Ensysce™ biosciences

IMPROVING PRESCRIPTION DRUG SAFETY THROUGH CHEMISTRY

NASDAQ: ENSC

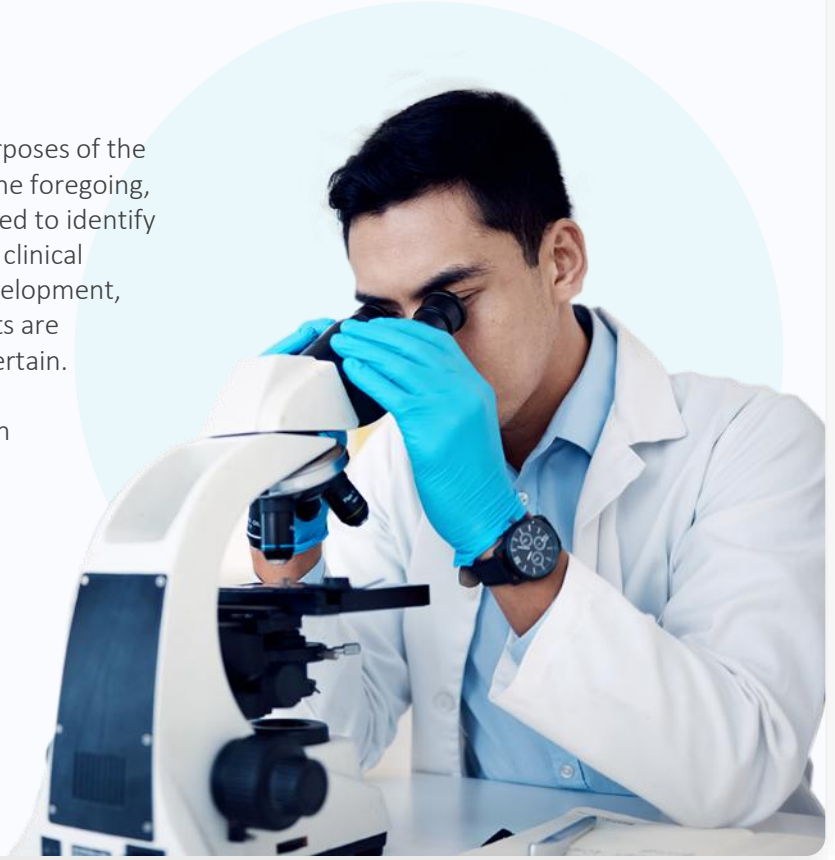
Investor Presentation July 2025

Disclaimer

Ensysce's PF614 and nafamostat are currently in clinical trial and pre-clinical studies, involving both the TAAP platform and MPAR platform. Accordingly, PF614 and nafamostat have the risks and uncertainties inherent in any drug in trial-phase, which include, but are not limited to, a failure to show sufficient efficacy to obtain FDA approval, the risk that clinical trials may not confirm any safety, potency or other product characteristics described or assumed herein and the possibility that presently unknown safety risks may occur. The statements made concerning PF614, nafamostat, TAAP and MPAR are subject to the complete set of risks set forth in the Risk Factors disclosure found in the Company's most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 15, 2024.

Forward Looking Statements

Statements contained in this presentation that are not purely historical may be deemed to be forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. Without limiting the foregoing, the use of words such as "may," "intends," "can," "might," "will," "expect," "plan," "believe" and other similar expressions are intended to identify forward-looking statements. The product candidates discussed are in clinic and not approved and there can be no assurance that the clinical programs will be successful in demonstrating safety and/or efficacy, that Ensysce will not encounter problems or delays in clinical development, or that any product candidate will ever receive regulatory approval or be successfully commercialized. All forward-looking statements are based on estimates and assumptions by Ensysce's management that, although Ensysce believes to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that Ensysce expected. In addition, Ensysce's business is subject to additional risks and uncertainties, including among others, the initiation and conduct of preclinical studies and clinical trials; the timing and availability of data from preclinical studies and clinical trials; expectations for regulatory submissions and approvals; potential safety concerns related to, or efficacy of, Ensysce's product candidates; the availability or commercial potential of product candidates; the ability of Ensysce to fund its continued operations, including its planned clinical trials; the dilutive effect of stock issuances from fundraising; and Ensysce's and its partners' ability to perform under their license, collaboration and manufacturing arrangements. These statements are also subject to a number of material risks and uncertainties that are described in Ensysce's most recent Annual Report on Form 10-K. Any forward-looking statement speaks only as of the date on which it was made. Ensysce undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required under applicable law



Ensysce Summary

Clinical-stage company – 'Next generation opioids' - disrupting analgesia using transformative trypsin-controlled chemistry.

Targeted therapy areas focus on products with blockbuster potential with FAST TRACK and BREAKTHROUGH THERAPY designation.

Lead Product near term launch with demonstrated safety and efficacy, **reducing clinical risk**.

Shortened development timeline with 505(b)(2) regulatory pathway, **de-risked** with **positive clinical data** demonstrating the novel approach.

Strong global patent estate

Highly experienced management team - broad biopharma background, from drug development to commercialization.

