AVENUE THERAPEUTICS, INC. | NASDAQ: ATXI

Forward Looking Statements

Statements in this presentation that are not descriptions of historical facts are forward-looking statements within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. We have attempted to identify forward-looking statements by terminology including “anticipates,” “believes,” “can,” “continue,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “should,” or “will” or the negative of these terms or other comparable terminology. Forward-looking statements are based on management’s current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition and stock price. Factors that could cause actual results to differ materially from those currently anticipated are risks relating to: us obtaining regulatory approval from the U.S. Food and Drug Administration for our product candidate; our growth strategy; results of research and development activities; uncertainties relating to preclinical and clinical testing; our dependence on third party suppliers; our ability to obtain, perform under and maintain financing and strategic agreements and relationships; our ability to attract, integrate, and retain key personnel; the early stage of products under development; our need for substantial funds; government regulation; patent and intellectual property matters; competition; as well as other risks described in the “Risk Factors” section of our Annual Report on Form 10-K for the year ended December 31, 2018 (“Form 10-K”) and other periodic reports filed from time to time with the Securities and Exchange Commission. We expressly disclaim any obligation or undertaking to update or revise any statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances after the date of this presentation. You should read carefully our “Special Cautionary Notice Regarding Forward-looking Statements” and the factors described in the “Risk Factors” sections of our Form 10-K and other periodic reports to better understand the risks and uncertainties inherent in our business.

Value Proposition

1. Contingent acquisition agreement with InvaGen provides substantial profit to shareholders upon 2nd stage closing
    - PDUFA action date of October 10, 2020
2. Shareholders may also have upside from Contingent Value Rights (CVRs) based on IV tramadol sales
3. Strong IP position on our proprietary dosing regimen expected to protect exclusivity in the U.S. into the mid 2030's

Why IV Tramadol?

Uniquely Positioned to Address a Clear and Significant Need for New Therapies for Post-operative Pain Amidst Opioid Crisis

- Dual MOA delivers opioid efficacy with less abuse potential and risk of dependence
- **If approved, IV Tramadol will be *the only intravenous Schedule IV opioid* in the U.S.**
- Provides convenient bridge to widely prescribed oral tramadol, which has established efficacy and safety
- Fills in the gap in acute care space between IV acetaminophen/NSAIDS and conventional narcotics

Broad Applicability with Potential to Replace Conventional Narcotics in Wide Range of Patients

- A new option for patients with contraindications to NSAIDS, those who can't tolerate strong narcotics, and those unwilling to take strong narcotics, etc.

Unique Dual Mechanism of Action Among IV Analgesics

IV TRAMADOL

OPIOID AGONIST

Blocking pain signal transmission at both the spinal and brain levels

Opioid Efficacy with Less Abuse Potential

INHIBITOR OF NOREPINEPHRINE & SEROTONIN RE-UPTAKE

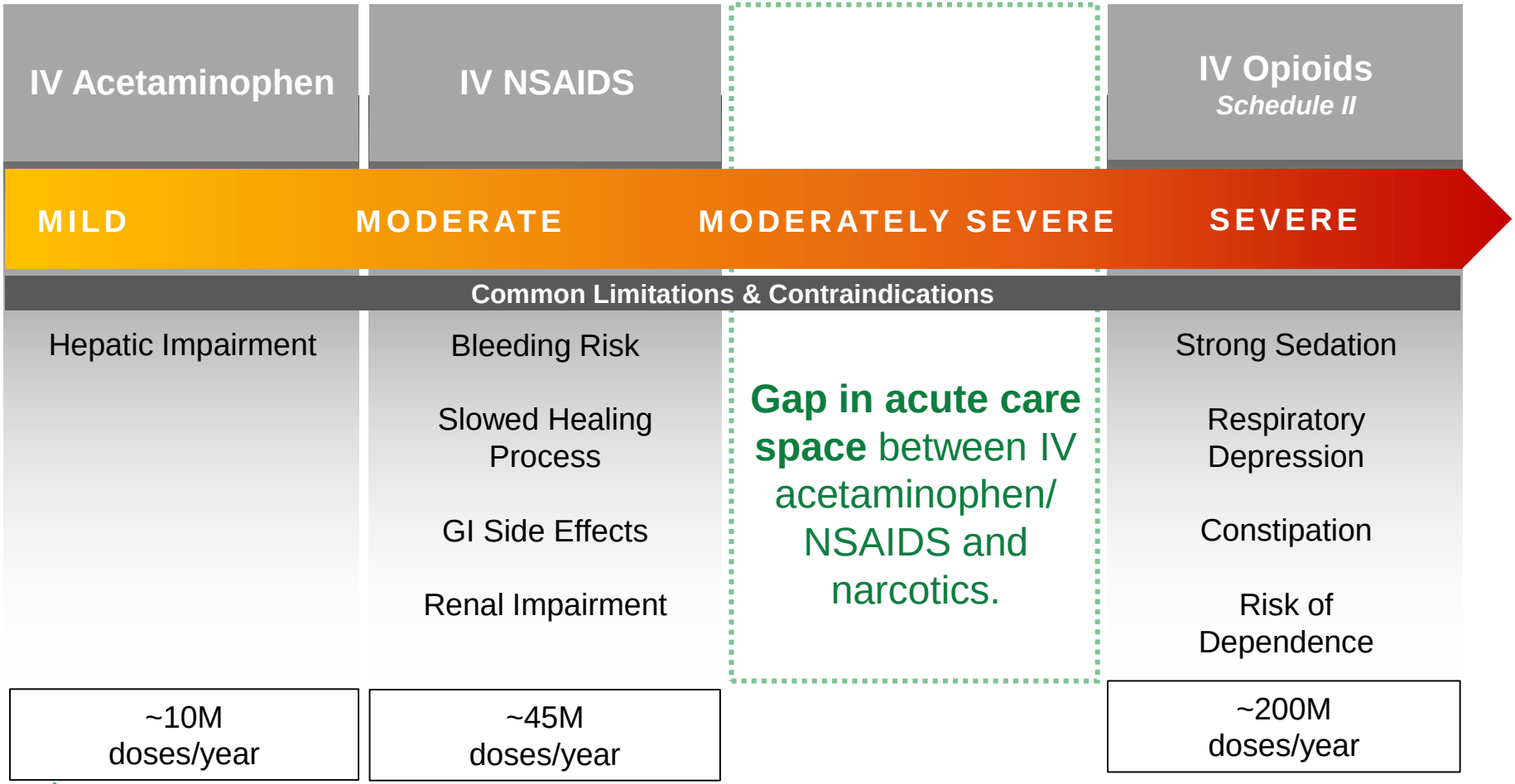
Blocking pain signal transmission at the spinal level

