



AcelRx

Pharmaceuticals, Inc.

March 3, 2014



Forward Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to the process and timing of anticipated future clinical development of our product candidates, the therapeutic and commercial potential of Zalviso™ and ARX-04, planned regulatory pathways for Zalviso, including potential MAA submission for Zalviso and regulatory approvals and other potential regulatory events and the timing thereof, the potential market opportunity for Zalviso and ARX-04 and our related commercial goals and planned segmentation strategy, the expected patent protection for our product candidates and the sufficiency of our cash resources and our anticipated cash consumption. Forward-looking statements represent our estimates and assumptions only as of the date of this presentation. Actual results may differ materially due to the risks and uncertainties inherent in our business, including the outcome, cost and timing of our product development activities and clinical trials; the uncertain clinical development process, including the risk that clinical trials may not have an effective design; our ability to obtain and maintain regulatory approvals of our product candidates; our ability to fund our operations; our plans to research, develop and commercialize our product candidates; our ability to attract additional collaborators with development, regulatory and commercialization expertise; the size and growth potential of the markets for our product candidates; our ability to successfully commercialize our product candidates and the timing of commercialization activities; the rate and degree of market acceptance of our product candidates; our ability to develop sales and marketing capabilities; the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for financing; our ability to continue obtaining and maintaining intellectual property protection for our product candidates; and other risks detailed in our filings and reports with the SEC including our Quarterly Report on Form 10-Q filed with the SEC on November 5, 2013. You may obtain these documents for free by visiting EDGAR on the SEC's website at www.sec.gov. The statements presented in this presentation speak only as of March 3, 2014. We undertake no duty or obligation to update publicly any forward-looking statements contained in this presentation for any reason.

AcelRx – Improving Acute Pain Management

Strong Zalviso™ profile from Phase 3

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- **Adverse events:** similar incidence to placebo, low incidence of O₂ desaturation events
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- **Terms:** \$250M upfront and potential milestones, mid-teens to mid-twenties % royalty
- **Other Territories:** Continue to seek additional partnerships in Asia, South America

Clear regulatory pathways in US and EU

- **US:** 505(b)2 NDA, CDER lead, CDRH consult, July 27, 2014 PDUFA date
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Zalviso EU Partnership: Grünenthal GmbH

Grünenthal brings its pain-focused organizational capability to support a successful launch of Zalviso in EU and Australia

- #2 pain company in Europe
- Zalviso success strategically relevant for Grünenthal
- EU pain business growing, 25% growth in 2012 over 2011
- Patient-centric and innovation based culture matches AcelRx culture well
- Mid 2014 centralized MAA submission planned for drug product approval

Attractive deal terms

- \$30M upfront payment
- \$220M in potential sales and development milestone payments
- Mid-teens to mid-twenties percent royalty on net sales

Zalviso™

(sufentanil sublingual
microtablet system)

**Proposed Indication: Management of
Moderate to Severe In-Hospital Acute Pain**



IV PCA – A Troubled Standard of Care

IV-PCA

- In-hospital, post-operative moderate to severe pain control
- Higher Patient satisfaction when patients control their own pain



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Limitations

- IV opioids - unfavorable side effects
 - Sedation, oxygen desaturation, respiratory depression
- Invasive route of delivery
 - IV infiltration causes analgesic gaps
 - IV connection restricts patient mobility
 - Risk of IV site infection
- Programming errors
 - Infusion pumps large source of morbidity / mortality¹
 - 1/9 harmful hospital errors due to IV PCA²

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6
1. FDA / AAMI Summit Meeting held October 2010; http://www.aami.org/infusionsummit/AAMI_FDA_Summit_Report.pdf

2. Calculated from "The rate and costs attributable to intravenous patient-controlled analgesia errors." Brian Meissner et al, Hospital Pharmacy April 2009

Zalviso: Sufentanil NanoTab

- **High Therapeutic Index Opioid**

- In animal studies

OPIOID	THERAPEUTIC INDEX
Morphine	71 ¹
Hydromorphone	232 ²
Fentanyl	277 ¹
Sufentanil	26,716¹

- **High Lipophilicity**

- Enables rapid transmucosal uptake
- 6 minute brain:plasma equilibration

- **No active metabolites**

- **Sufentanil NanoTab**

- Sublingual avoids IV peaks & troughs
- Small size minimizes swallowed drug
- Results in high bioavailability
- Provides consistent dose delivery

- **Supplied in cartridge of 40 NanoTabs**

- 2 days for average patient



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1. Mather, Clin Exp Pharmacol Physiol 1995; 22:833.