TAAP™

Anti-abuse chemistry

MPAR®

Overdose protection

A New Solution: Treat Pain AND Provide Abuse and Overdose Protection

— Delivering 'Next Generation' opioid products

USING TWO CORE TECHNOLOGY PLATFORMS

TAAP™
Trypsin-Activated Abuse Protection

MPAR®
Multi-Pill Abuse Resistance: Combination Product for Overdose Protection

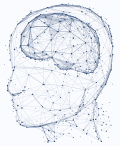
…to deliver improved drug performance.

Immediate focus – severe pain

Two Clinical Programs in Development

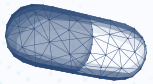
Dueling Crises: Severe Pain vs Abuse/Overdose

— Pain is the Leading Cause of Doctor Visits



35 Million
Americans in severe pain

10 Million
Misuse Opioids



143 Million
Opioid Rx in USA

Severe Pain is **#1 fear** in Cancer Patients

https://drugabusestatistics.org/opioid-epidemic/ | https://www.cnn.com/2022/12/14/health/drug-overdose-deaths-slowing/index.html

Supply Crisis for Pain Sufferers

NEWSWEEK MAGAZINE

How the Opioid Backlash Went Wrong

BY DAVID H. FREEDMAN ON 05/03/23 AT 5:00 AM EDT

About 8 million patients in the U.S. who depend on opioids to face constant, intense pain are at risk of losing access to the one treatment that seems to make the pain bearable. That includes Barcelona. "I don't think I could have lived without the drugs I've been taking," he says.

My Story: A Bone Cancer Survivor's Search for Pain Relief

PAIN NEWS NETWORK

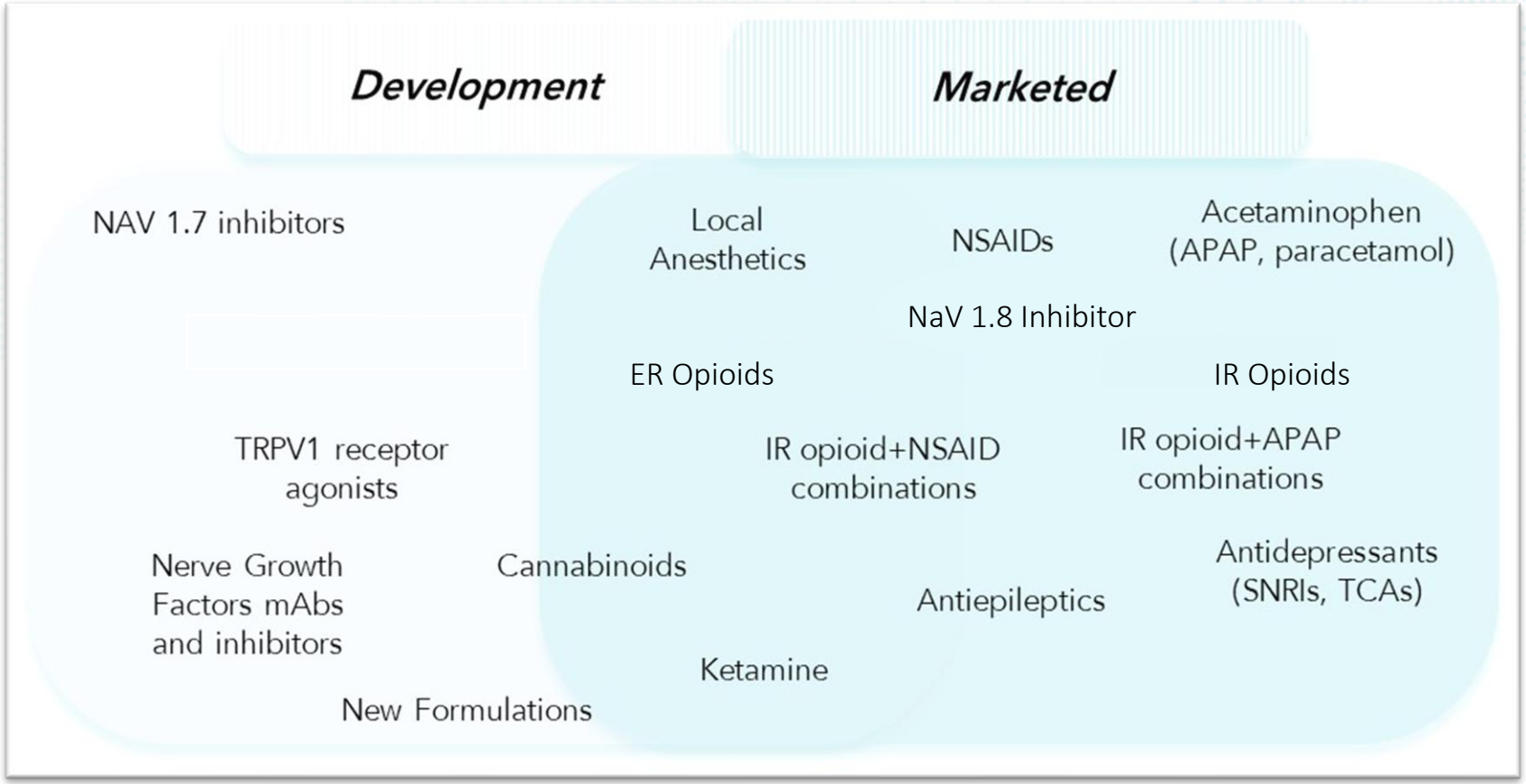
August 04, 2023

By Kristen Hernandez

The past three weeks have been the most challenging since my cancer diagnosis 20 years ago. Shortages of opioid pain medication have taken their toll, costing me weeks of productivity, mental and physical anguish, and a negative bank account.