Schedule IV versus Conventional Narcotics (Schedule II)

Note: Schedule IV means a low potential for abuse and low risk of dependence. Schedule II drugs have a high potential for abuse, with use potentially leading to severe psychological or physical dependence.
Source: https://www.dea.gov/druginfo/ds.shtml

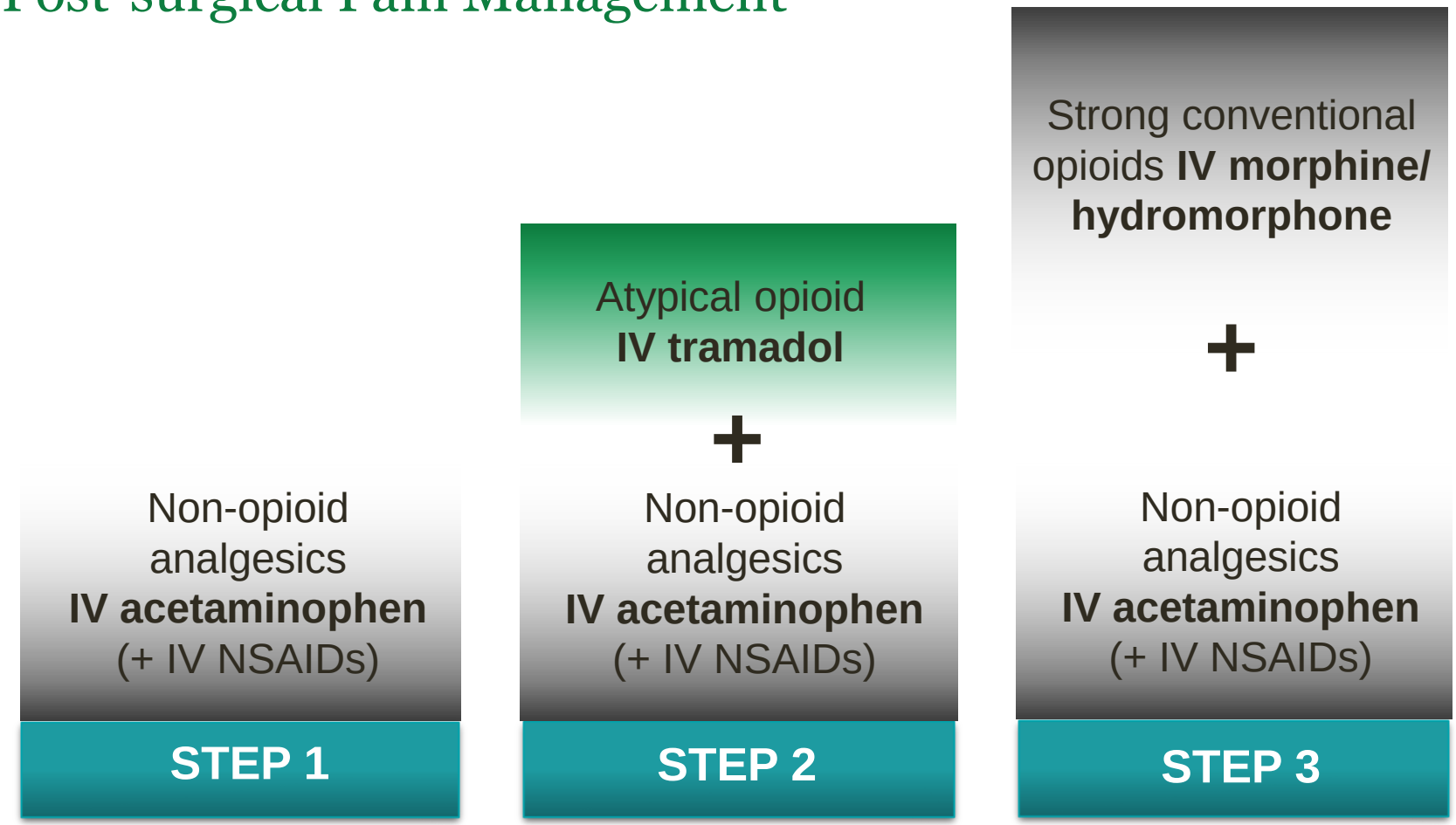
What is the Unmet Need in Post-op Pain Care?

