



Preventing Prescription Opioid Overdose

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FIRST OPINION

Needed: an Operation Warp Speed for the opioid epidemic

The New York Times

Overdose Deaths Have Surged During the Pandemic, C.D.C. Data Shows

The latest numbers surpass even the yearly tolls during the height of the opioid epidemic and mark a reversal of progress against addiction in recent years.

76

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The Washington Post

Democracy Dies in Darkness

The Post's View

Opinion: The deadly opioid epidemic is getting worse. It must not be forgotten.



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OPINION

America is still in the middle of an opioid epidemic. Why did we stop talking about it?

The social isolation brought on by the COVID-19 pandemic is making treating the opioid epidemic so much harder.

THE OPIOID CRISIS IS FUELED BY ALCOHOL

A critical yet unaddressed dimension of the crisis.

500%

Opioid patients with alcohol problems are **500%** more likely to overdose on their medication¹

22.1%

22.1% of fatal prescription opioid overdoses are mediated by concurrent alcohol consumption²

¹Landsman-Blumberg et al. Burden of Alcohol Abuse or Dependence Among Long-Term Opioid Users with Chronic Noncancer Pain. J Manage Care Spec Pharm., 2017; 23:718-724.

²Jones et al. Alcohol Involvement in Opioid Pain Reliever and Benzodiazepine Drug Abuse-related Emergency Department Visits and Drug-related Deaths. Morbidity Mortality Weekly Report, 2014; 63:881-885.

SafeRx Has Designed Alcohol-Resistant Opioids (AROs)

A revolutionary new formulation which combines the opioid with a second drug that discourages alcohol consumption.

Each ARO tablet includes:

- ▶ An effective dose of an FDA-approved opioid (e.g., oxycodone) for pain relief
- ▶ An effective dose of disulfiram, an FDA-approved alcohol-deterrent
- ▶ A binding matrix (excipient) that prevents separation of the two active pharmaceutical ingredients

[View a video animation of our technology](#)



SafeRx Has Designed Alcohol-Resistant Opioids (AROs)

If patient avoids alcohol with the ARO:

- Opioid (pain killer) works as prescribed (normal analgesic profile)
- Disulfiram remains inert & unnoticed by patient

Patients who avoid alcohol with their prescription experience the intended pain relief and no perceptible effects from disulfiram.

If patient consumes alcohol with the ARO:

- Disulfiram interferes with normal breakdown of alcohol
- A toxic byproduct- acetaldehyde- rapidly accumulates in the body, producing a noxious experience referred to as the disulfiram-alcohol reaction.

Patients who, against medical advice, drink with their prescription experience an extremely unpleasant reaction characterized by dizziness/vertigo, headache, and severe nausea/vomiting.

SafeRx Has Patented Its ARO Platform

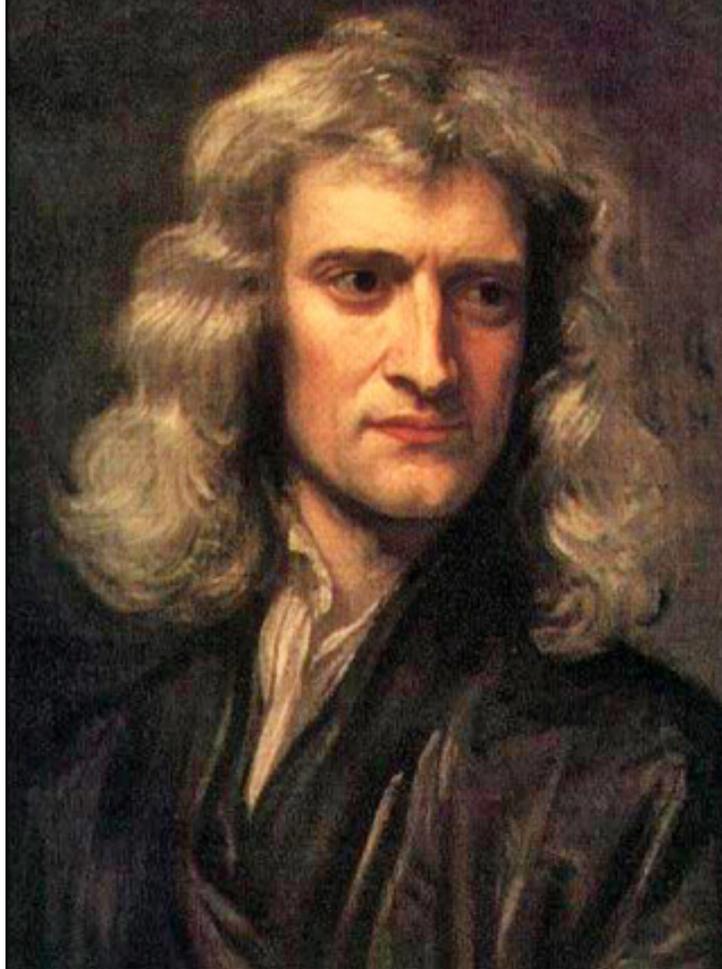
	REFERENCE #	TITLE	ISSUE DATE
ISSUED PATENTS (U.S.)			
	US 10,478,408	Combination Treatments for Opioid Crisis	Issued 11/19/2019
	US 10,881,625	Combination Treatments for Opioid Crisis	Issued 1/5/2021
PENDING APPLICATIONS (INTERNATIONAL)			
	PCT 15/881,475	Combination Treatments for Opioid Crisis	
FILED IN:			
CANADA	CANADA 3,089,071		Pending
EUROPEAN UNION	EPO 19 74 4389.8		Pending
INDIA	IN202047035537		Pending
MEXICO	MX/A/2020/007860		Pending

