

AcelRx analyst and investor day

December 11, 2018

AcelRx
Pharmaceuticals, Inc.

Forward-looking 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 timing of and approach to the planned commercial launch of DSUVIA in the U.S.; 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; and the therapeutic and commercial potential of AcelRx's product candidates, including potential market opportunities for DSUVIA, DZUVEO and ZALVISO; projected cash flows; as well as the Company's expected financial discipline as it continues preparation for commercial launch. 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 delays in 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 9, 2018 and its Quarterly Report on Form 10-Q filed with the SEC on November 5, 2018. 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 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.



Agenda for the day

Introduction	<i>Vince Angotti</i>	8:30
Multimodal approaches to acute pain management	<i>Dr. Eugene Viscusi</i>	8:45
DSUVIA™ PK and clinical data	<i>Dr. Pam Palmer</i>	9:00
Expert Panel	<i>Moderator: Dr. Pam Palmer</i>	9:10
DSUVIA commercialization	<i>Vince Angotti</i>	10:25
Conclusion and Q&A	<i>ACRX management</i>	10:45



Introduction

Vince Angotti



DSUVIA[™]
(sufentanil)
sublingual tablet 30 mcg 

DSUVIA[™]
(sufentanil)
sublingual tablet 30 mcg 

DSUVIA REMS 

Important Safety Information 

U.S. Prescribing Information 

Directions for Use 

For U.S. Residents Only

NOW APPROVED

DSUVIA (sufentanil) sublingual tablet 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.

PRESCRIBING INFORMATION 

DIRECTIONS FOR USE 





5 mg IV morphine

One DSUVIA is approximately equivalent to a standard dose of 5 mg IV morphine





0.5%

Percentage of misused opioids stolen from a healthcare setting⁽¹⁾

DSUVIA will ONLY be used within a certified medically supervised healthcare setting with a REMS

Opioid related medication errors continue to plague the acute care setting



2005



2017



Opioid dosing is the
second
most frequent
medication error within the
acute hospital setting

DSUVIA is the only transmucosal opioid indicated for acute pain in settings such as hospitals, surgical centers and emergency departments



Other transmucosal opioids



Indication

Opioid agonist indicated for the management of breakthrough pain in cancer patients 18* years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy

Contraindication

Acute or postoperative pain including headache/migraine and dental pain, or acute pain in the emergency department.

Continued intravenous opioid shortage issue in hospitals



Hospitals Face Prolonged Injected Opioid Shortage
The other opioid crisis: Hospitals are frequently running out of widely used injected painkillers, and some patients are feeling the pain.
June 27, 2018

Los Angeles Times

The other opioid crisis: hospitals are running short of powerful painkillers

By PAULINE BARTOLONE
MAY 16, 2018



Pfizer manufacturing ills mean ongoing shortages for hospitals

by [Eric Palmer](#) | Oct 30, 2018

STAT

Hospitals are confronting a new opioid crisis: an alarming shortage of pain meds

By CASEY ROSS
MARCH 15, 2018



Urgent action necessary to address opioid drug shortage

August 25, 2018
Jai N. Patel, PharmD, BCOP



Survey Report
Survey conducted April 2018.

98.4% of respondents have experienced severe or moderate shortages of morphine, hydromorphone, and fentanyl.



In the midst of a massive opioid crisis, hospitals are experiencing an opioid shortage

By [Aaron Schachter](#) May 14, 2018

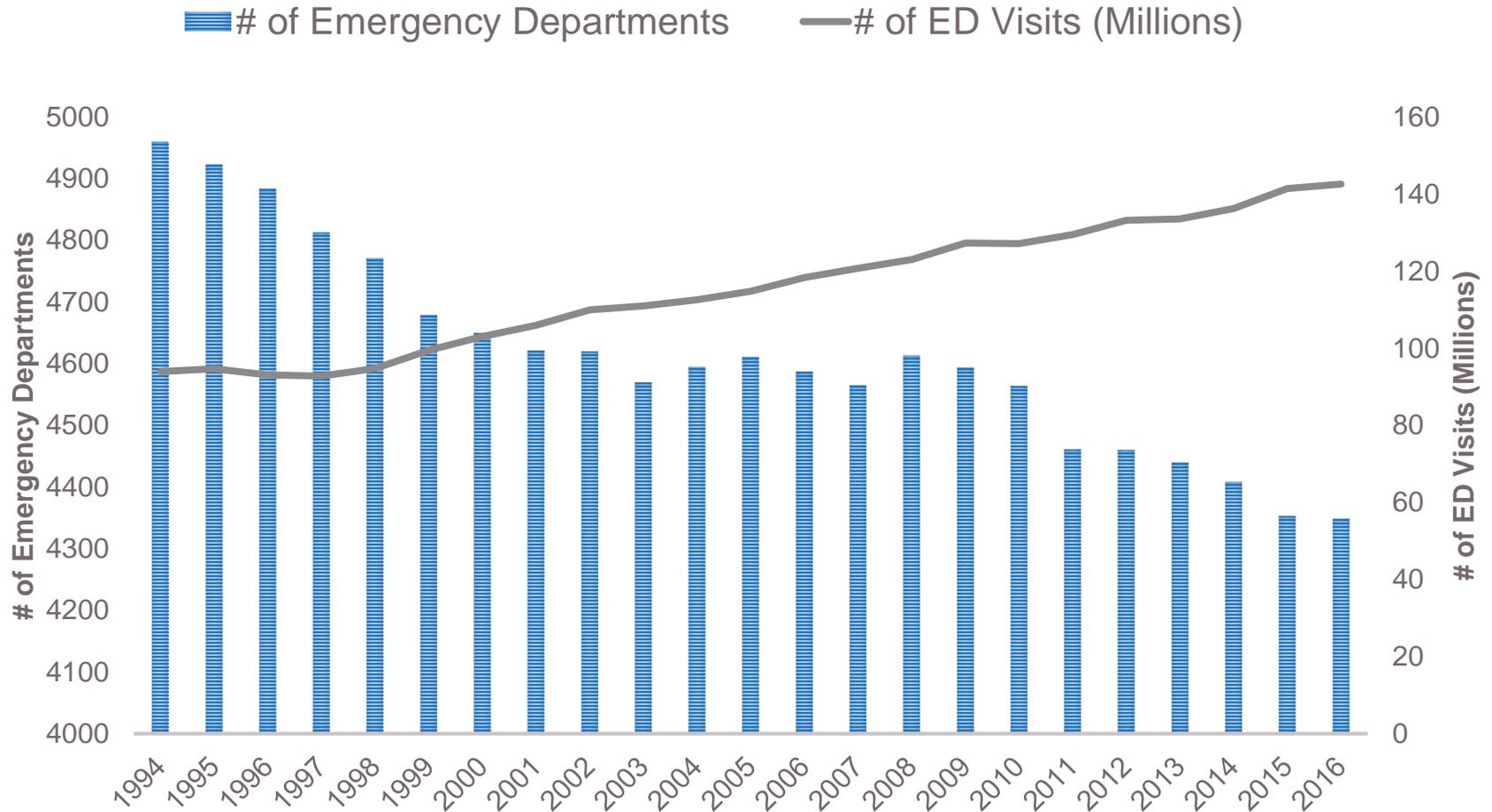


DSUVIA[™]
(sufentanil)
sublingual tablet 30 mcg 

EFFECTIVE PAIN RELIEF,

Efficiently Delivered.