The Search for a New Gold Standard to Treat Severe Pain

- FDA encouraging companies to make opioid analgesics as safe as possible for patients



FDA U.S. FOOD & DRUG ADMINISTRATION

The FDA is encouraging the development of prescription opioids with abuse-deterrent properties to help combat the opioid crisis. Abuse-deterrent formulations target known or expected routes of abuse. FDA is working with many drug makers to support advancements in this area and helping drug makers navigate the regulatory path to market as quickly as possible.

https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/abuse-deterrent-opioid-analgesics

The Next Generation of Opioids for Powerful Pain Relief

> **New class of opioid**

> **Low abuse –** Prescriber confidence/reassurance to patients

> **Reduced risk of overdose,** *first time ever*

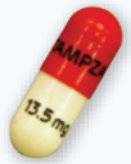
3400 B.C.

Originally identified

1900s

Pharmaceuticals
Immediate release opioids

1990s



Abuse Deterrent Formulations (ADFs)
Extended-release formulations claimed to reduce abuse and addiction

2020s

TAAP™ and MPAR®
Immediate and extended-release chemistry to deliver pain relief when needed

How is the Ensysce Solution Different?

— TAAP™ & MPAR®: Smart, Unique and Extensible Platforms Improving Drug Performance and Safety

TAAP™

Trypsin-Activated Abuse Protection*

PROTECTIVE	Trypsin **TURNS ON RELEASE** only in small intestine.
CONTROLLABLE	Chemically engineered to provide immediate or extended-release products.
ANTI-ABUSE	Reduces ability to tamper with drug product.
PERFORMANCE	TAAP™ to improve product delivery.

MPAR®

Multi-Pill Abuse Resistance: Combination Product for Overdose Protection *

SMART	**TURNS OFF RELEASE** only with overdose.
COMBINATION	Trypsin inhibitor, nafamostat added to TAAP products.
UNIQUE	Platform based on trypsin control of activation and release.
MULTI-USE	TAAP™ and MPAR® can be applied to numerous drug classes.

*For mechanism see appendix

Diversified Pipeline

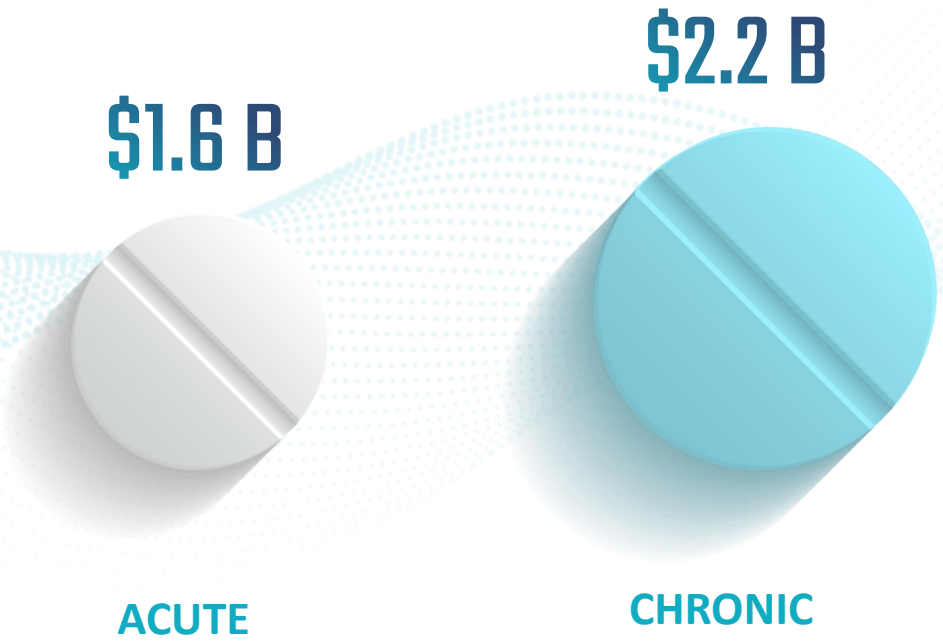
Neuroscience and Respiratory Diseases

Program	Therapeutic Target	Discovery	Phase 1	Phase 2	Phase 3
PF614	Pain with abuse protection	TAAP-Oxycodone			FDA Fast Track
PF614-MPAR	Pain with overdose protection	TAAP-MPAR-Oxycodone			FDA Breakthrough Therapy
PF329	Pain with abuse protection	TAAP-Hydromorphone			
PF8001	ADHD - Immediate release	TAAP-Dexamphetamine			
PF8026	ADHD - Extended release	TAAP-Dexamphetamine			
PF9001	Opioid Use Disorder	TAAP-Methadone			
Nafamostat*	Infectious diseases				

TAAP™ and MPAR® platforms with 505(b)(2) regulatory development path; *Nafamostat in development for MPAR®, infections and respiratory diseases. ER = Extended Release, IR = Immediate Release

Market Opportunity – US

US Pain Management Drugs Market *



*Ref: IQVIA 2023 Market Data

LAUNCH STRATEGY

- **Launch PF614** for acute severe pain use to provide superior pain control over limited period of time**.
- **Launch PF614-MPAR** for chronic pain
- **Cross reference** NDAs to support acute/ chronic use for both PF614 and MPAR

** PF614 used for post-surgical pain is anticipated to have four key advantages over traditional opioids: (a) pre-dosing at the start of surgery to reduce pain generation from the beginning vs. chasing pain that is already moderate to severe at the end of surgery, (b) having a longer duration of action to allow patients to stop or transition off opioids before leaving the hospital or clinic and continue using only non-opioid drugs at home, (c) reducing overall opioid use, and (d) potentially reducing overall healthcare costs.