2. Kumar, Eur J Pharmacol 2008; 597:39 (ED50) and Purdue Pharma MSDS, 2009 (LD50)

Zalviso: Delivery Device Design and Feature Set

Non-invasive (sublingual) delivery

- Eliminates IV infection risk
- Enhances ease of ambulation

Pre-programmed delivery

- Factory set 20-minute lockout period
- Eliminates programming error risk

Design safety features

- Set-up tablet, RFID cartridge provides full inventory loop tracking of NanoTabs
- RFID thumb tag co-located to device prevents proxy dosing
- HCP controlled access, device tether reduces risk of product loss
- Battery power ensures 72-hour function even in the event of power outage



Investigational drug and delivery system not FDA approved for commercial use

Zalviso: A strong clinical profile

Strong Efficacy

- Faster onset than IV morphine
- Sustained pain relief over 48-72 hours
- Consistent effect across surgery types

Attractive Tolerability

- AE profile similar to placebo
- Itching only AE different to placebo
- Lower oxygen desaturation rate

High Nurse Ease of Care

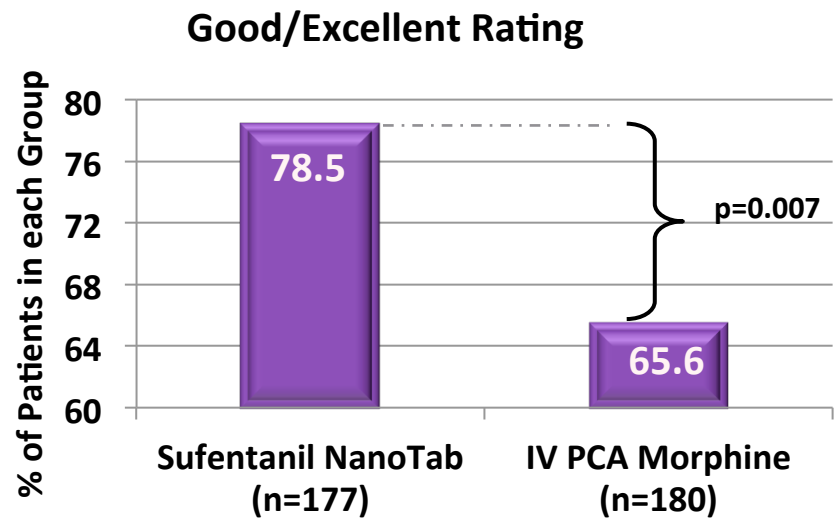
- No programming
- No IV eliminates infiltration alarms
- Less bothersome, time consuming

High Patient Satisfaction

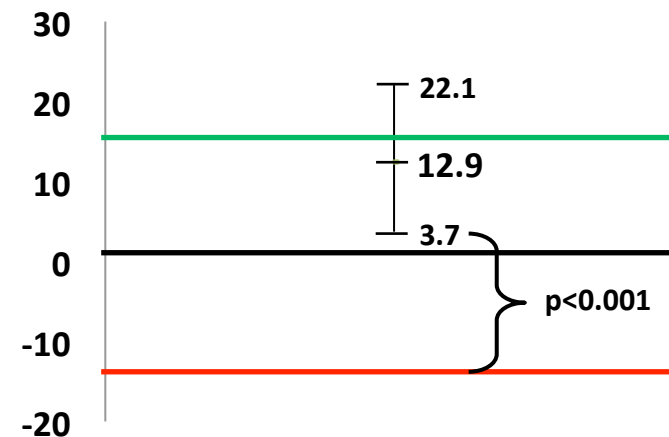
- Patient control heightens satisfaction
- Rapid onset controls pain quickly
- No IV supports easier ambulation



Zalviso Non-Inferior and Superior to IV Morphine Patient Global Assessment – 48 hours (ITT Population)