The number of emergency departments are declining while annual visits continue to increase



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

Delays in the Emergency Department: time is money



Overcrowding in the ED results in patients leaving without being seen and diverted ambulance patients – both leading to lost revenue to the hospital



Estimates of annual lost revenue for every 1-hour ED delay: Per 50,000 annual ED visits - ranges from \$4.1M to \$10.0M^{1,2}

IV access delays treatment in the Emergency Department



64

Minutes
(n= 144)

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

199

Minutes
(n=91)

Median time from triage to IV access for patients requiring advanced IV techniques (IQR 131 to 350 minutes)^{1*}

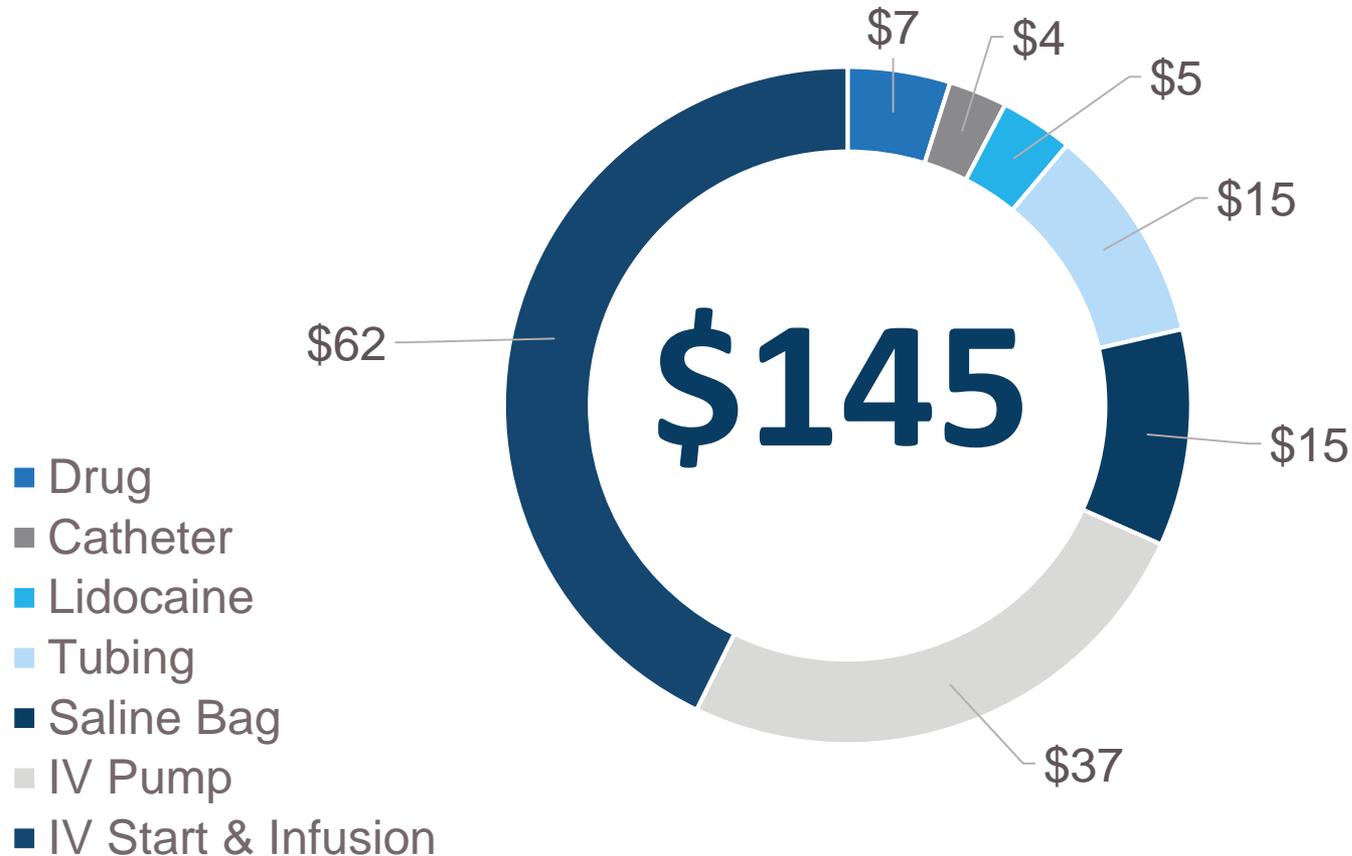
Reference: 1. Witting et al., 2017

* Advanced IV techniques includes such things as ultrasound guidance for peripheral IV access or external jugular vein catheterization

IV administration is resource and cost intensive



Component cost of IV dose¹



Watch the ease of administering a DSUVIA





Multimodal approaches to acute pain management

Dr. Eugene Viscusi



DSUVIA PK and clinical data

Dr. Pam Palmer

Indication and limitations of use

For U.S. Residents Only

NOW APPROVED

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[PRESCRIBING INFORMATION](#)

[DIRECTIONS FOR USE](#)



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



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 Risk Evaluation and Mitigation Strategy (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 only available 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 healthcare setting.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with 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 each patient's risk prior to 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 all 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

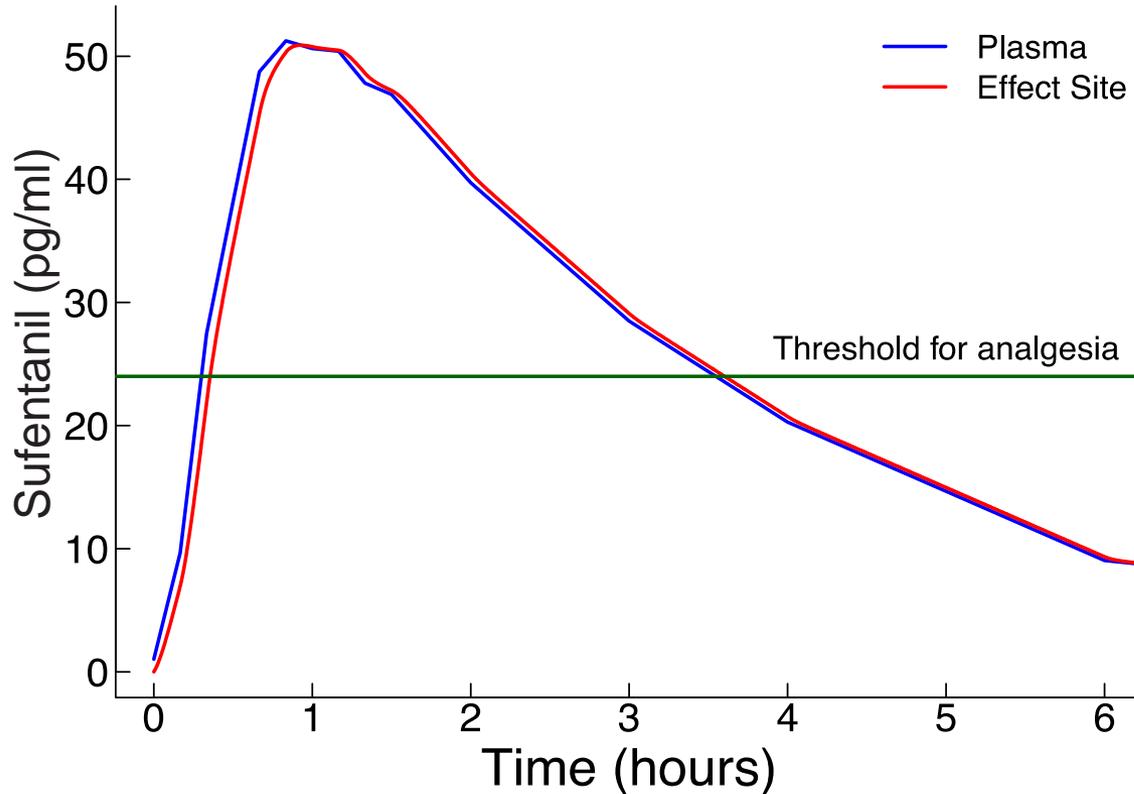
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.

- Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

DSUVIA pharmacokinetics matches the pharmacodynamics



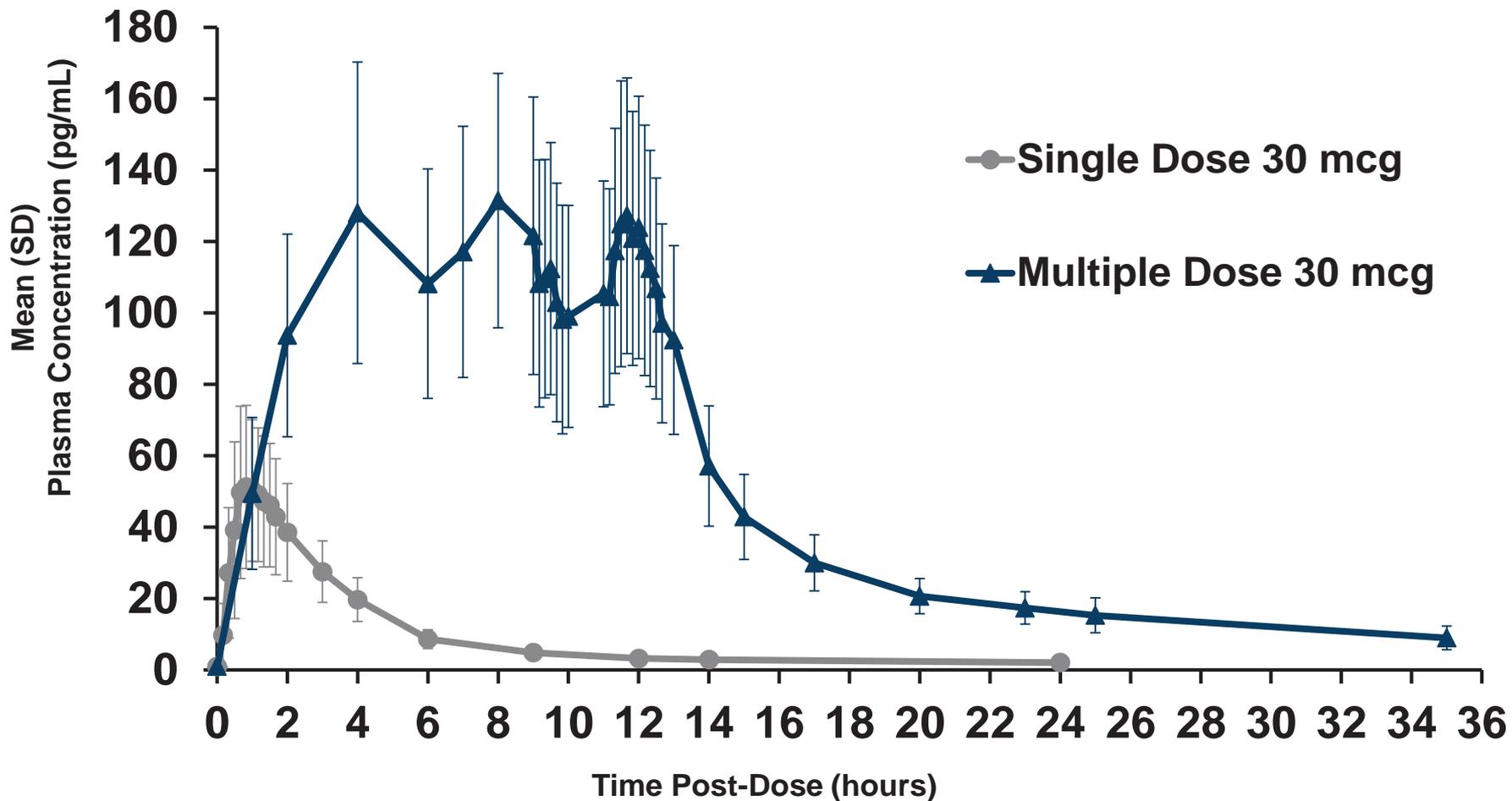
Sufentanil Sublingual (30 mcg)¹



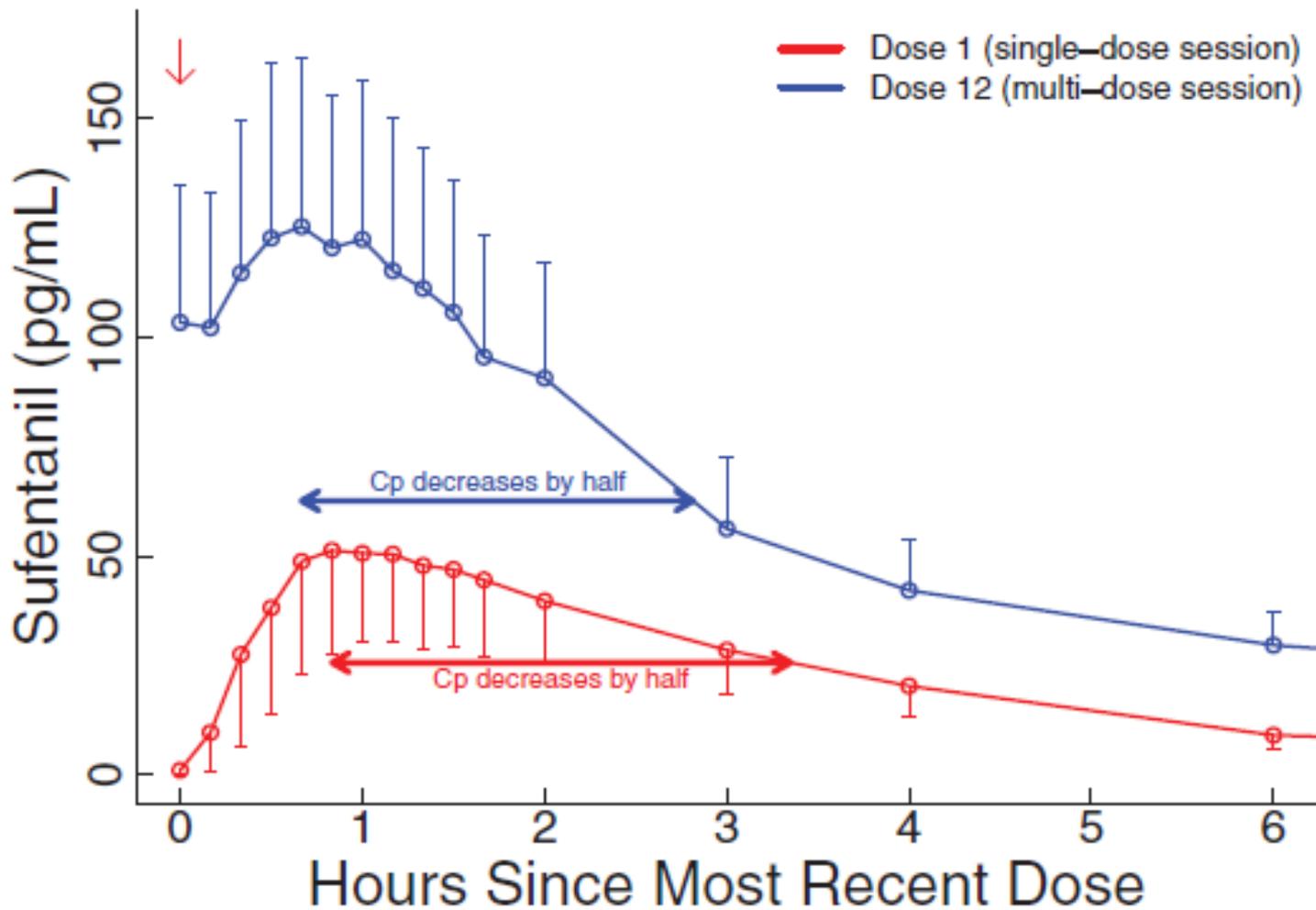
The PK profile suggests analgesia as early as 15 minutes and with a duration of ~3 hours