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PF614

TAAP OXYCODONE

Fast Track Designation

Grant by FDA January 2018

PF614 for Severe Pain

Strong Efficacy – Less Abuse

PF614

- **TAAP™ Prodrug**
  - > Delivers potent pain relief – equivalent to Oxycontin with reduced abuse potential
- **Fast Track granted**
- **505(b)(2)**
  - > Shortened path to registration

PF614: The IDEAL Analgesic for Severe Pain

PF614

Bioequivalent to OxyContin[1]

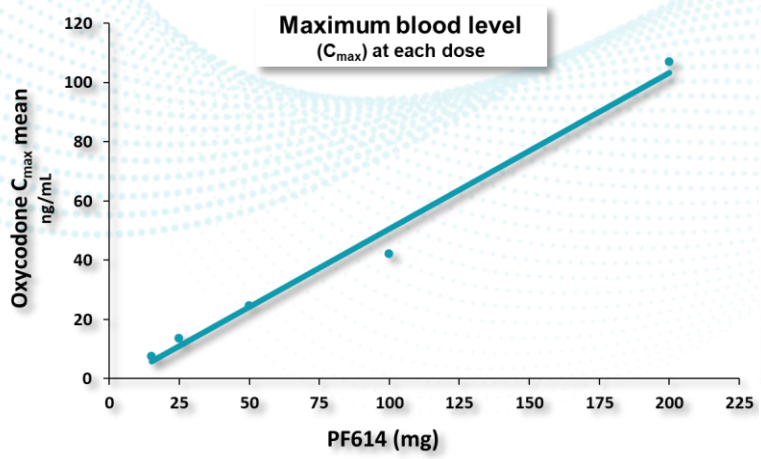
1) Clinical support; Potential 505(b)(2) path
2) Retaining Abuse Deterrence

- Efficacy = oxycodone
- Slow to reach blood levels – not "liked"
- No Food Effect
- Real 12-hour half-life for twice daily dosing
- Can dissolve in water for easy dosing
- Can "Switch on" to start activation
- Can "Switch off" to stop overdose

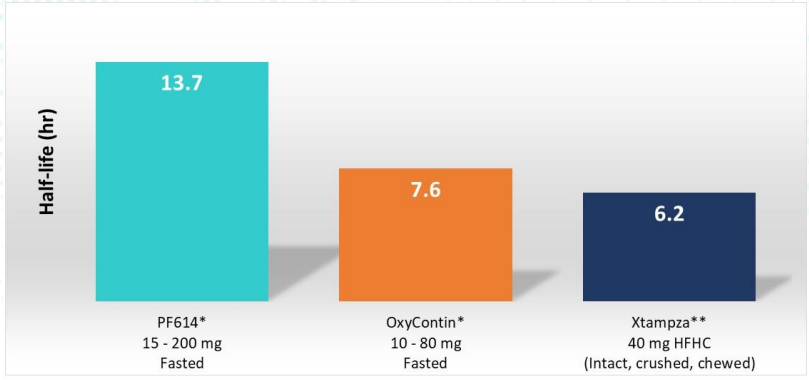
PF614 – 12 hour pain relief/reduced abuse

PF614 Clinical Data

PF614 efficiently delivers oxycodone

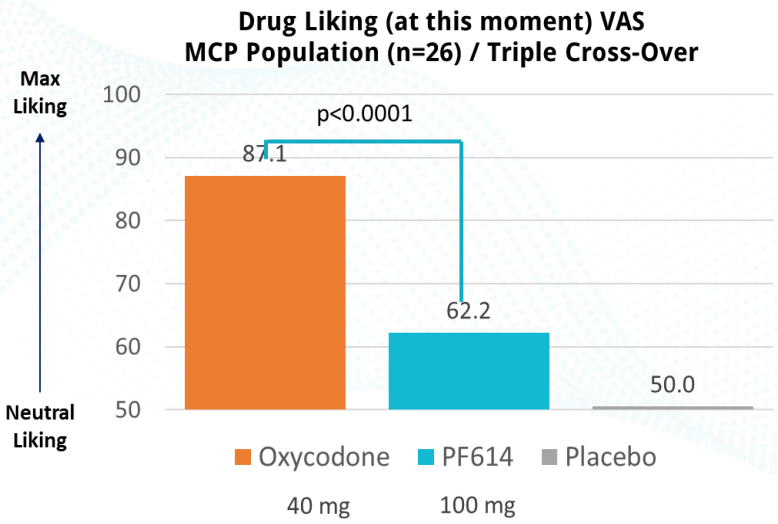


Longer oxycodone half-life supports BID dosing



* From PF614-101, Phase 1 SAD trial
** From Application 208090Orig1s000 CDER pg 11