Why SafeRx is Selling Its Stock Through Crowdfunding

Because we recognize the extraordinary power of community

- ▶ We believe grassroots, community-supported solutions to the opioid crisis will succeed where institutional investments have not
 - ▶ “small money” vs “Big Pharma”
- ▶ We want to give communities that have lost so much to this crisis a chance to participate in developing a solution, and to potentially benefit financially in so doing
 - ▶ beyond the immense cost of life, non-fatal overdoses have also caused economic devastation
- ▶ By relying on equity crowdfunding, SafeRx can maintain the autonomy to stay true to our mission
 - ▶ this helps to ensure our ARO products will reach the patients who need them and enables re-investment of proceeds into research and development of other lifesaving solutions to this multi-dimensional crisis

DEVELOPING ALCOHOL-RESISTANT OPIOIDS (AROs)



“If I have seen further
it is by standing on
the shoulders of giants”

Sir Isaac Newton

Scientist, born January 4, 1643

[O.S. December 25, 1642]

Portrait by Sir Godfrey Kneller

Developing AROs

“On the Shoulders of Giants”

➤ Expedited Development and Approval Process

- All active pharmaceutical ingredients in the ARO platform of products are already FDA-approved for their intended functions

Hatch-Waxman Amendments of Drug Price Competition and Patent Term Restoration Act established abbreviated FDA approval pathways, including 505(b)(2)

“A 505(b)(2) application is an NDA... where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use.”

-Reduced scope of new clinical trials can reduce time and cost dramatically

- The opioid crisis remains a national public health emergency

Because ARO products address a designated health emergency they are expected to qualify for Priority Review with the FDA

-Reduces new drug application review time to <6 months



Developing AROs “On the Shoulders of Giants”

MEDIAN NME AND PAA DEVELOPMENT TIMES (2010-2018):

DEVELOPMENT PROGRAM	DEVELOPMENT TIME
New Molecular Entity	7.7 Years
Previously Approved API(s)	
Efficacy/Safety Trials	5.1 Years
Bioequivalence Trials (505b2)	2.3 Years

Modified by Bossart, J. Drug Development Times, What it Takes–Part 3. *Drug Development & Delivery*. April 2020