Reference: 1. Fisher DM, et al. Pharmacokinetic Properties of a Sufentanil Sublingual Tablet Intended to Treat Acute Pain. Anesthesiology 2018; 128:943-52; *note Fisher et al., modeled the Effect site from the pop PK data

Mean Sufentanil Plasma Concentrations: Single vs. Multiple Doses

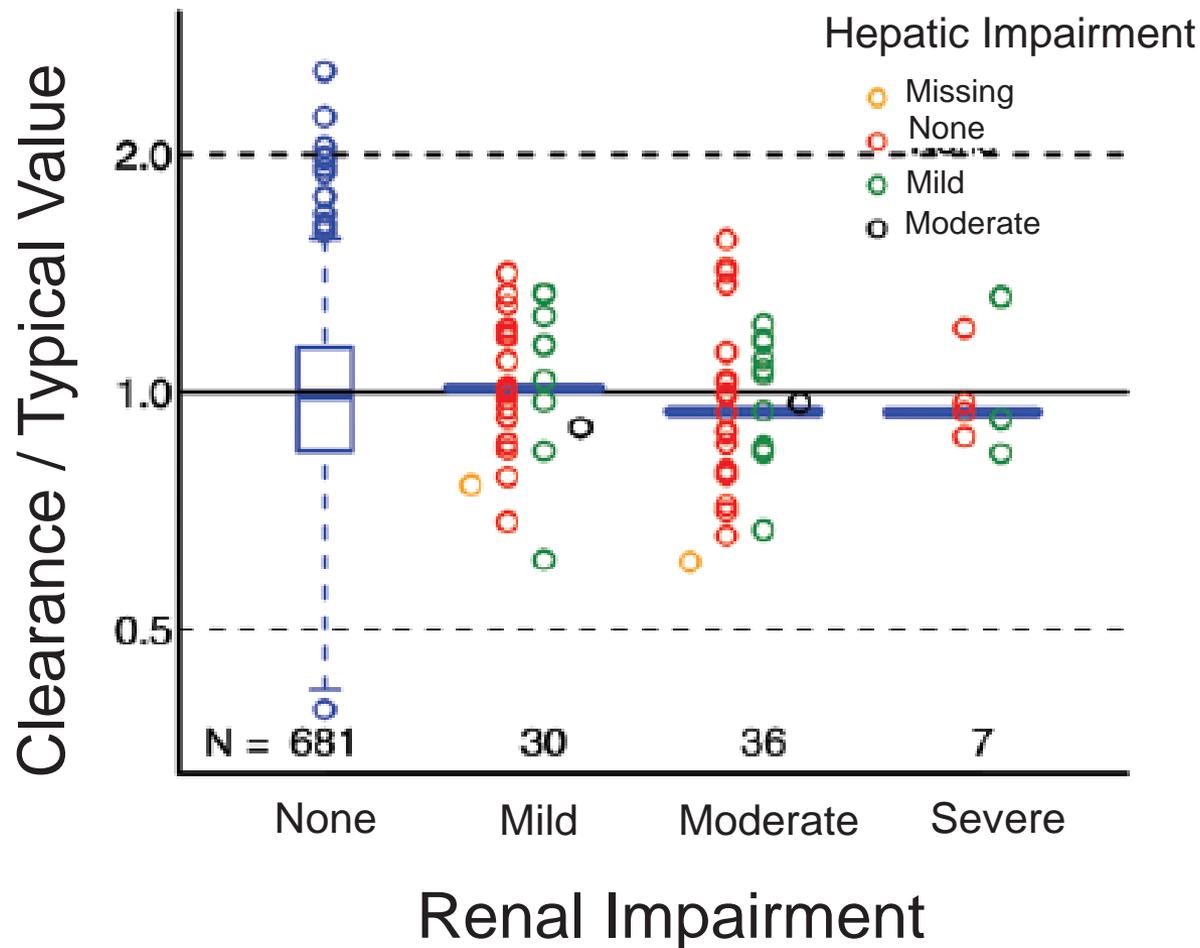


Consistent plasma clearance of sufentanil following first and last DSUVIA dose



Cp = Plasma concentration

Sufentanil clearance by severity of renal impairment



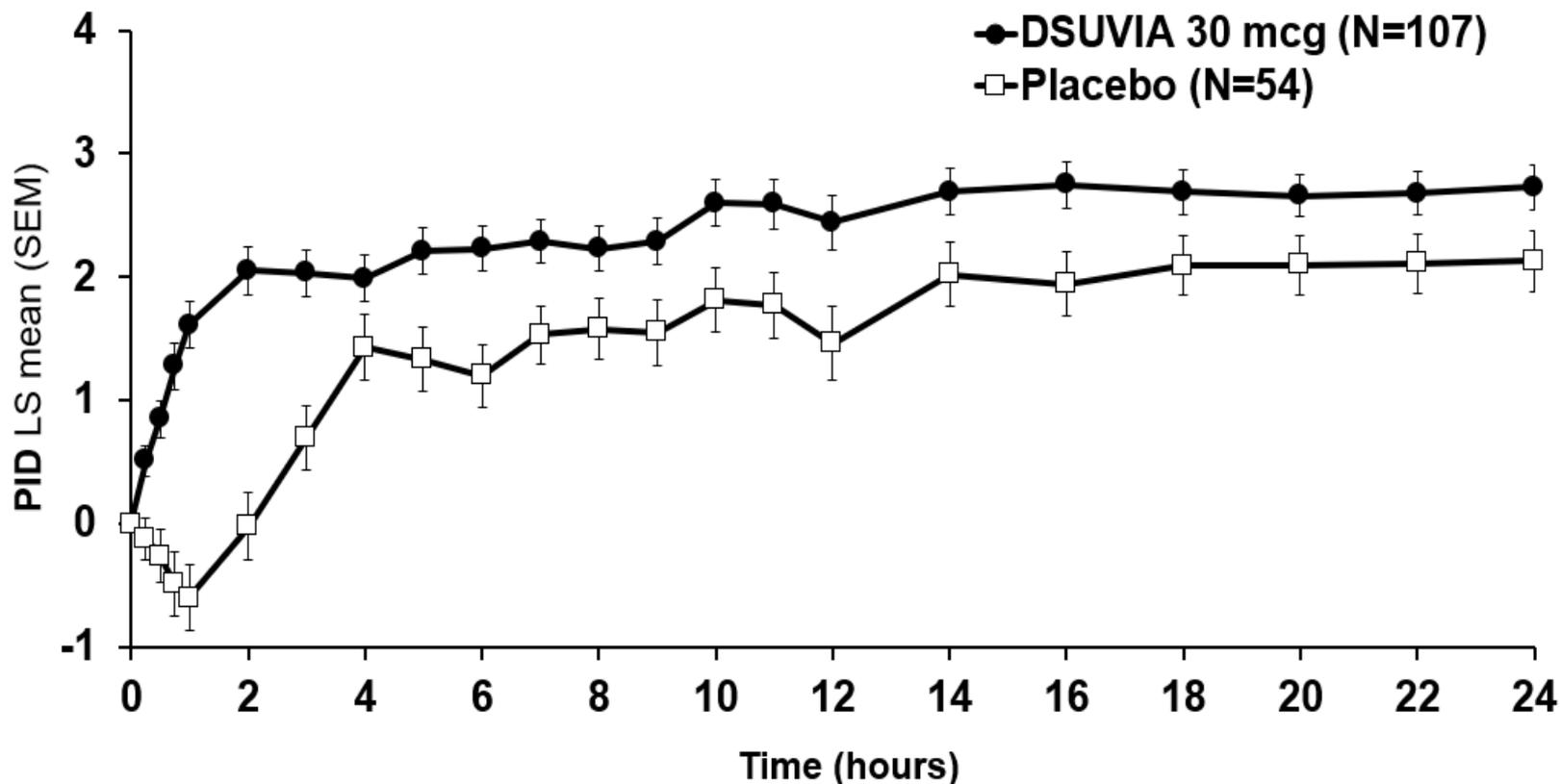
DSUVIA
clearance **not**
significantly
affected by:

- mild or moderate renal impairment
- race
- gender

Clinical study demonstrating greater pain intensity difference from baseline compared to placebo



- Over the first 12 hours (primary endpoint), $p < 0.001$
- Observed at the first timepoint (15 min), $p = 0.002$



DSUVIA adverse reactions



Adverse Reactions Occurring in $\geq 2\%$ of Patients and for Which Rate Is Higher in DSUVIA than Placebo Group: Placebo-Controlled Study SAP301

Possibly or Probably Related Adverse Reactions	DSUVIA* n=107	Placebo* n=54
Nausea	29.0%	22.2%
Headache	12.1%	11.1%
Vomiting	5.6%	1.9%
Dizziness	5.6%	3.7%
Hypotension	4.7%	3.7%

- Evaluated in **646 patients** exposed to ≥ 30 mcg sufentanil in first hour of treatment
- **20% aged 65-74** years of age
- **11% aged ≥ 75 years**

* Morphine 1 mg IV was permitted as rescue medication



Questions? 1-855-925-8476 Directions for Use Prescribing Information

DSUVIA™
(sufentanil) sublingual tablet 30 mcg

REMS Overview ENROLLMENT FORM On-Site Support Resources

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

Online REMS enrollment is straightforward



Questions? 1-855-925-8476

Directions for Use

Prescribing Information

DSUVIA[™]
(sufentanil) sublingual tablet 30 mcg

REMS Overview

ENROLLMENT FORM

On-Site Support

Resources

DSUVIA Healthcare Setting Enrollment Form

Download and complete the enrollment form to submit it 1 of 3 ways:

- **By email:** DSUVIAREMS@acelrx.com
- **By fax:** 1-650-649-1855
- **By mail:** AcelRx Pharmaceuticals, Inc.
Attn: REMS Administrator
351 Galveston Drive
Redwood City, CA 94063

DOWNLOAD FORM

Complete and submit the enrollment form online.

ENROLL ONLINE

[Privacy Policy](#) | [Terms of Use](#) | [Contact Us](#)

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AcelRx
Pharmaceuticals, Inc.



Expert panel perspective

Experts: Dr. Louis Guzzi
Dr. Jasmine Jones
Dr. Michael Ritter
Jean Tersteeg, RN

Moderator: Dr. Pam Palmer



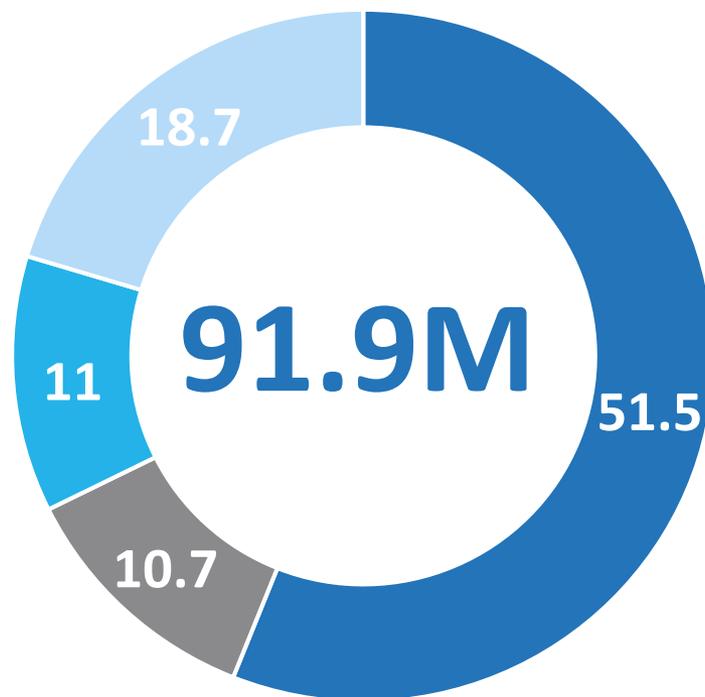
Commercializing DSUVIA

Vince Angotti

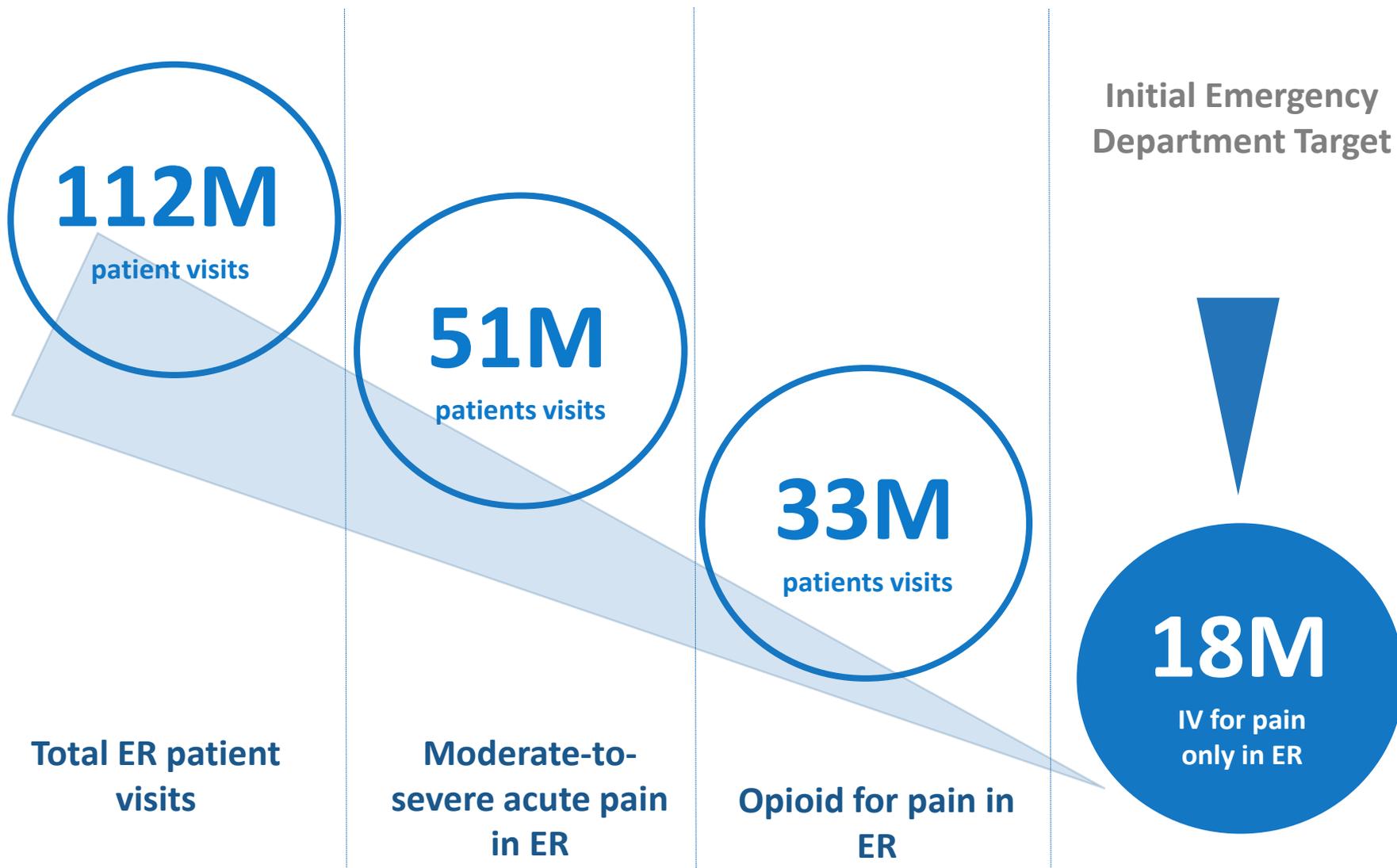
91.9M adult moderate-to-severe acute pain patient visits in medically supervised settings