Reduced nasal abuse potential



Clinical Milestones

COMPLETED STUDIES	SIGNIFICANCE
PF614-101/102 Single and multi-ascending dose and Bioequivalence study Positive bioequivalence data between PF614 and OxyContin	**Shortened 505(b)(2) regulatory path possible**
PF614-103 *Nasal Human Abuse Potential studies:* Significantly Reduced 'Drug Liking' for PF614 vs oxycodone comparator	**Abuse-deterrent labeling possible – inhalation**
PF614-104 *Oral Human Abuse Potential studies:* Significantly Reduced 'Drug Liking' for PF614 vs oxycodone comparator	**Abuse-deterrent labeling possible – oral**
PF614-201 *Efficacy/Time of Onset Study* Time of efficacy onset and pain reduction for 50 and 100 mg PF614	**Provides information for Phase 3 study design**

Next Steps for PF614

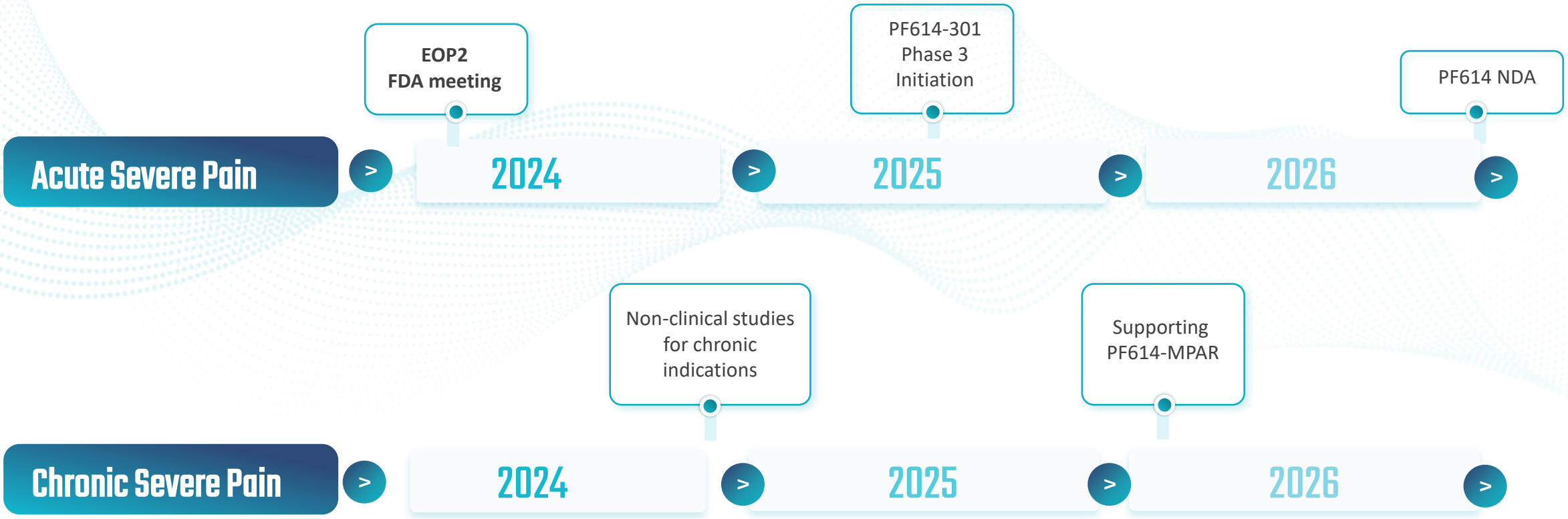
— Preparation for Phase 3

2024/2025	DESCRIPTION	SIGNIFICANCE
Regulatory	End of Phase 2 meeting held to discuss Phase 3 plans for Acute Pain indication	**FDA input into non-clinical, CMC and pivotal trials leading to NDA***
PF614-301	Phase 3 study Abdominoplasty: Post-surgical pain	**Pivotal study leading to NDA**

*NDA = New Drug Application submitted for approval to the FDA.

