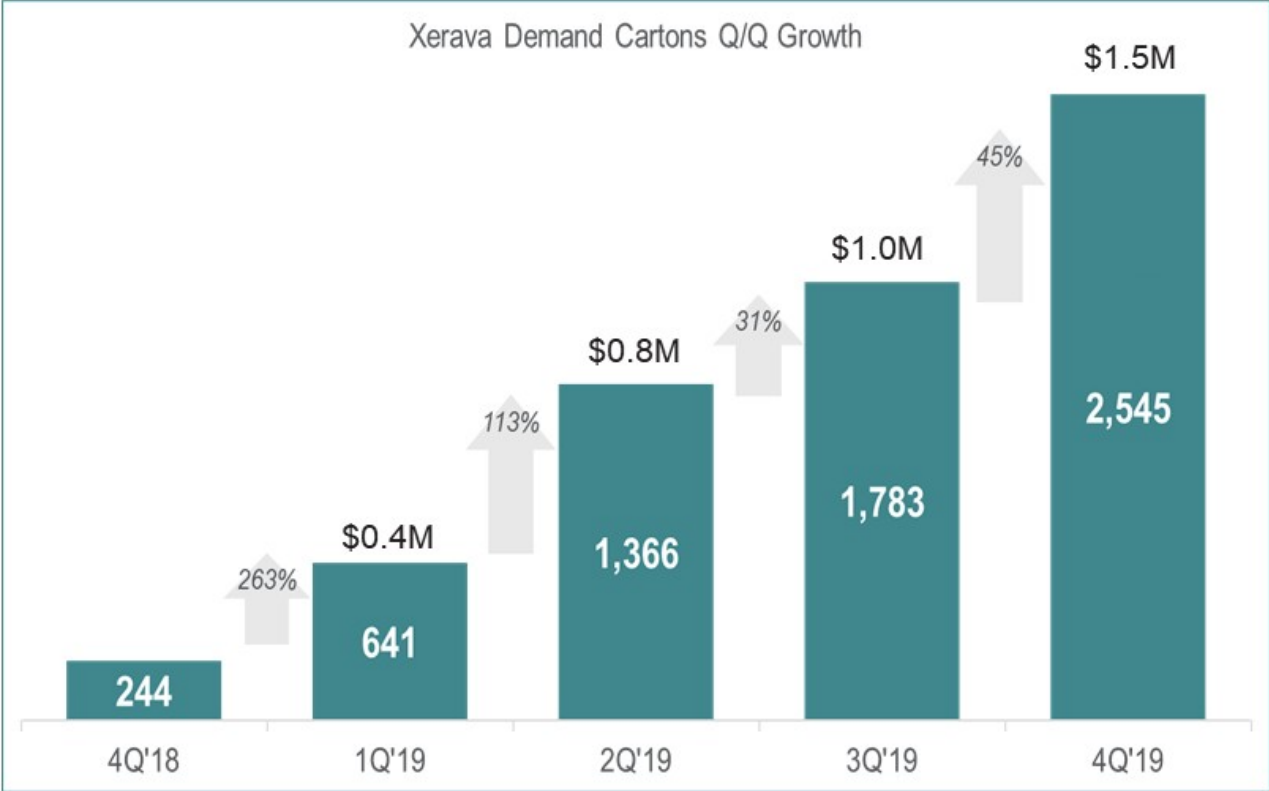






- A different molecule leads to a different antibiotic launch
  - No stocking the retail channels to inflate revenue, Demand revenue mirrors Wholesaler revenue
- Patient days of Therapy for IV antibiotics are **>3 fold** any recent launch
- **Triple to Double digit** quarter over quarter growth in 2019
- On formulary or available at **1200** institutions
- Strong start to 2020 trending to have **double digit** quarterly growth vs Q4 2019
- Ample supply to address the challenges we are currently facing

# XERAVA quarterly carton growth



Source: 867 thru 12/31/19

# Achieved 2019 objectives, building the foundation for growth in 2020



125 formulary approvals / REMS-certified facilities by year-end \*\*



Hire 25 new hospital account managers, targeting 40 by beginning of Q3



Resubmit Zalviso NDA

*\* awaiting FDA opioid approval policy finalization*

Quarterly operating expense not exceeding \$15M to \$18M \*



Refinance senior debt



\* Combined R&D and SG&A, including ~\$2M/qtr of non-cash stock-based comp; \$13M to \$16M quarterly operating expense excluding stock-based compensation