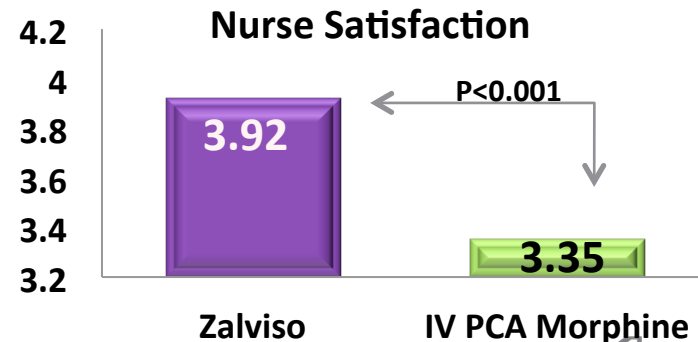
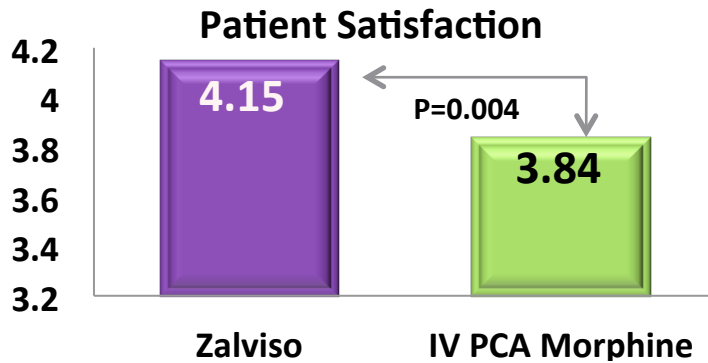
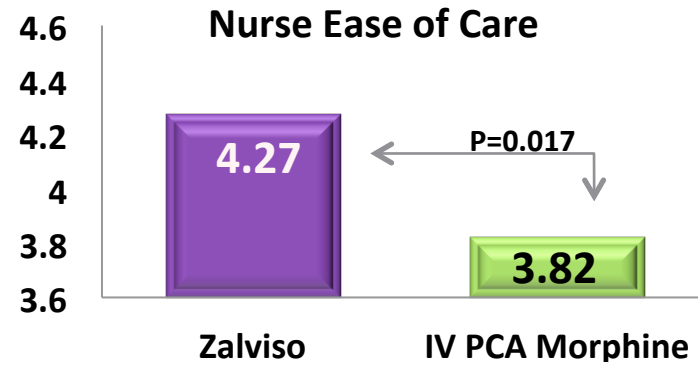
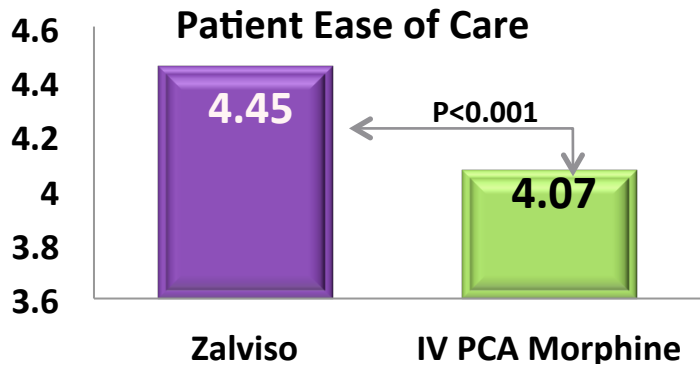


Primary Endpoint Non-Inferiority Comparison



- PGA 48 among completers demonstrates superiority for Zalviso
- PGA 24 and 72 hour also statistically superior in favor of Zalviso