Current Post-Op Pain Management Paradigm



Potential Paradigm: Simplified IV "Analgesic Ladder" Post-2020

Systemic Pharmacotherapy to Remain the Mainstay of Post-surgical Pain Management

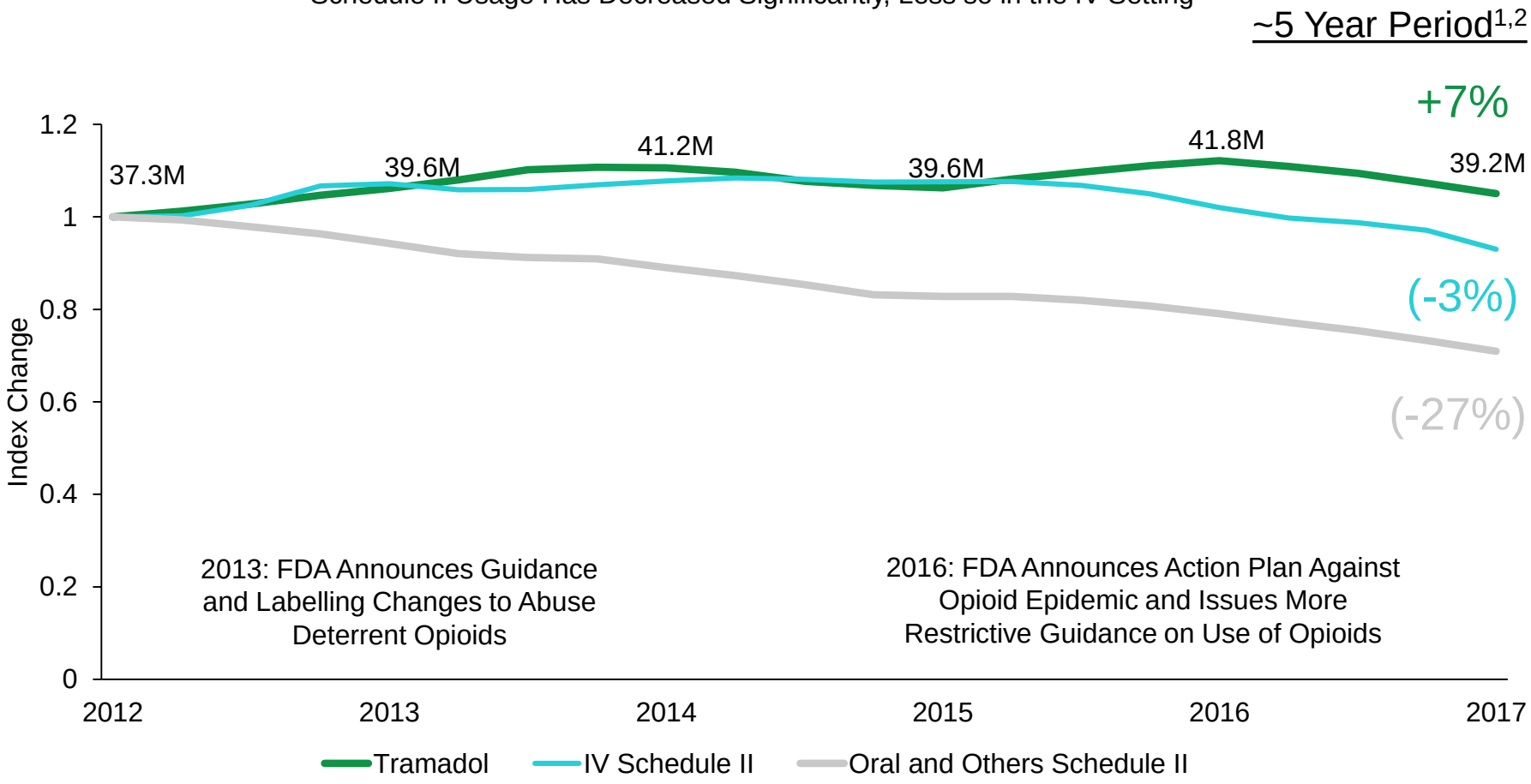


Source: Can Fam Physician. 2010 Jun; 56(6): 514–517; Avenue research

Oral Tramadol is Widely Prescribed in the U.S.