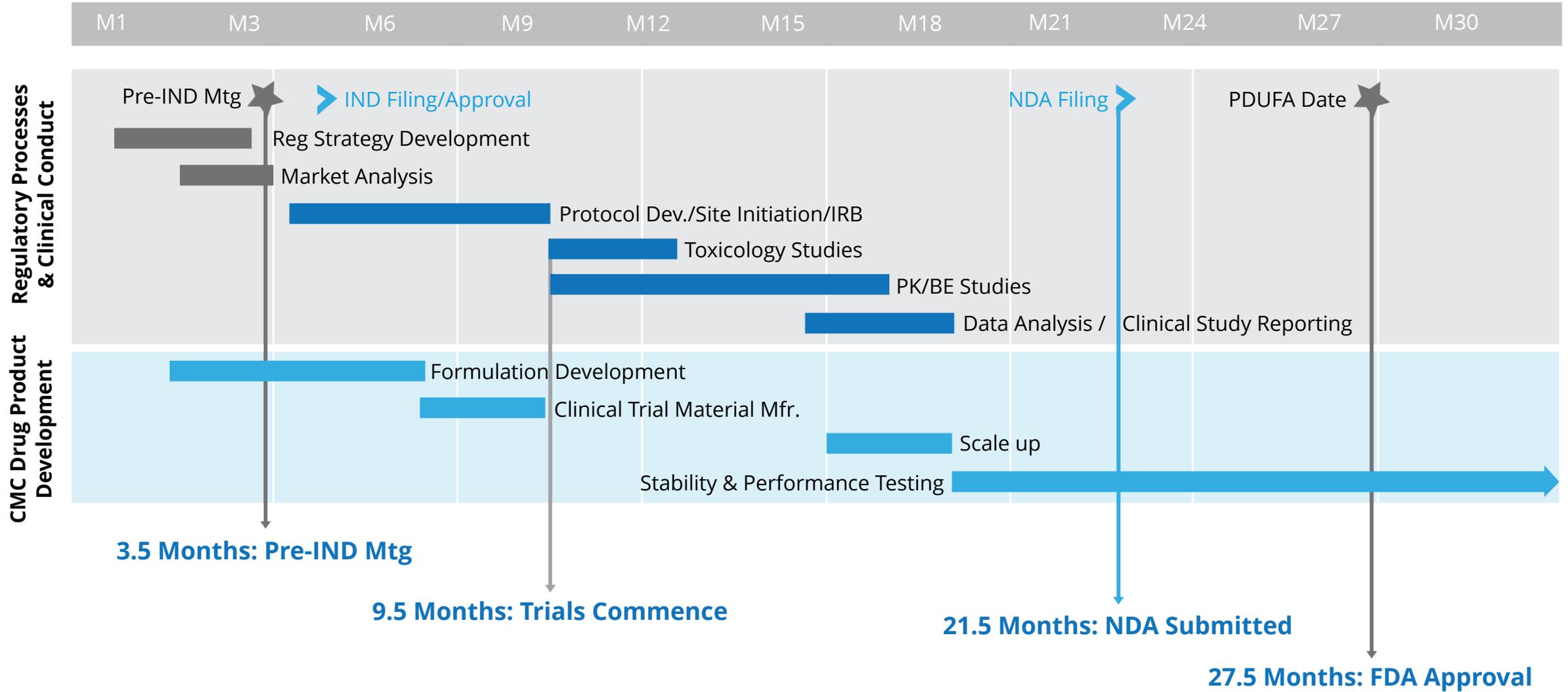
➤ OxARO® IR & MethARO® IR approvals expected in <3 years

The SafeRx Platform Consists of 7 Products:

1. OxARO[®] IR (oxycodone hydrochloride-disulfiram tablets, immediate-release)
2. MethARO[®] IR (methadone hydrochloride-disulfiram tablets, immediate-release)
3. HydARO[®] IR (hydrocodone bitartrate-disulfiram tablets, immediate-release)
4. MorphARO[®] IR (morphine sulfate-disulfiram tablets, immediate-release)
5. OxARO[®] ER (oxycodone hydrochloride-disulfiram tablets, extended-release)
6. HydARO[®] ER (hydrocodone bitartrate-disulfiram tablets, extended-release)
7. MorphARO[®] ER (morphine sulfate-disulfiram tablets, extended-release)

- We plan to seek FDA approval of these products in the order listed above.
- Capital raised from the current equity crowdfunding campaign is intended to support the OxARO[®] IR and MethARO[®] IR development programs.

OXARO® IR DEVELOPMENT TIMELINE



There Are No Direct Competitors

- ▶ Currently, after scouring the market, we are not aware of any companies in (or planning to enter) the market with products specifically designed to address the risk of alcohol consumption with opioids
- ▶ Closest 'competing' RX: Abuse-Deterrent Formulation opioids, which are designed to make inappropriate use less rewarding or more difficult
 - ▶ Existing products target improper routes of administration (IV, IN)
 - ***None prevent concurrent alcohol-opioid consumption***

...and Alternatives Don't Work

STRATEGY	MECHANISM	EFFICACY
Counseling	Education, Support	Weak
Patient-Signed Contract	Written Agreement, UDS	Weak
Antabuse™	ALDI (monotherapy)	Weak

Physicians currently have no effective means of preventing patients from drinking with their opioid.