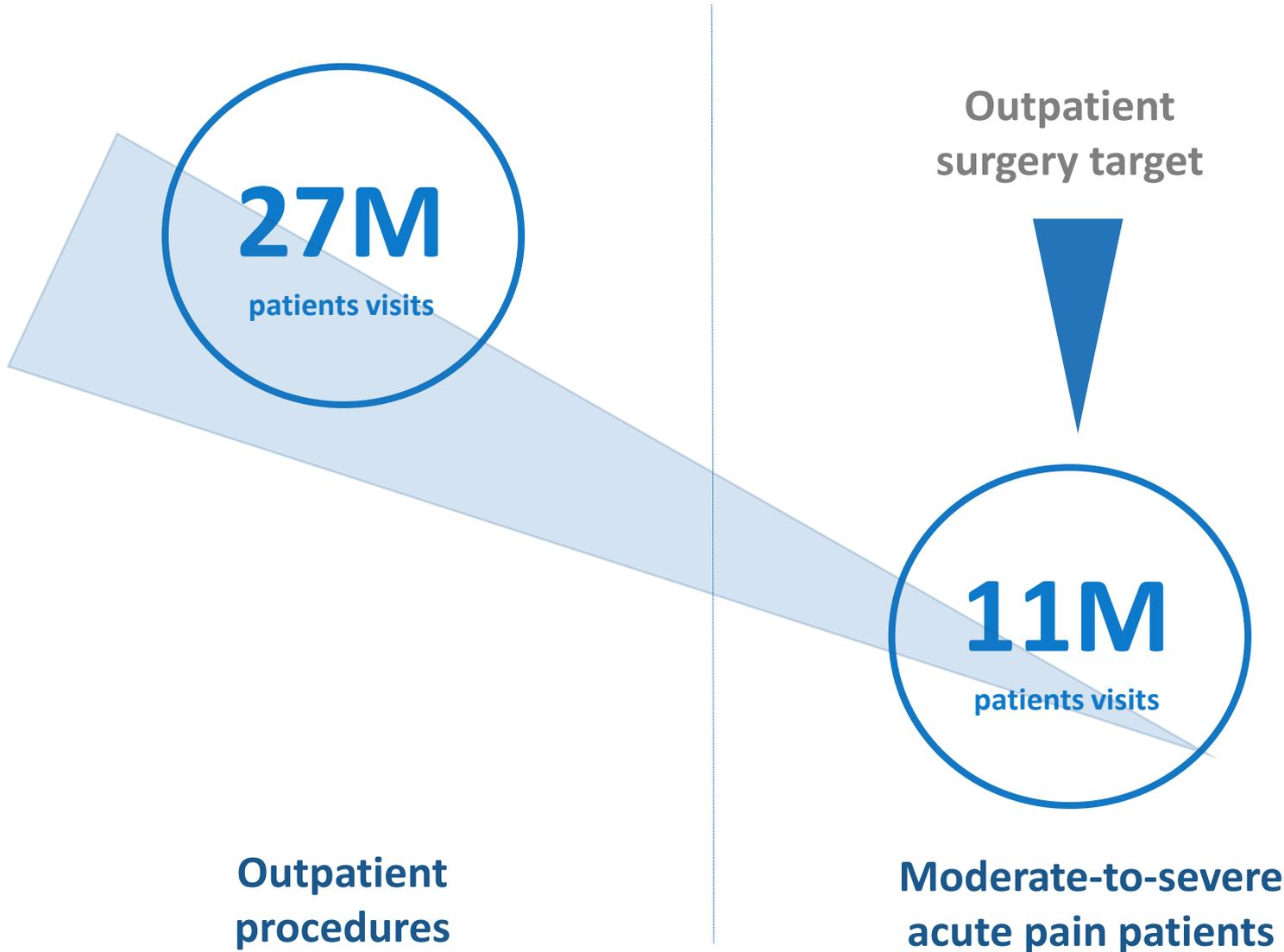
- Emergency department
- Outpatient surgery
- Inpatient/other surgery
- Other procedures



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



DSUVIA outpatient surgery opportunity is estimated at 11M adult patient visits annually



Approximately 1,200 hospitals will be our initial focus for 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

1,260
Hospitals

*70% of
potential
opportunity*



Staged approach to launching DSUVIA in the U.S. planned for early Q1 2019



15

**Hospital account
managers**

+

4 MSLs
Q1 2019

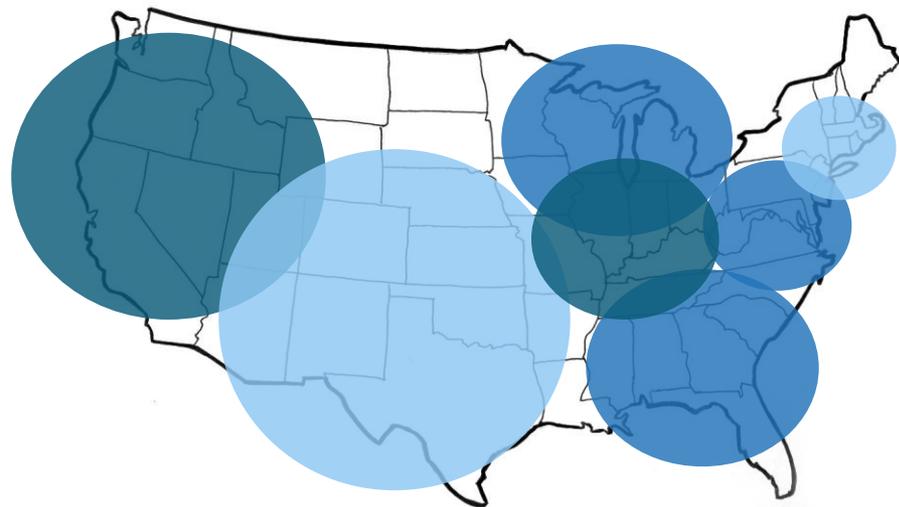
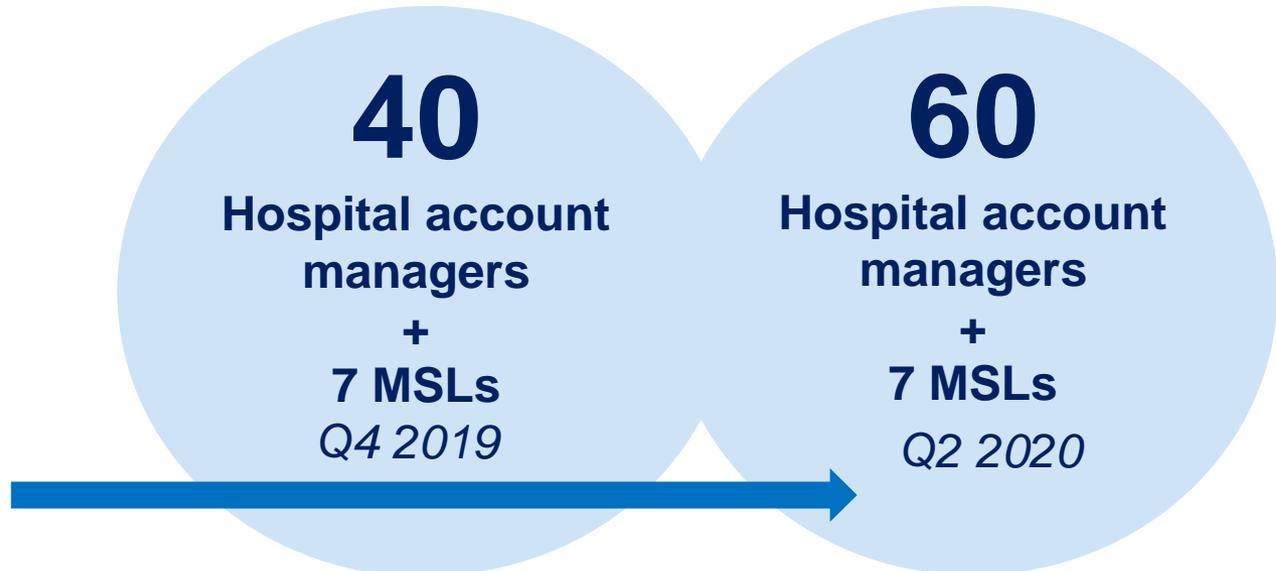
9 Hospital Account Managers today