Oral Tramadol Usage Has Increased During the Opioid Crisis

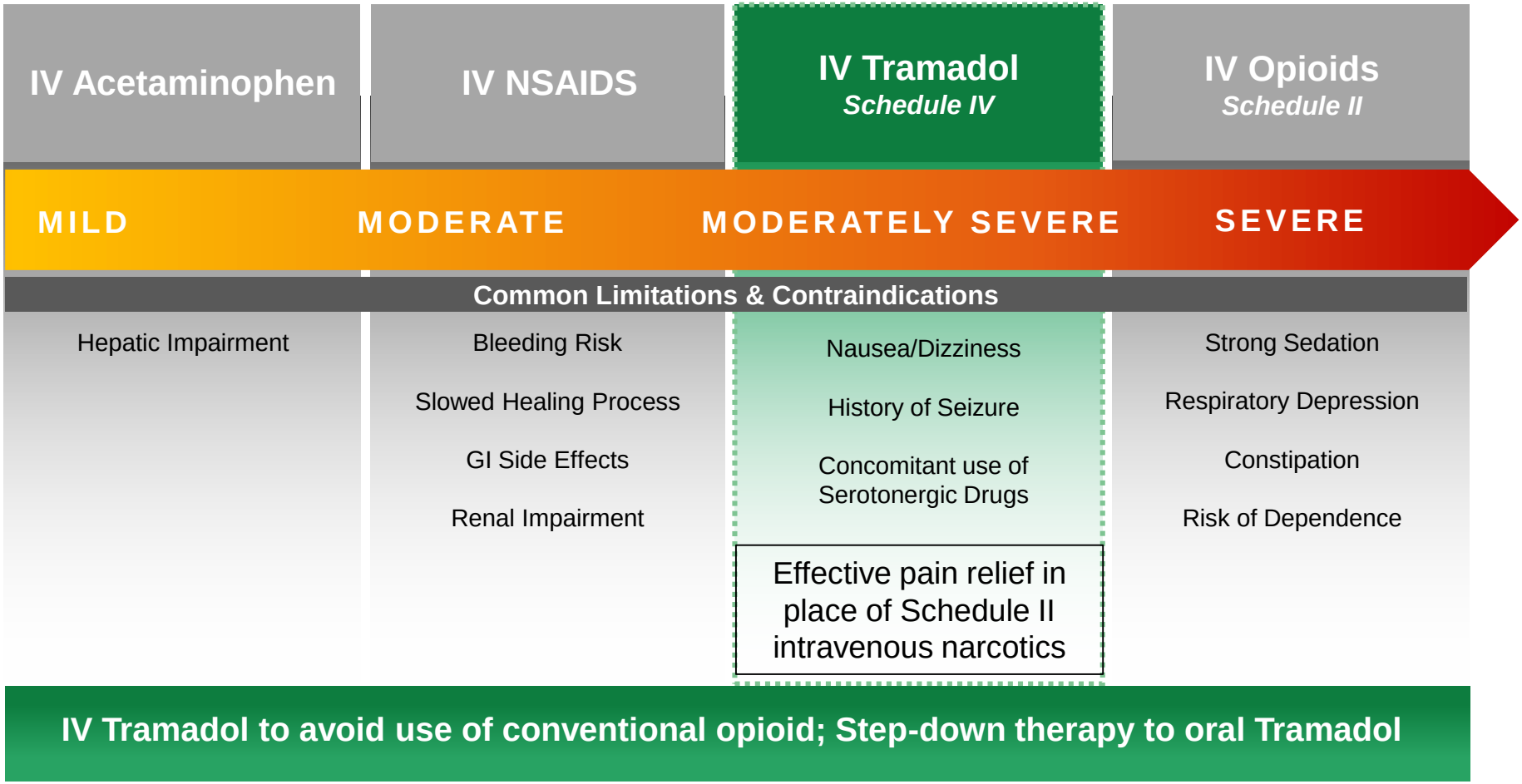
Schedule II Usage Has Decreased Significantly, Less so in the IV Setting



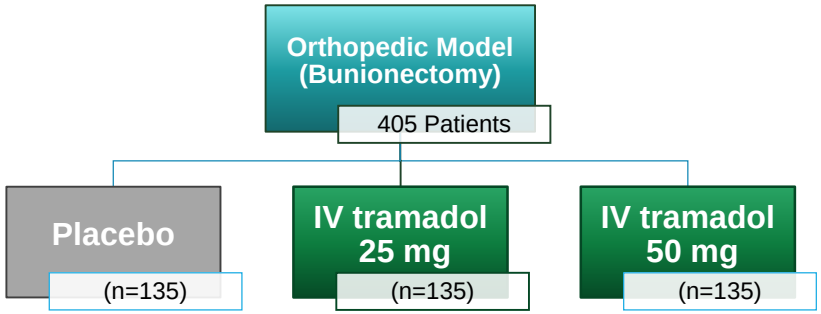
Source: Symphony Health Solutions; Note: 1. Decline shown as of 9/30/2017 2. Constraints at Pfizer's McPherson site have affected IV product supply since November 2017

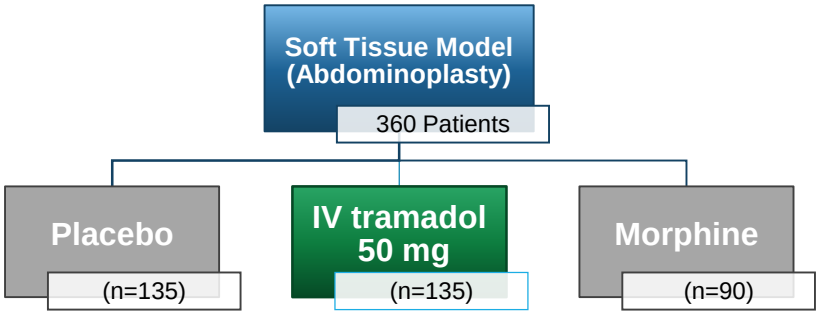
IV Tramadol Favorably Suited for Multi-modal Pain Management