High Patient Satisfaction & Nurse Ease of Care



IAP 309: Ease of Care Subscales

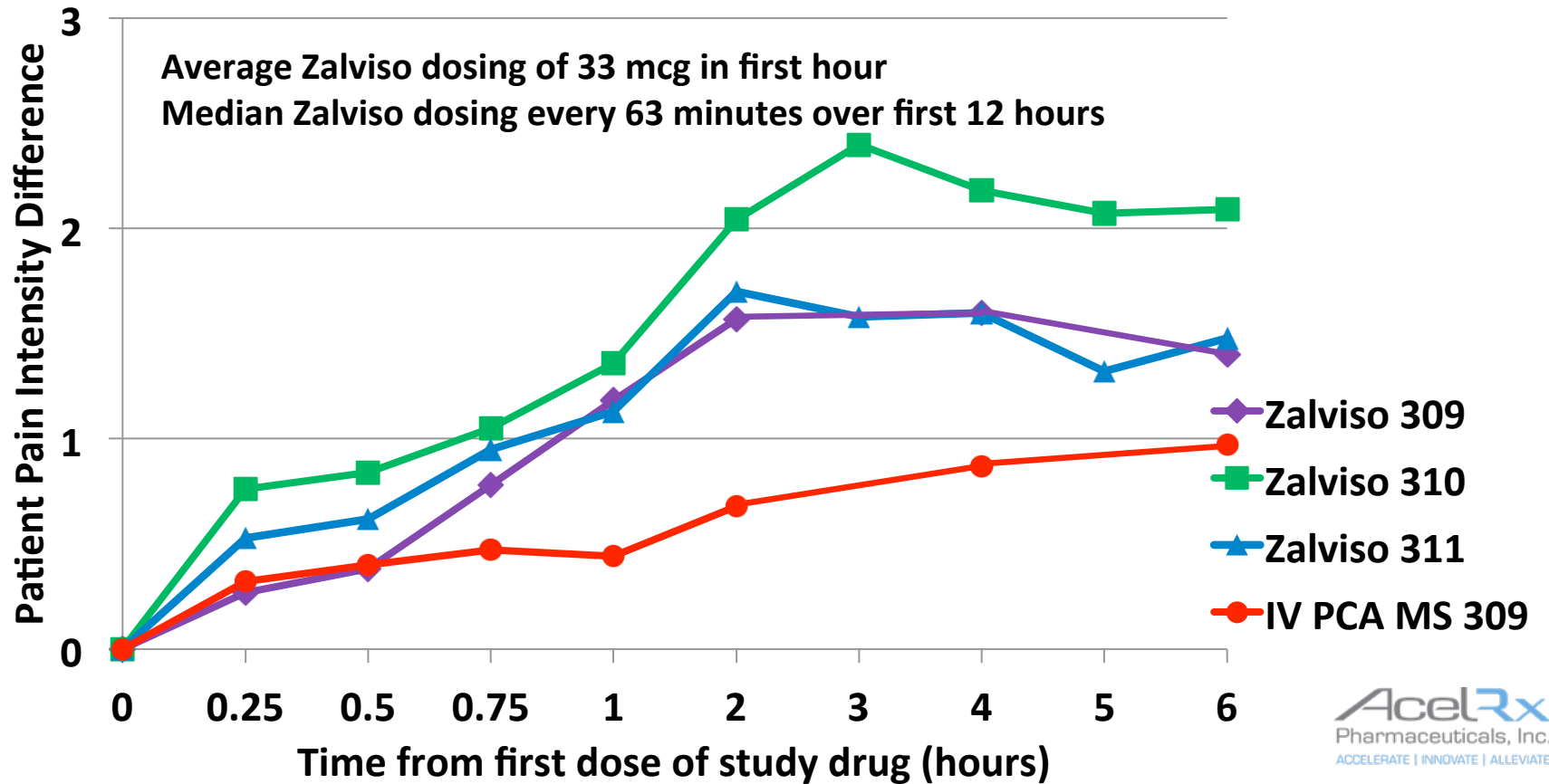
Patient and Nurse Ease of Care

Patient Subscale	Zalviso (n=177)	IV PCA MS (n=180)	P Value
Confidence with Device	4.69	4.51	0.015
Comfort with Device	4.47	4.33	0.041
Impact on Movement	4.73	3.88	<0.001
Dosing Confidence	4.74	4.47	0.003
Pain Control	3.58	3.16	0.004
Knowledge & Understanding	4.47	4.05	<0.001

Nurse Subscale	Zalviso (n=43)	IV PCA MS (n=41)	P Value
Bothersome	0.54	1.09	0.006
Time-Consuming	0.92	1.24	0.076

Zalviso: Rapid Control of Pain

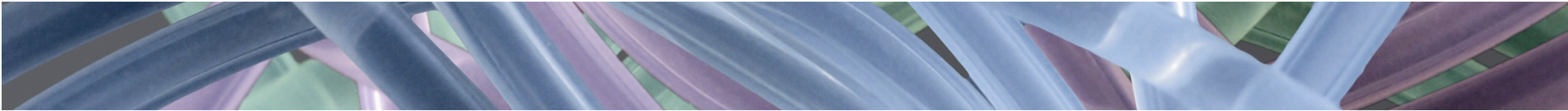
Across all Phase 3 Studies



Adverse Reactions >2% in Placebo Studies

Possibly or Probably Related Adverse Reactions	Zalviso N=429	Placebo N=162
Nausea	29.4%	22.4%
Vomiting	8.9%	4.9%
Oxygen Saturation Decreased	6.1%	2.5%
Itching*	4.7%	0%
Dizziness	4.4%	1.2%
Constipation	3.7%	0.6%
Headache	3.3%	3.7%
Insomnia	3.3%	1.9%
Hypotension	3.0%	1.2%
Confusional State	2.1%	0.6%

* Significantly Different between Zalviso and Placebo (p<0.05)



Zalviso™

(sufentanil sublingual microtablet system)



Large Commercial Opportunity

Investigational drug and delivery system not FDA approved for commercial use

Moderate-to-Severe Pain in US Hospital Settings^{1,2}

Hospital in-patient, moderate-to-severe acute pain, post-operative

- 12M procedures per annum, Zalviso potentially usable in ~95% cases

Hospital in-patient, moderate-to-severe acute pain, not post-operative

- 7.4M patients per annum, Zalviso potentially usable in ~66-80% cases
- IV push opioid is current standard for acute non-post-op pain, not IV PCA
- Physicians reported Zalviso may be supplementary to IV push

Hospital affiliated hospice, moderate-to-severe acute pain

- 300k patients per annum, Zalviso potentially usable in ~40% cases
- Zalviso is a potential replacement for liquid morphine

Formulary Adoption after FDA Approval Based on Clinical Data Earliest – 2 Months; Typical – 8-10 Months