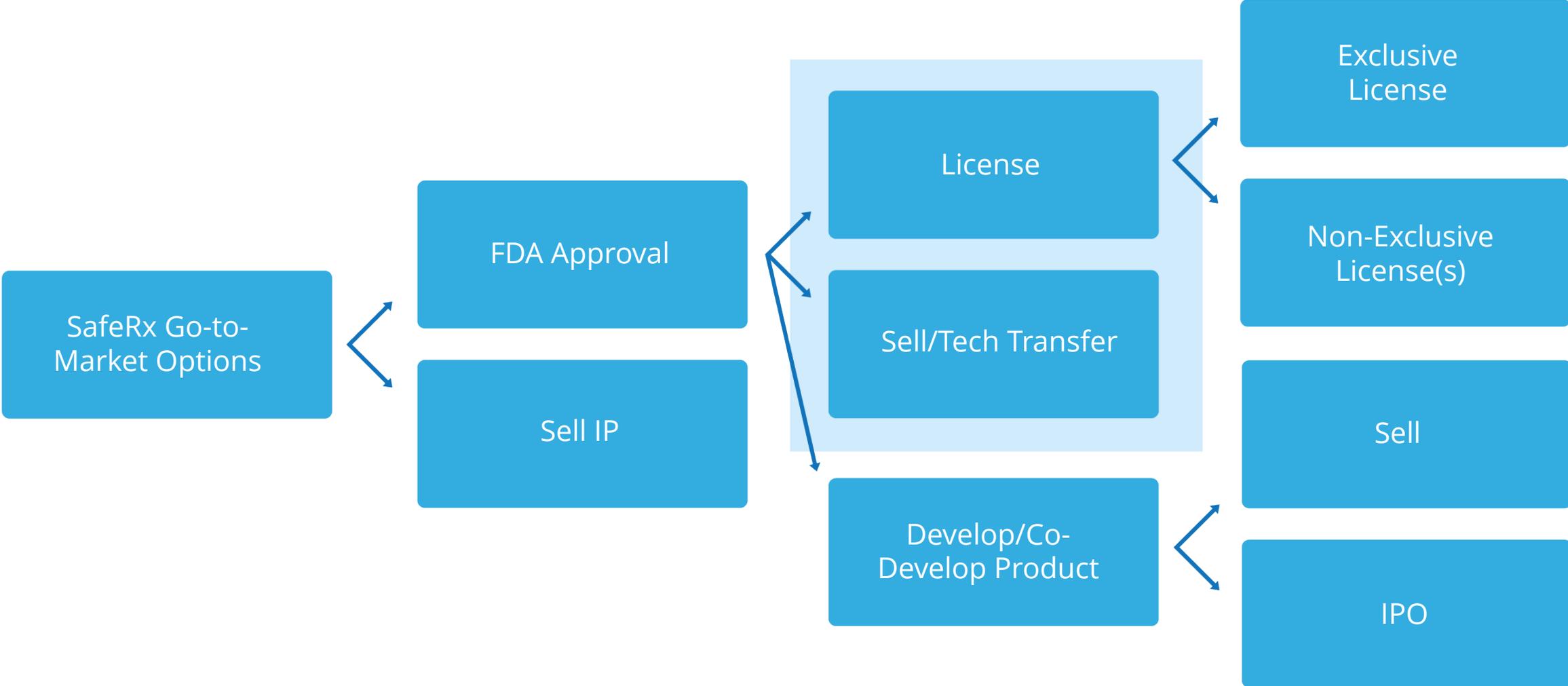
“Alcohol-resistant opioids protect both the patient and prescriber. They will be enthusiastically adopted.”

Brett Miller, M.D.; Vice-Chair,

Department of Anesthesiology; Santa Clara Valley Medical Center

Clinical Associate Professor; Stanford Anesthesiology, Perioperative, and Pain Medicine

SafeRx Product Approval and Revenue Path



Addressable Market

% patients likely to benefit from conversion to an ARO product depends on patient group:

▶ Chronic

- ▶ 36 – 58% drink with opioid^{1,2}
- ▶ 24% binge drink

▶ Opioid Use Disorder

- ▶ 76 – 81% drink with opioid^{3,4}
- ▶ 23 – 41% alcohol-dependent^{3,4,5}



“There is no safe level of alcohol use for people using opioids.”

Centers for Disease Control and Prevention

¹Saffier, K., C. Colombo, D. Brown, M. Mundt & M. Fleming. Addiction Severity Index in a chronic pain sample receiving opioid therapy. *J Subst Abuse Treat.*, 2007; 33:303-311.