Future Post-Op Pain Management Paradigm



2 Phase 3 Trials – Completed in 2Q2019





PRIMARY ENDPOINT
Sum of Pain Intensity Differences (SPID) through 48 hours post first dose

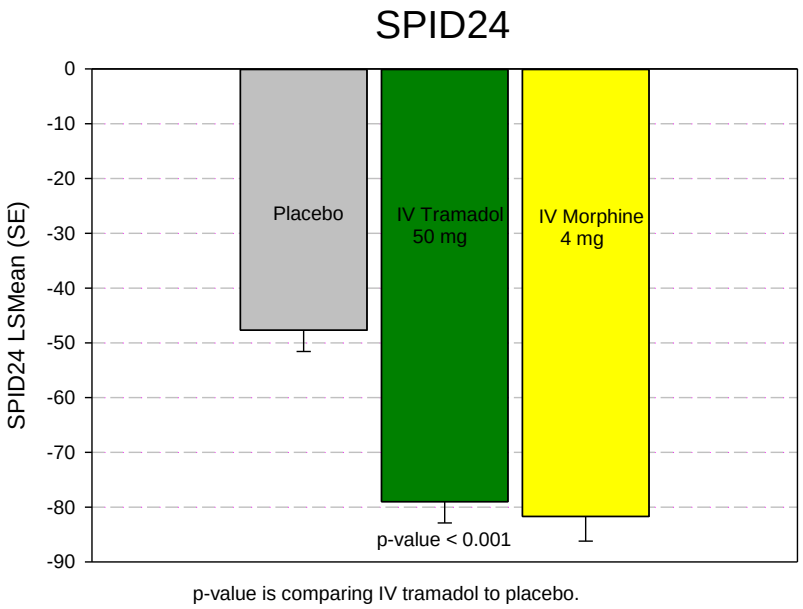
PRIMARY ENDPOINT
Sum of Pain Intensity Differences (SPID) through 24 hours post first dose

Safety Study
(n=250)

Abdominoplasty Study Results

IV Tramadol 50 mg Achieved Primary Endpoint and All Key Secondary Endpoints in this soft-tissue model

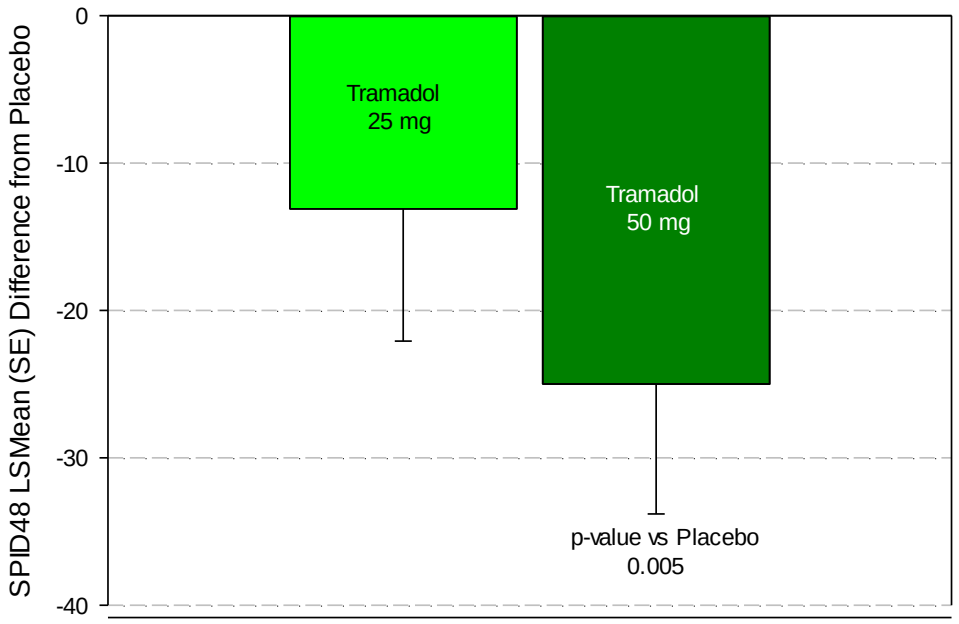
- P<0.001 for the primary endpoint of SPID24 (Sum of Pain Intensity Difference over 24 hours)
- Key secondary endpoints included:
  - PGA
  - SPID48
  - Total consumption of rescue medicine
- Similar efficacy benefit to IV morphine 4 mg, a standard-of-care IV opioid



Bunionectomy Study Results

IV Tramadol 50 mg Achieved Primary Endpoint and All Key Secondary Endpoints in this orthopedic model

- P=0.005 for the primary endpoint of SPID48 (Sum of Pain Intensity Difference over 48 hours)
- Key secondary endpoints included:
  - SPID24
  - Total consumption of rescue medicine
  - Patient Global Assessment (PGA)
- Rapid onset of efficacy
  - Statistically significant pain reduction seen as early as 30 minutes after dosing