- Average 8 years hospital sales experience; 20 yrs pharma
- All have customer specific experience in their existing region

5 Add'l Hospital Account Manager positions accepted

- Average 16 years hospital sales experience; 20 yrs pharma
- All have customer specific experience in their existing region

Staged approach to launching DSUVIA in the U.S. planned for early Q1 2019



- Stage 1
- Stage 2
- Stage 3

Experienced commercial leadership has successfully launched products together as a team



11 yrs pharma + 7 yrs agency

Marketing

*22 yrs market access;
14 product launches;
6 start-ups*

Market Access

MSLs

*11 yrs in hospital pharmacy before joining industry;
22 yrs med affairs; 3 start-ups*

*27 yrs pharma;
hospital rep;
military rep; CEO*

CEO

Sales

*29 yrs healthcare;
19 products launched;
2 start-ups*

Marketing campaign sneak-peek



NO NEEDLE



NO LINE



NO VIAL



NO DOSE
CALCULATIONS



NO FREQUENT
REDOSING

Efficient, effective pain relief for your adult patients who require an opioid



EXTENDED REDOSING INTERVAL

DSUVIA showed an average of 3 hours between doses over a 12-hour period, with a minimum redosing interval of 1 hour.^{2,†}

TIMELY PAIN REDUCTION

DSUVIA showed a greater pain intensity difference to baseline vs placebo ($P=0.002$) at 15 minutes, the first assessment.^{2*}

SINGLE FIXED DOSAGE

DSUVIA comes in one strength and avoids calculations that can complicate dosing and lead to errors.^{1,6}

NON-IV OPTION

DSUVIA is administered sublingually with a single-dose applicator, and can be given after an IV line is removed.¹

SUBLINGUAL DELIVERY

Sublingual delivery may circumvent the risks associated with IV lines, such as infiltration and phlebitis.^{1,4}

PREFILLED APPLICATOR

The prefilled applicator delivers one tablet of DSUVIA, so there's no leftover drug to waste and witness after administration.^{1,5}

*The efficacy and safety of DSUVIA were demonstrated in a pivotal trial of 161 post-operative abdominal surgery patients. The primary endpoint was time-weighted summed pain intensity difference to baseline over 12 hours (SPID₁₂). A secondary endpoint was pain intensity difference to baseline at each evaluation time point. Redosing interval (time between doses) was also recorded.^{1,2}

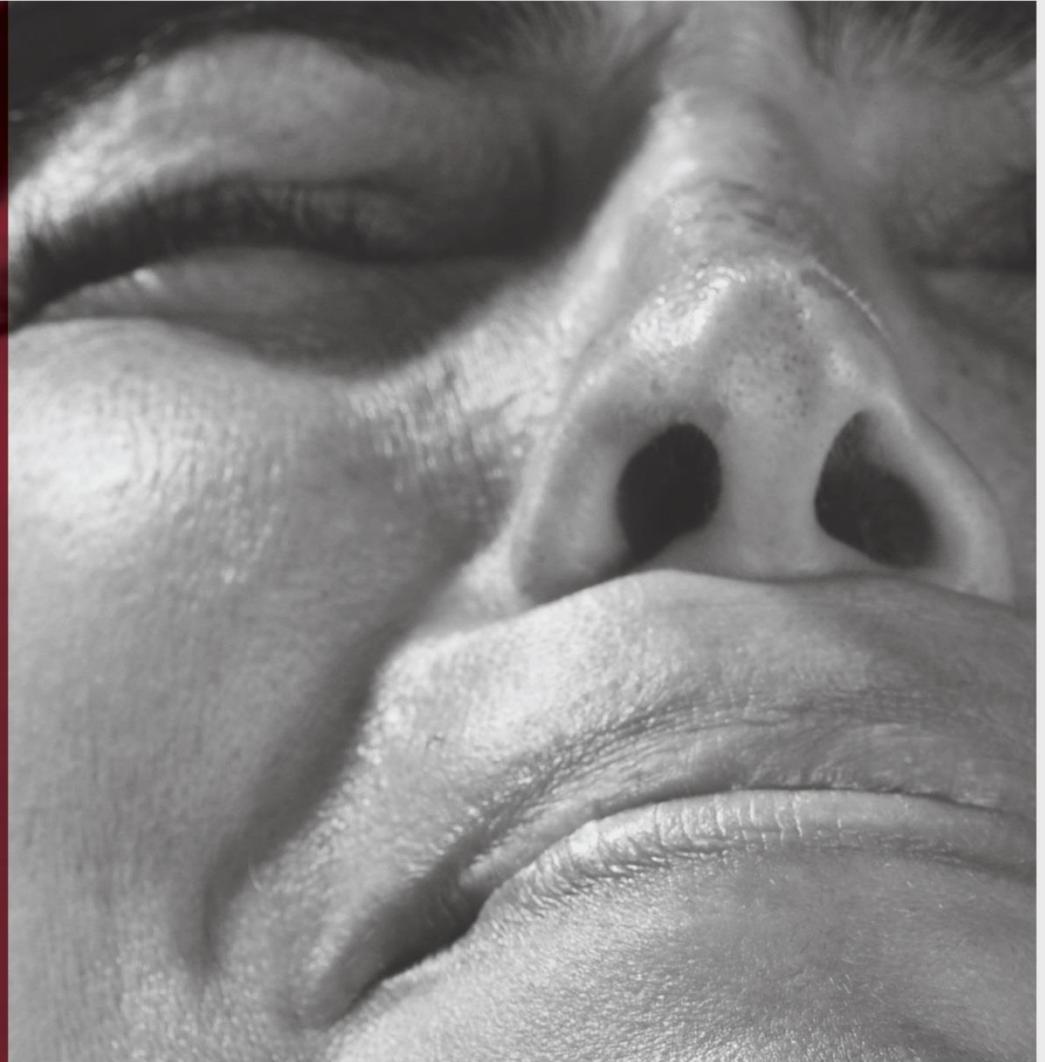
†Patients may require more frequent redosing (minimum interval 1 hour) than the 3-hour average when initiating DSUVIA.¹

Dislocated shoulder with acute pain

Patient needs IV only for analgesia

- 43-year-old female
 - 115 lb (BMI 20)
 - No relevant medical history
 - Pain score at triage: 9/10
-

Physician attempts reduction without analgesia. Patient experiences increased pain and muscle contraction, and attempt fails. Physician orders IV placement for procedural analgesia.



Hip fracture with acute pain

Patient has difficult-to-access veins

- 65-year-old female
 - 190 lb (BMI 35)
 - History of hypertension
 - Pain score at triage: 8/10
-

Nurse attempts IV cannulation for fluids and analgesia. After 2 failed attempts, she calls another nurse for assistance. Patient's blood pressure rises rapidly as they wait for second nurse to arrive and place the IV.