PF614 Development Plans in US

- Development Pathway for Acute and Chronic Pain Indications



Bold text: Completed
Non-bold text: Planned studies

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PF614-MPAR

TAAP Oxycodone with overdose protection

Breakthrough Therapy Designation

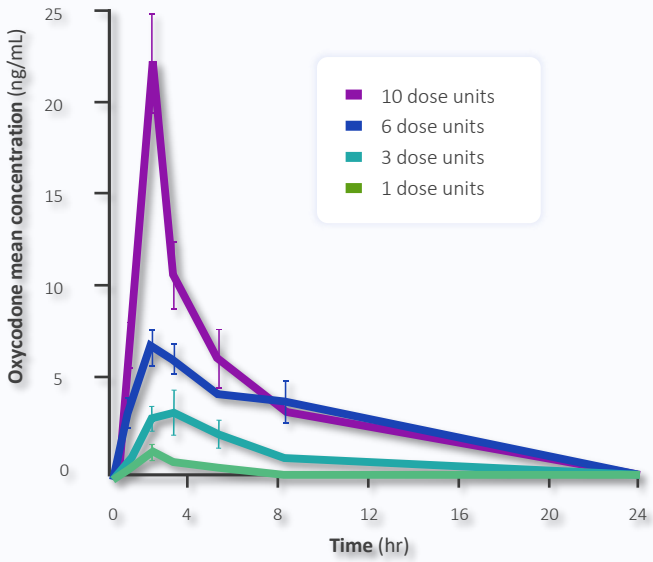
Grant by FDA January 2024

PF614-MPAR Pre-Clinical Data

— Blocks Activation of PF614 and Oxycodone Release if Overdosed

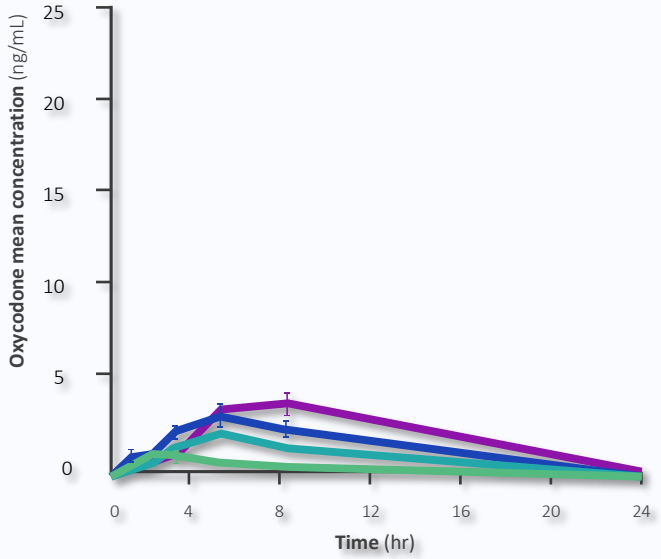
Oxycodone levels *without* MPAR®

PF614 without nafamostat



Oxycodone levels *with* MPAR®

PF614 with nafamostat

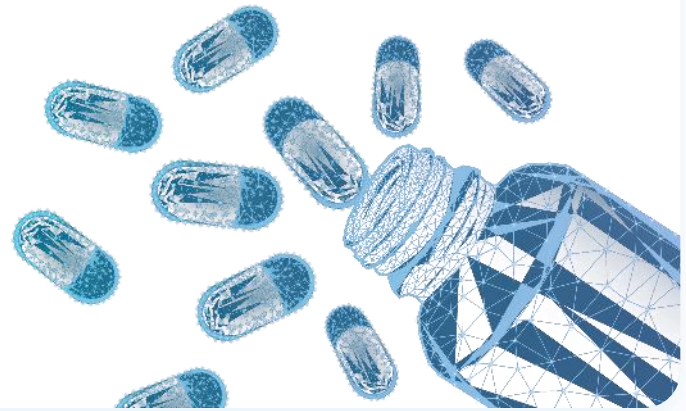


in rats n=4 / dose

TAAP + MPAR™: PRECLINICAL DATA

PRE-CLINICAL MPAR SUPPORT DATA

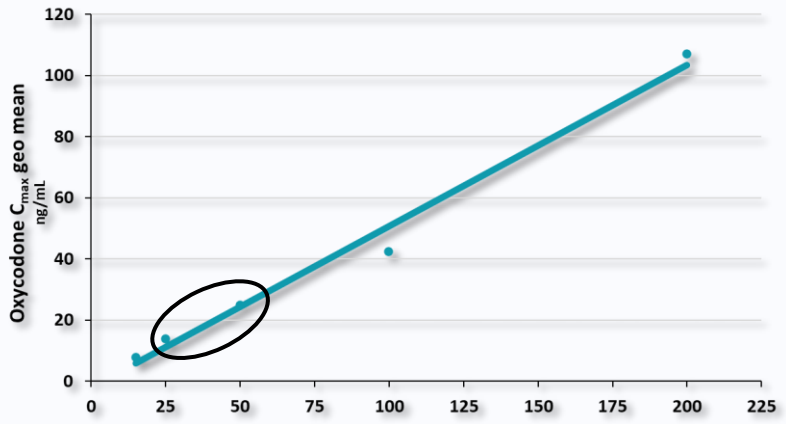
- Combination product of PF614 with an ultrapotent trypsin inhibitor, nafamostat
- Taken at prescribed doses there is no change in oxycodone release from PF614
- With increasing dose unit administration, increasing amounts of nafamostat blocks trypsin release of oxycodone and prevents opioid overdose



PF614-MPAR Pain Relief with Overdose Protection

— Phase 1 Clinical Study Demonstrating Overdose Protection

PF614 alone no MPAR® overdose protection

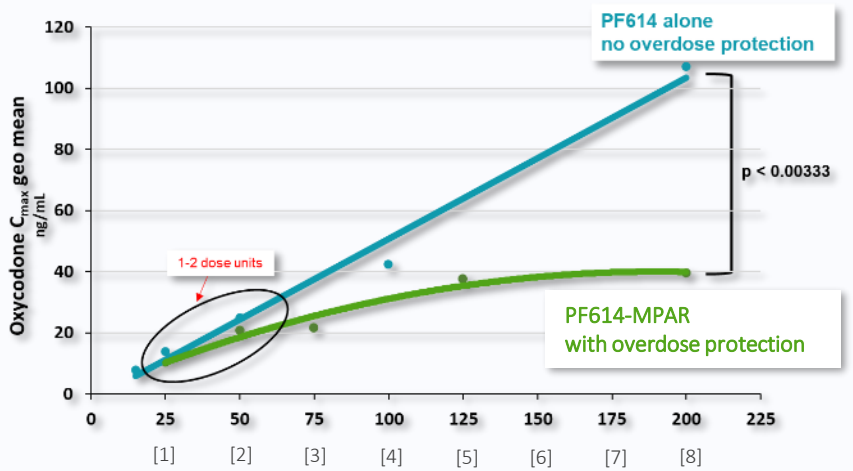


PF614 mg

PF614 alone (SAD-MAD studies)