\*\* Added REMS certified facilities metric in Q2



**223**

Formulary approvals  
at March 15, 2020

**218**

REMS certified  
facilities at March  
15, 2020

**465**

target formulary  
approvals and  
REMS certs. by  
year-end 2020

**\$2.3M**

FY19 revenues

**\$9-12M**

2020 operating expense  
guidance\*

**\$66.1M**

Dec 2019 cash

*\* Combined R&D and SG&A, excluding  
non-cash stock-based comp*

# AcelRx investment highlights



- **DSUVIA commercial launch in late February 2019; with full 40 rep salesforce beginning in Q3 2019**
  - European approval received in June 2018 (DZUVEO); in discussion with potential partners
  - US market opportunity is over 91M patients in multiple settings<sup>1</sup>
- **Zalviso FDA resubmission timing awaiting new FDA opioid approval policy finalization**
  - Successfully completed IAP312 study in 7/2017; awaiting DSUVIA REMS reporting and EU study data for use in an expected Adcom
  - Commercial launch in Europe – over 50,000 patients in 300 hospitals since launch
- **74 issued patents (24 in US); 16 Orange Book listed patents expiring from 2027 to 2031**
- **\$66.1 million of cash at December 31, 2019**
- **223 formulary approvals and 218 REMS-certified facilities at March 15, 2020 increasing to a planned 465 for each by end of 2020**





For more information, visit:  
**[www.aceIrx.com](http://www.aceIrx.com)**

For Important Safety Information including full prescribing information, visit: [www.DSUVIA.com](http://www.DSUVIA.com).

**AceIrx**  
Pharmaceuticals, Inc.



# Important safety information for DSUVIA



## 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.



#### **Additional Information and Where to Find It**

In connection with the proposed transaction between AcetRx Pharmaceuticals, Inc. (AcetRx) and Tetrphase Pharmaceuticals, Inc. (Tetrphase), AcetRx will file with the SEC a registration statement on Form S-4 that will include a document constituting a prospectus of AcetRx and will also contain a proxy statement of Tetrphase. AcetRx and Tetrphase also plan to file other relevant documents with the SEC regarding the proposed transactions. After the registration statement on Form S-4 is declared effective by the SEC, a definitive proxy statement/prospectus will be mailed to the stockholders of Tetrphase. INVESTORS AND SECURITY HOLDERS ARE URGED TO READ THE PROXY STATEMENT/PROSPECTUS AND OTHER RELEVANT DOCUMENTS FILED WITH THE SEC CAREFULLY AND IN THEIR ENTIRETY WHEN THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION. Investors and security holders will be able to obtain free copies of the registration statement on Form S-4 and the proxy statement/prospectus (when available) and other relevant documents filed or that will be filed by AcetRx or Tetrphase with the SEC through the website maintained by the SEC at <http://www.sec.gov>. Copies of the documents filed with the SEC by AcetRx will be available free of charge within the Investors section of AcetRx's website at <http://ir.acetrx.com>. Copies of the documents filed with the SEC by Tetrphase will be available free of charge within the Investors section of Tetrphase's website at <https://ir.tphase.com/investor-relations>.

#### **Participants in the Solicitation**

Each of AcetRx and Tetrphase and their respective directors and executive officers may be deemed to be participants in the solicitation of proxies from Tetrphase stockholders in connection with the proposed transaction. Information about AcetRx's directors and executive officers is included in the definitive proxy statement for its 2019 annual meeting of stockholders, which was filed with the SEC on May 14, 2019. Information about Tetrphase's directors and executive officers is included in Tetrphase's Annual Report on Form 10-K for the fiscal year ended December 31, 2019, which was filed with the SEC on March 12, 2020. Other information regarding the participants in the solicitation of proxies in connection with the proposed transaction and a description of their direct and indirect interests, by security holdings or otherwise, will be contained in the proxy statement/prospectus and other relevant materials to be filed with the SEC regarding the proposed transaction when they become available. When available, investors may obtain free copies of these documents from AcetRx or Tetrphase as indicated above.

#### **No Offer or Solicitation**

This communication is being made in respect of the proposed transaction involving AcetRx and Tetrphase. This communication does not constitute an offer to sell or the solicitation of an offer to buy any securities nor a solicitation of any vote or approval with respect to the proposed transaction or otherwise. No offering of securities shall be made except by means of a prospectus meeting the requirements of Section 10 of the Securities Act of 1933, as amended, and otherwise in accordance with applicable law.