42% Very Likely to Approve

convinced by the clinical benefit demonstrated

assume ability to demonstrate economic benefit or set cost aside

42% Quite Likely to Approve

looking for relevant experts to champion the product

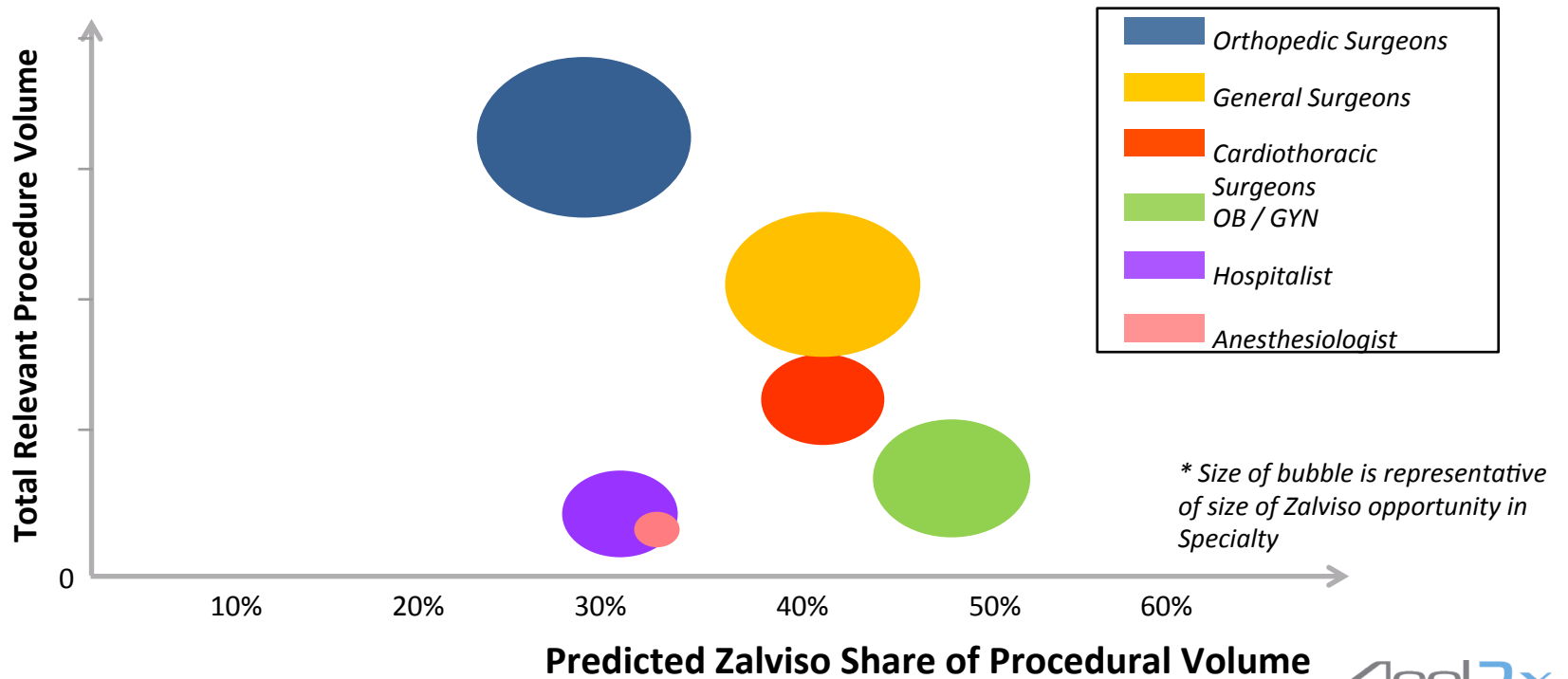
unsure of cost, looking for favorable cost-benefit analysis