No Surprise in Safety Outcomes

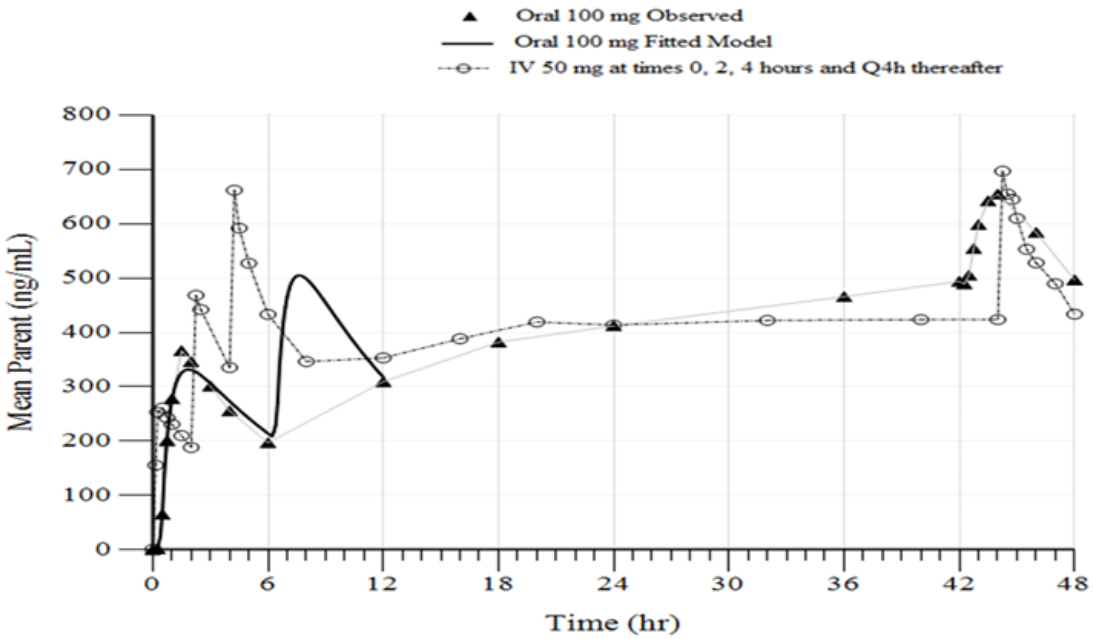
IV Tramadol 50 mg was Well Tolerated in both studies

- There were no drug-related serious adverse events (SAEs)
- AE profile was consistent with known tramadol pharmacology
- The most common AEs (>10%) in the abdominoplasty study:

	Nausea (%)		Vomiting (%)		Headache (%)		Dizziness (%)	
	As reported	Placebo-adjusted	As reported	Placebo-adjusted	As reported	Placebo-adjusted	As reported	Placebo-adjusted
Placebo	37.0		6.7		14.8		6.7	
IV tramadol	69.7	32.7	38.7	32.0	18.3	3.5	12.7	6.0
IV morphine	78.5	41.5	45.2	38.5	23.7	8.9	18.3	11.6

Novel Dosing Regimen Maximizes Efficacy and Tolerability

- IV tramadol 50 mg is infused intravenously over 15 minutes at Hours 0, 2, 4, and once every 4 hours thereafter
- Similar C_{max} and AUC to that of 100 mg oral tramadol given every 6 hours at steady state



Strong Patent Portfolio

- U.S. Patents No. 8,895,622, No. 9,561,195, No. 9,566,253, No. 9,962,343
  - Expire in 2032

- U.S. Patents No. 9,693,949, No. 9,968,551, No. 9,980,900
  - Expire in 2036

Post-Surgical Pain Management is a Gateway to Opioid Dependence

Approximately 6% of patients who are prescribed an opioid become new persistent opioid users in the post-surgical setting

"In this population-based study of 36,177 surgical patients, the incidence of new persistent opioid use after surgical procedures was 5.9% to 6.5% and did not differ between major and minor surgical procedures."[1]

Regimens initiated with conventional narcotics have a significant association with opioid misuse

"After adjusting for covariates, other risk factors… including benzodiazepines …as well as regimens initiated with hydromorphone… and oxycodone …had a statistically significant association with opioid misuse."[2]