²Larance B, Campbell G, Peacock A, Nielsen S, Bruno R, Hall W, Lintzeris N, Cohen M, Degenhardt L. Pain, alcohol use disorders and risky patterns of drinking among people with chronic non-cancer pain receiving long-term opioid therapy. *Drug Alcohol Depend.*, 2016; 162:79-87.

³Hillebrand, J., J. Marsden, E. Finch & J. Strang. Excessive alcohol consumption and drinking expectations among clients in methadone maintenance. *J Subst Abuse Treat.* 2001; 21:155-160.

⁴Dobler-Mikola, A., J. Hattenschwiler, D. Meili, T. Beck, E. Boni & J. Modestin. Patterns of heroin, cocaine, and alcohol abuse during long-term methadone maintenance treatment. *J Subst Abuse Treat.*, 2005; 29:259-65.

⁵Hser YI, Mooney LJ, Saxon AJ, Miotto K, Bell DS, Huang D. Chronic pain among patients with opioid use disorder: Results from electronic health records data. *J Subst Abuse Treat.*, 2017; 77:26-30.

Addressable Market

- ▶ At least 1/3 of opioid RXs should be converted to an ARO formulation
 - ▶ Rx/year “convertible” to ARO: 51.09M
- ▶ Current Average Market price/MME = \$0.20/MME
- ▶ Current Average MME/Rx = 1187/MME
 - ▶ Current Average Market price per ARO Rx: \$237.34

\$12.1 billion

Annual revenue if all “at-risk” patients converted from a traditional opioid formulation to an ARO formulation, based on stated assumptions.

Summary: Competitive Advantages

- ▶ Disruptive Solution to Public Health Emergency
 - ▶ Previously unaddressed dimension of the opioid crisis with no effective alternatives
 - ▶ Reduces medico-legal liability for opioid prescribers
- ▶ First Mover with Intellectual Property
 - ▶ New, paradigm-shifting class of alcohol-resistant opioids that will save thousands of lives
 - ▶ Issued USPTO utility patents (#10,478,408 and #10,881,625); enforceable through 2038
- ▶ Straightforward Regulatory Pathway
 - ▶ 505-b2 NDA; Priority Review given public health emergency
 - ▶ FDA approval expected within 3 years of funding
- ▶ Capital-Efficient
 - ▶ Abbreviated regulatory pathway; clinical trials limited in size/scope
 - ▶ No costly technology required; “virtual pharmaceutical company” model
- ▶ Quality Team
 - ▶ Sophisticated, mission-driven founding team and board
 - ▶ Extensive industry experience and track record of success

Thank You!



www.InvestInSafeRx.com



FOUNDING TEAM



Michael Presti, MD PhD

Founder-CEO

- MD and PhD (Neuro) from University of Florida
- NIH National Research Service Awardee
- Master's in Business Management from Warrington School, University of Florida
- Neurology residency and fellowship training at Mayo Clinic Rochester
- Diplomat of the ABPN and ABSM
- Inventor with multiple USPTO issued patents



Ray Sison

Chief Product Officer

- 25+ yrs in pharmaceutical formulation dev, product launch and commercialization
- Created licensing, acquisition & commercialization opportunities for OptiNose, Lonza Group, Teva Pharma
- Expert in outsourced pharma development and virtual supply chain coordination
- Involved in product launches of Roxybond and Morphabond, both ADF-labeled opioids

ADVISORY BOARD



Jamie Grooms

Executive Board Member

- ▶ Co-founded two highly successful life science companies: RTI Surgical, Inc. and AxoGen, Inc., both now publicly traded (NASDAQ: RTIX, AXGN)
- ▶ Former CEO of Florida Institute for Commercialization of Public Research
- ▶ Visionary and innovator in medical technology, regenerative medicine
- ▶ Successfully launched, managed, or advised numerous biotech startup companies



Marlo Tan Walpole

Board Member

- ▶ Over two decades Product Development experience in Medical Device, HCT/PS, Biologic, and Pharmaceutical industries
- ▶ Directed R&D at AuxThera Inc., AxoGen Inc. (NASDAQ: AXGN), RTI Surgical, Inc. (NASDAQ: RTIX) and other biotechnology companies
- ▶ Brings practical expertise especially for startup and small to mid-size companies



Jim Parrino, MBA PhD

Board Member

- ▶ Managing director and co-head of the M&A Buyside Advisory at Fifth Third Securities
- ▶ Managing director at Praxis Partners LLC
- ▶ Expert in corporate valuation, M&A, venture finance, entrepreneurship, corporate strategy, cross-border acquisitions
- ▶ CPA with 30+ years of operational, strategic and transactional M&A advisory experience