16% Early approval unlikely

might be swayed by additional, independent clinical literature

assume product expensive, might accept favorable cost-benefit analysis

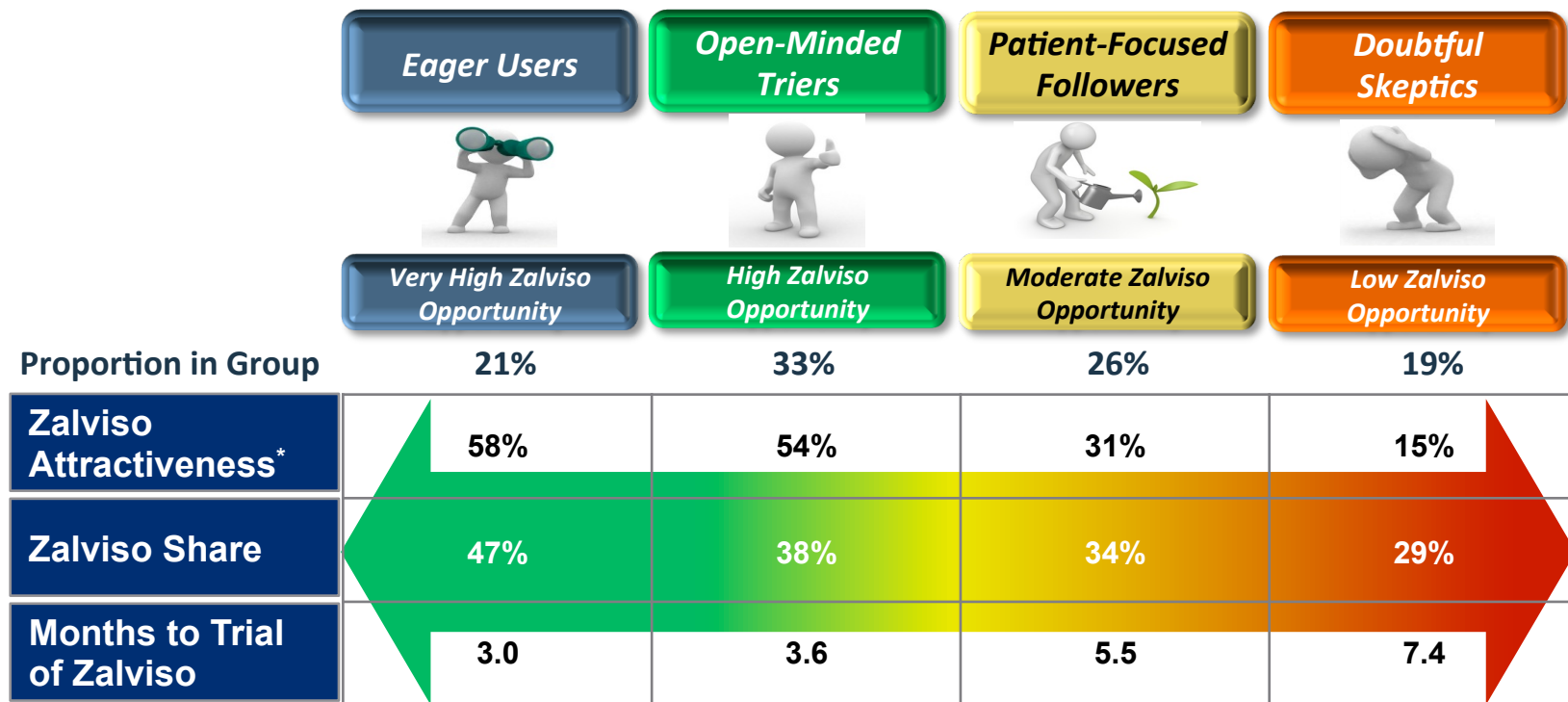
Strong Positive Reaction to Zalviso Clinical Profile Market Research Among Hospital Specialists (n=244)¹



1. ZS Associates Quantitative Survey Among Hospital Specialists, Winter 2013.

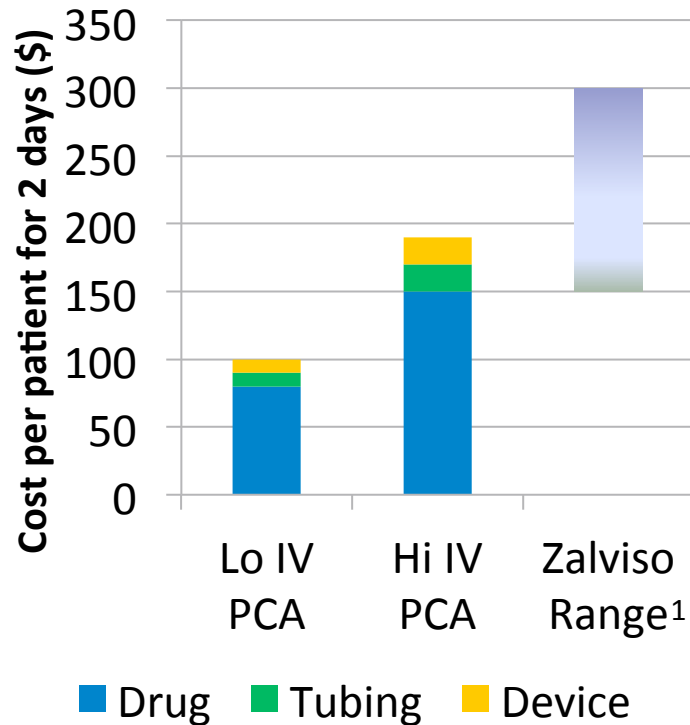
Adoption will depend on individual surgeon profile

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* Percentage who rate Zalviso a 6 or 7 on a 1-7 scale