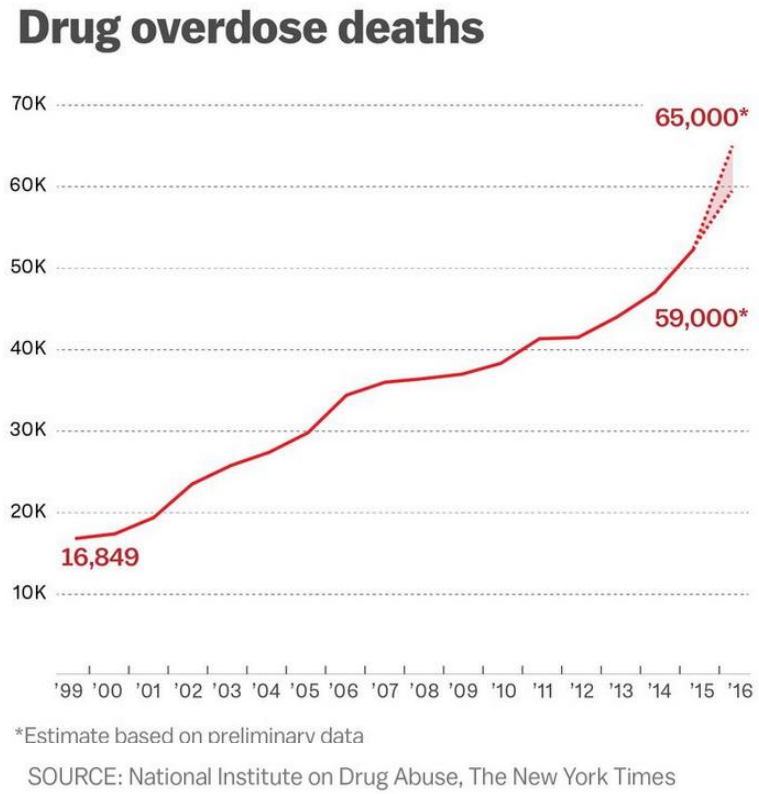
(1) *Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. JAMA Surg. 2017;152(6):e170504.*

(2) *Brat GA, Agniel D, Beam A, et al. Postsurgical prescriptions for opioid naïve patients and association with overdose and misuse: retrospective cohort study. BMJ. 2018:Jan 17;360:j5790.*

Opioid Crisis Puts Pressure on the Use of Conventional Narcotics

"IV to Oral" Tramadol is Positioned to Help Reduce Conventional Opioid Usage in the Postoperative Setting

- **Release of the CDC guidelines:**
  - *"When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed."*
- **DEA has proposed a 20% reduction** in the manufacture of opioids for 2018
- **CVS/other pharmacies limiting opioid (new) prescriptions** to 7 days and the daily dosage (mg)



Physician Enthusiasm for IV Tramadol Product Profile

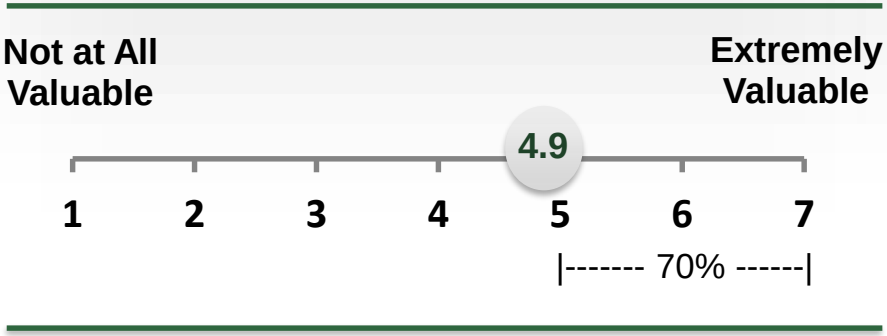
70% of physicians rated IV Tramadol "5 or higher" on the Value Scale (1-7)

- 80% of orthopedic surgeons and 76% of general surgeons rated IV Tramadol "*5 or higher*"

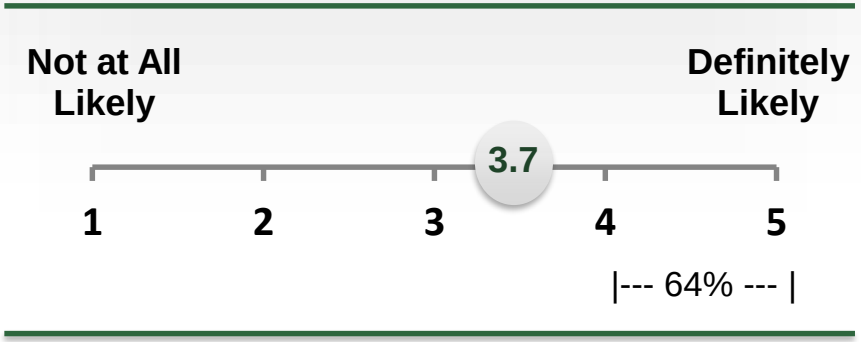
Strong interest in prescribing IV Tramadol

- Almost two-thirds (64%) were "*probably-definitely*" likely to prescribe;
- Orthopedic surgeons displayed the highest prescribing intent (74% - "*probably-definitely*")