Linear dose increase after each dose

PF614-MPAR 25 mg with MPAR® overdose protection



PF614 (mg) or PF614-MPAR [# dose units]

PF614 + nafamostat (PF614-MPAR study)

MPAR- Reduced activation after two dose units

Goal to deliver two doses up to twice daily

Trypsin controlled opioid release

Clinical Milestones

COMPLETED STUDIES	SIGNIFICANCE
PF614-MPAR-101 Part A and B: PF614 and nafamostat Positive PK data to define drug product and overdose protection	**First demonstration of overdose protection for a prescription opioid: 25 mg dose unit**
PF614-MPAR-102 Part A *Escalating 100 mg PF614-MPAR dose units*	Confirmation of overdose protection 25 to 100 mg PF614-MPAR
PF614-MPAR-102 Part B *Evaluating Food effect*	**Further evaluation of PF614-MPAR with and without food (ongoing)**
PF614-MPAR Breakthrough Therapy Designation	Granted by FDA

PF614-MPAR Development Plans

— Clinical Development for Overdose Protection

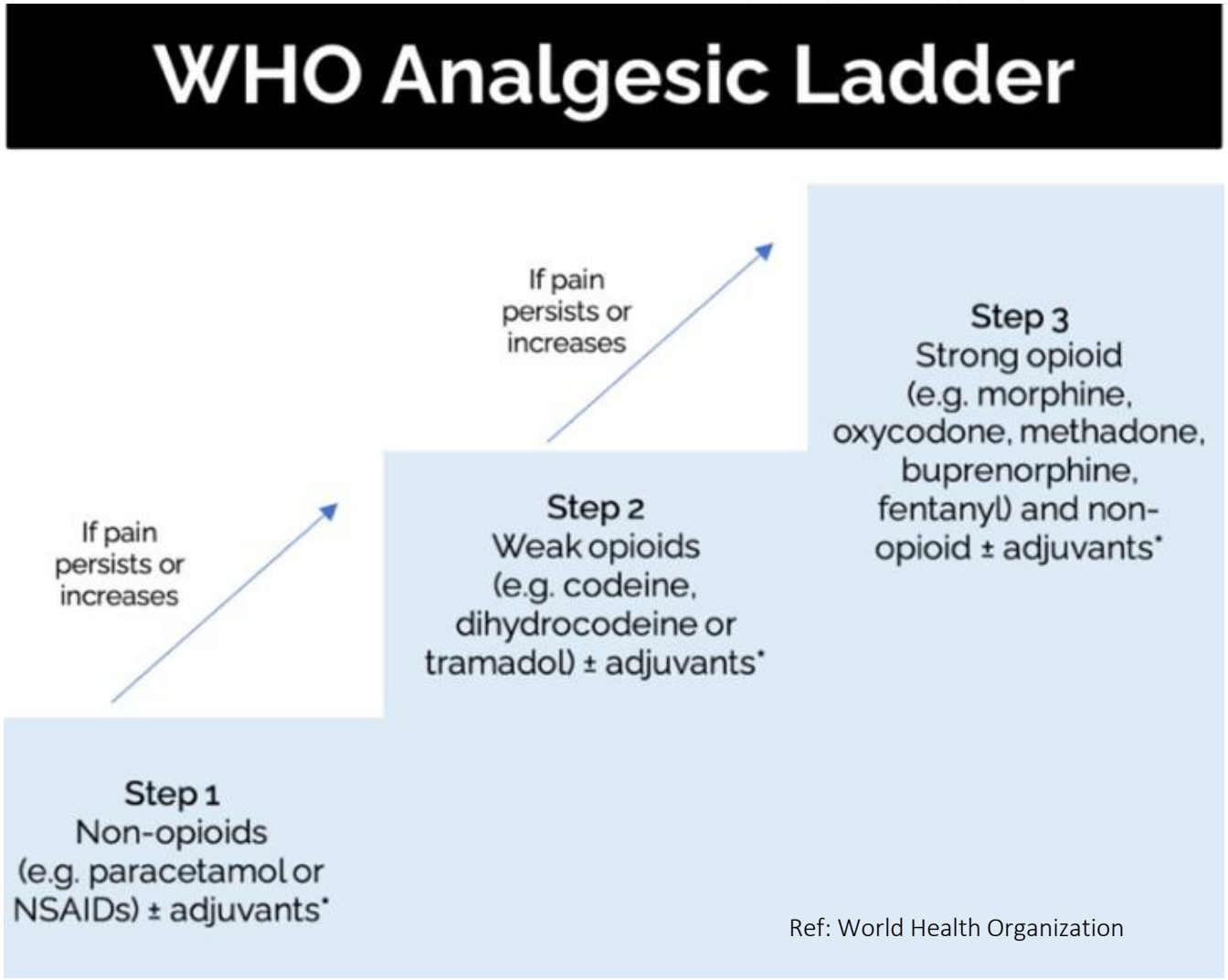
2024/2025	OUTCOME	SIGNIFICANCE
PF614-MPAR-102	Continue Phase 1b SAD 100 mg dose followed by MAD	Confirm overdose protection followed by MAD study to support Type B FDA meeting
PF614-MPAR	Meeting held with FDA to discuss development plans	Outline path to commercialization

Bold text: Completed
Non-bold text: Planned studies
OD: Overdose
SAD: Single Ascending dose study
MAD: Multi-Ascending dose Study

Analgesic Landscape– where will PF614 and new analgesics fit?