Pricing and Pharmacoeconomics



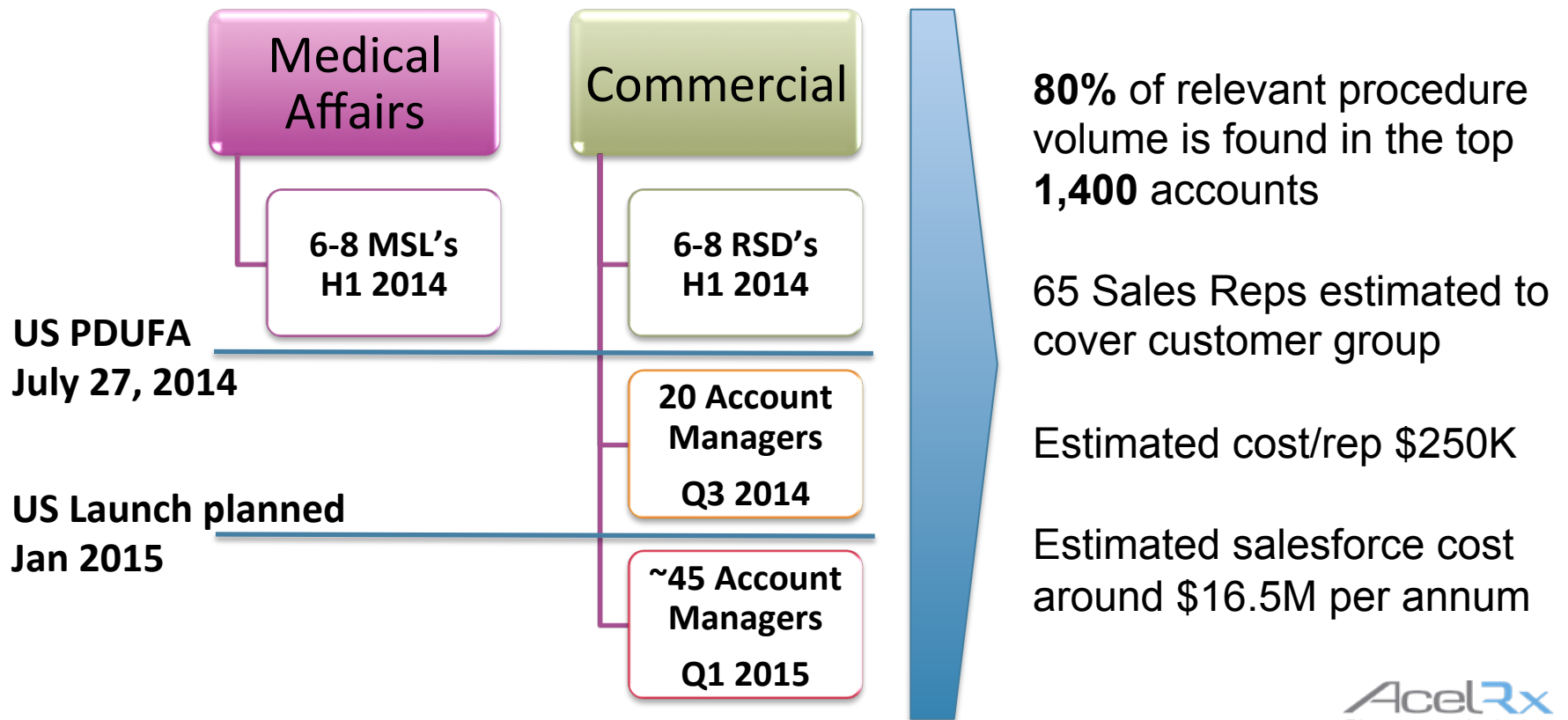
Option to price in line with IV PCA

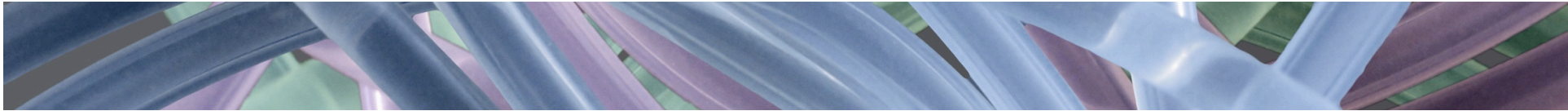
- Margins on disposable elements allow pricing flexibility
- Pharmacoeconomic model will illustrate value to hospital

Pharmacoeconomic value created by:

- Elimination of programming errors
- Elimination of PCA IV site infection risk
- Earlier and easier ambulation potentially accelerates hospital release
- Early onset of pain relief should lower opioid dosing, less overshoot
- Enhanced Patient Satisfaction results in improved CMS reimbursement