Edward, abdominal laparoscopy

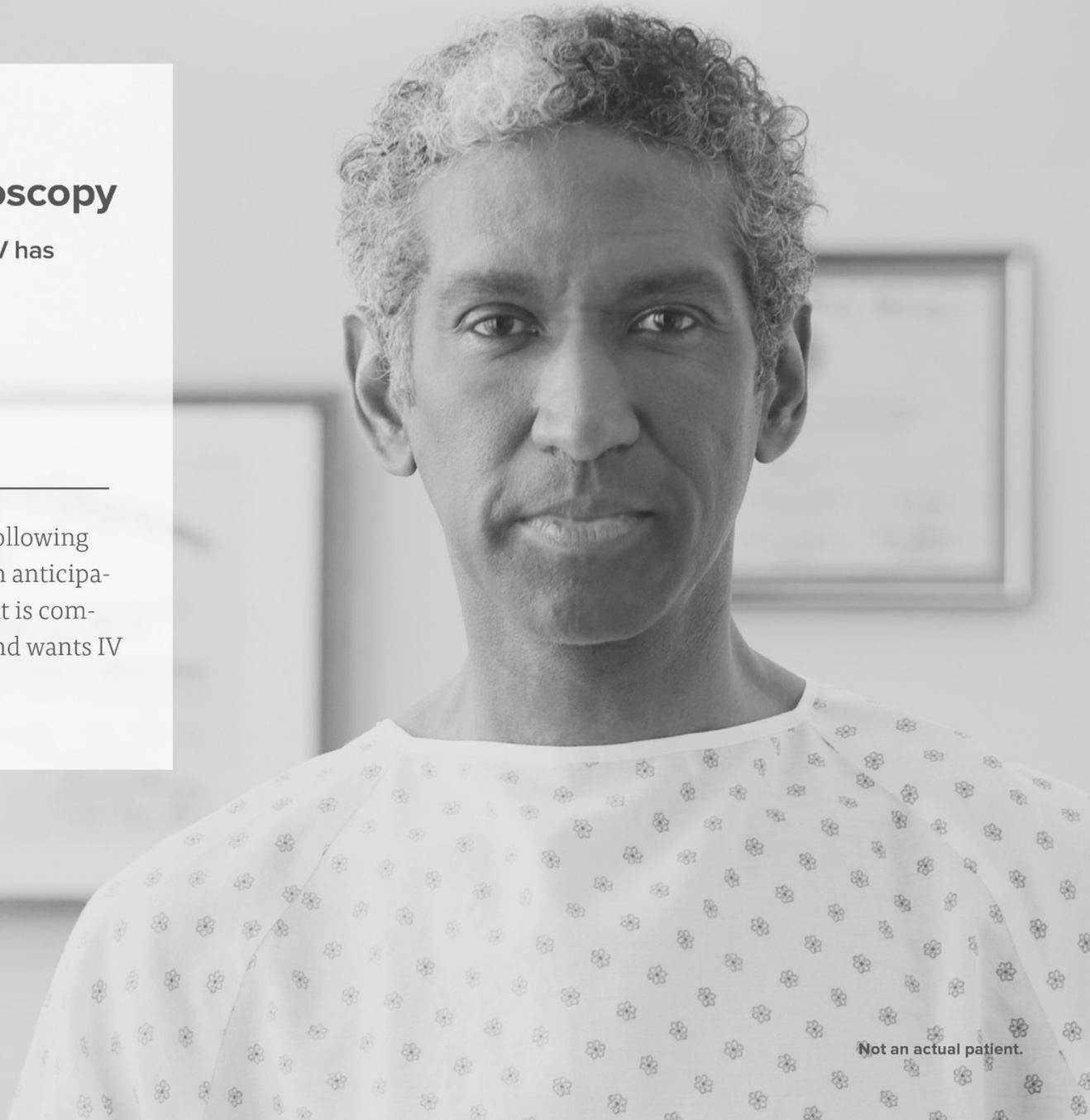
Patient has acute pain and IV has
been removed

Age: 48

BMI: 21

Pain score: 6/10

Patient receives IV fentanyl following surgery. IV is then removed in anticipation of discharge. Now patient is complaining of worsening pain and wants IV put back in place.



Not an actual patient.

Reimbursement of DSUVIA is expected as part of the hospital's packaged payment



The goal of packaging is to incentivize hospitals to make cost-efficient treatment choices

Feb-June 2019

For the first 90 – 150 days, REMS-certified institutions can submit billing for DSUVIA as either part of the 'packaged' bundle or separately payable

Post-July 2019

CMS will complete their evaluation of DSUVIA's pass-through application

We expect it will be considered part of the package as it must be (a) administered by an HCP, (b) incident to physician's services, and (c) below per diem threshold

Mid-November 2019

AcelRx will receive written notification from CMS on DSUVIA's J-code application, with expectation it will be issued a J-code with an 'N' modifier solidifying its 'packaged' status

DSUVIA will be launched in the second-half of February 2019



Production

Outsourced production contracted and running; Semi-automated shifting to fully automated production in 2020



3PL

Outsourced 3rd party logistics for distribution to wholesalers/hospitals contracted and ready



Wholesalers

Launching with three wholesalers - two contracted with the third under final review



GPOs

Focused on 9 GPOs at launch – top 4 represent 94% of AcelRx targeted accounts; completion expected in January

Department of Defense and other government agencies

PHASE 1

Military Treatment Facilities (MTFs)

- 63 MTFs in the United States
- 10 of the 63 account for ~70% of branded pain medication use in the MTF's in 2016

Military

Integration of DSUVIA into the Army, Navy, and Air Force deployment sets



2019

2020

PHASE 2

Veterans Administration

There are 152 VA Medical Centers and

Other Govt. Agencies (OGAs)

Coast Guard, National Guard, FEMA, HHS, CERT, Indian Health, Bureau of Prisons, Public Health Service, Tribal Health, Department of Justice

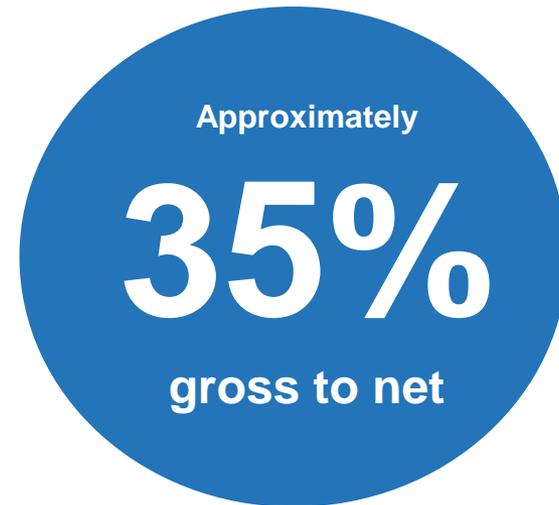


2021

Launch metrics



100 hospitals
with DSUVIA
on formulary
by year-end



Gross to net sales
percentage will
vary quarterly
depending upon
customer mix

Achieved our stated milestones set for 2018



AcelRx investment highlights



- **DSUVIA FDA approval on November 2, 2018**
 - European approval received in June 2018 (DZUVEO)
 - US market opportunity is over 91M patients in multiple settings¹
- **ZALVISO FDA resubmission timing being evaluated**
 - Successfully completed IAP312 study in 7/2017; NDA being updated
 - Commercial launch in Europe – approx. 31,000 patients in over 300 hospitals through Q3 2018
- **69 issued patents (22 in US) through at least 2027; 29 pending**
- **\$63.6 million in cash at Sept 30, 2018; est. \$116 million proforma Sept 30 (Q4 ATM proceeds and equity offering)**
- **\$12-13 million Q4 2018 expected cash burn**



1. Data on file. In-house commissioned market research. QuintilesIMS, "ARX-04 and ZALVISO US forecast" December 2016

For more information, visit:
www.aceIrx.com

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

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Important safety information for DSUVIA



LIMITATIONS OF USE

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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.