Value of IV Tramadol



Likelihood of Prescribing IV Tramadol

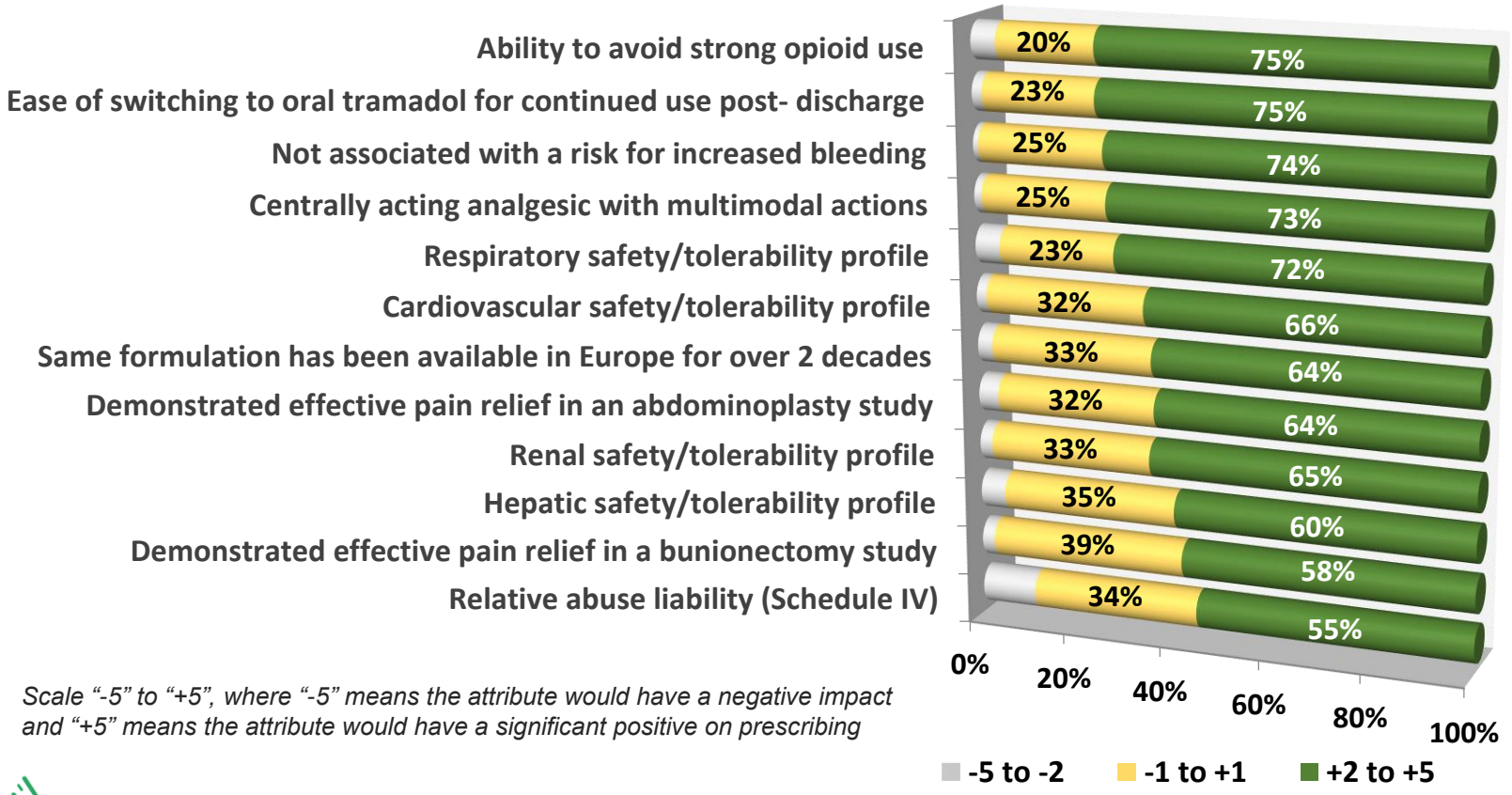


Characterizing the Acceptance of IV Tramadol in the Treatment of Acute (post-surgical) Pain. Internet survey - n=201 practitioners (orthopedic surgeons; general surgeons, anesthesiologists; and emergency medicine physicians)

Characteristics Supportive of IV Tramadol Usage

The potential for IV Tramadol to offer an alternative to use of strong opioids was viewed as the most significant enticement to prescribe

- A direct transition from an IV to oral formulation and potential safety benefits vs. both opioids and non-opioids would also be very meaningful to clinicians



Scale "-5" to "+5", where "-5" means the attribute would have a negative impact and "+5" means the attribute would have a significant positive on prescribing

Characterizing the Acceptance of IV Tramadol in the Treatment of Acute (post-surgical) Pain. Internet survey - n=201 practitioners (orthopedic surgeons; general surgeons, anesthesiologists; and emergency medicine physicians)

Acquisition Agreement signed with InvaGen (a Cipla subsidiary)

- At first stage closing in February 2019, Invagen acquired 5.8M shares @$6 per share for $35M representing a 33.3% stake in Avenue on a fully diluted basis
- At second stage closing, Invagen to purchase remaining shares for up to $180M subject to certain terms disclosed in the 8-k and proxy
- The four major conditions for second stage closing are:
    1. FDA approval by April 30, 2021
    2. No REMS
    3. General pain label (not specific to any surgery)
    4. Schedule IV

CVR's based on annual net sales and gross profits

- Each non-InvaGen shareholder at time of second stage closing is entitled to one CVR for each share owned

- CVR payments are on annual IV tramadol net sales (product launch to 2028):
    - 10% of all gross profits if net sales >$325M
    - 12.5% of all gross profits if net sales >$400M
    - 15% of all gross profits if net sales >$500M

- Beginning in 2029 if cumulative net sales of IV tramadol are at least $1.5B and annual net sales are >$100M, then annual payment of CVR is 20% of all gross profits

- As of September 30, 2019 – there are approximately 11M non-InvaGen shares outstanding

Milestones and Anticipated Timeframes

InvaGen agreement-Stage 1 Closing	1Q 2019	✓
Submission of NDA	Dec. 2019	✓
FDA acceptance of NDA submission	Feb 2020	✓
InvaGen agreement-Stage 2 Closing	2020-2021	

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