US Customer-focused Organization Build





ARX-04

HCP Administered

Single 30mcg dose

Sufentanil NanoTab

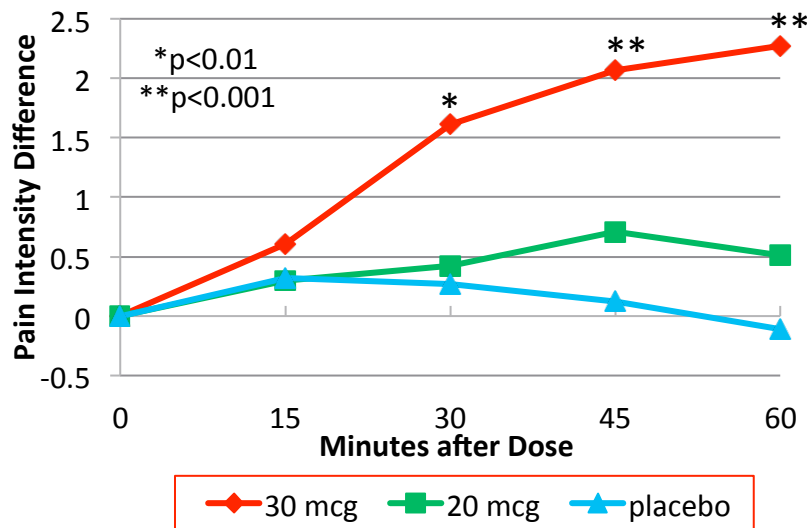
**Moderate to severe acute pain treatment
in medically supervised settings**



ARX-04 – Short Term Acute Pain Management

Phase 2

30mcg sufentanil NanoTab rapid onset of effect demonstrated



End of Phase 2 Meeting held Dec. '13

- 505(b)(2) submission
- 500 patient safety database requested, 100 multiple dose, 400 single dose
- Single Phase 3 placebo controlled study
 - Abdominal surgery, SPID-12 primary, follow for 48 hours
 - FPI in H2 2014
 - Results expected in H2 2015
- Single & repeat dose pk study

ARX-04 – Commercial Opportunity

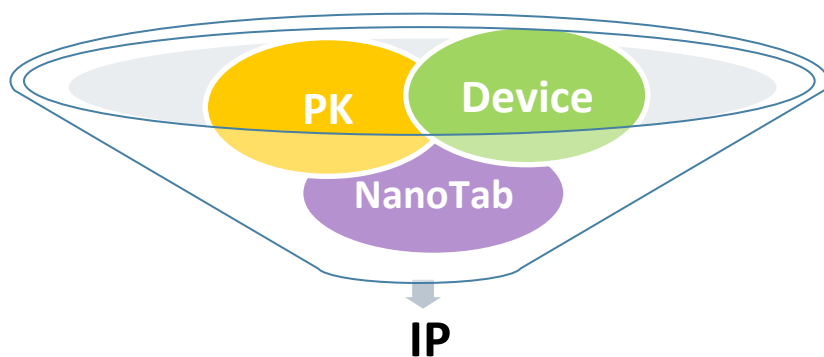
Peri-Hospital ARX-04 Market Opportunity Complements Zalviso

- ER Department
 - 130M visits annually, analgesics provided in 95M of these visits
 - Stomach Pain and Chest Pain two most common reasons to attend ER
- Ambulatory Surgery Center
 - 35M ASC visits per year
 - 1-6 hour recovery in ASC typical after procedure
- Paramedics
 - 15M patients transported/yr
 - 20% in moderate to severe pain

Broad Patent Strategy & Estate

Strategy

Drug-device combination allows overlapping & interlocking patents



Integrated IP and regulatory strategy designed to minimize ANDA exposure

Estate

6 US patents issued on NanoTab
4 US patents issued on Devices
▪ Coverage through 2027 - 2031

2 EU patents issued on NanoTab
1 EU Patent issued on Device
▪ Coverage through 2027 - 2029

7 issued patents in other territories

13 US applications plus 40 foreign and PCT applications in late stage prosecution

Financial Summary

Cash position at December 31, 2013: \$104 million

- Option to draw up to \$25 million in 2 tranches from debt facility
 - \$10 million available through 2Q 2014
 - \$15 million contingent on Zalviso approval, available through 1Q 2015

Currently available cash resources fund operations through breakeven

- Assumes timely regulatory approval of Zalviso in the US
- Supports execution of all planned US commercial launch efforts for Zalviso
- Provides ability to fund Phase 3 development of ARX-04 through NDA

Net 4Q 2013 cash usage of \$8.3 million

- Excludes \$30 million upfront from Grunenthal for Zalviso partnership in EU
- Excludes \$6 million received from renegotiated debt facility

43.1 million shares outstanding at December 31, 2013

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