Target market for PF614
ER opioid

Target market for suzetrigine
NaV 1.8 inhibitor



Ref: World Health Organization

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TAAP™ and MPAR®

Expanded Opportunities

Drug Development Opportunities with TAAP™

Improving Drug Delivery and Lifecycle Management

TAAP™ MODIFICATION ATTRIBUTES

- Reaches the gastrointestinal tract/epithelial cells intact
- Chemistry controlled GI delivery for 'Immediate' or 'Extended-Release'
- Improves aqueous solubility
- Enhances the drug's permeation through the epithelial lining

OPPORTUNITY

Our TAAP™ platform enables new chemical entity (NCE) solutions that allow our collaborators to obtain new patents and extend market positions, revitalize approved medications and repurpose approved medications for the benefit of patients and care givers.

Possible oral delivery of injectable drugs

Enhance activity of drugs on GI tract

Extend half-life to improve dosing

Ensysce™ biosciences

EXPERIENCED MANAGEMENT

Management Team — Highly Motivated, Experienced Team with Proven Record

D. LYNN KIRKPATRICK, PHD

Chief Executive Officer

- Co-founded 2 start up companies
- Developed three targeted small molecule oncology drugs from discovery to clinic
- Experience in private and public company raising funds from private, public and government sources

BIOMIRA | ONCOTHYREON | Yale University School of Medicine

DAVID HUMPHREY, CPA

Chief Financial Officer

- Extensive experience in entrepreneurial environments
- Multiple equity and debt financing, including IPOs
- Focused on financial infrastructure, internal controls with merger and acquisition strategies

senomyx | ACTIVX Biosciences | pwc

GEOFF BIRKETT

Chief Commercial Officer

- Large pharma leadership experience
- Launched 5 major market-leading brands, including:
  - Nicorette | Prozac | Seroquel | Zomig

Lundbeck | NEKTAR | AstraZeneca | Lilly | INSEAD

LINDA PESTANO, PHD

Chief Development Officer

- Experienced in the design of pre-clinical programs focused on building IND-enabling data packages for lead candidate compounds intended for the treatment or diagnosis of cancer and inflammatory diseases
- PhD in Immunology from Tufts, Postdoctoral Research at Dana Farber, Harvard Medical School

VIRIDIAN | ONCOTHYREON | Tufts University | Roche

WILLIAM K SCHMIDT, PHD

Chief Medical Officer

- Over 25 years of pharma industry experience, with special emphasis on discovery and development of novel analgesic and narcotic antagonist drugs
- Past President of the Eastern Pain Association, affiliate of the American Pain Society

DUPONT | Adolor | CrystalGenomics | UCSF

JEFFREY MILLARD, PHD

Chief Operating Officer

- Industrial experience in CMC (chemistry, manufacturing, and controls)
- 7 IND submissions (CDER, CBER, and IMPDs); directed CMC efforts from discovery, in-licensing to commercial launch
- PhD in Pharmaceutical Sciences from University of Arizona

Arizona | ONCOTHYREON | Cascadian Therapeutics | BIOMIRA

Clinical Advisory Board

Pain, Addiction and Abuse Expertise

DR. LYNN WEBSTER

Dr. Webster has dedicated more than three decades to becoming an expert in the field of pain management

DR. JEFFREY GUDIN

Dr. Gudin is Faculty Dept of Anesthesiology/Pain Management, Univ of Miami, and Co-Editor of Practical Pain Management.

DR. RICHARD DART

Dr. Dart is the Director of the Rocky Mountain Poison and Drug Center and specializes in emergency medicine and toxicology.

DR. WILLIAM SCHMIDT

Over 25 years of pharma industry experience, with special emphasis on discovery/development of novel analgesic and narcotic antagonist drugs

Board of Directors

Business, Finance, Healthcare & Regulatory Expertise

Dr. Lynn Kirkpatrick

Career focused on novel drug discovery and development

Dr. Bob Gower

Seasoned Executive and Entrepreneur

Andrew Benton

President Emeritus of Pepperdine University

William Chang

Entrepreneur, Realty Company & Movie executive

Dr. Adam Levin

Academic and clinical orthopedic surgeon at Johns Hopkins Univ.

Steve Martin

Experienced Senior Executive and Chief Financial Officer

Dr. Curtis Rosebraugh

Extensive FDA drug approval experience

Lee Rauch

Experienced CEO and Strategy Advisor

Cash Resources

NASDAQ: ENSC

As of May 8, 2024

Shares Outstanding	2.4M
Shares Public Float	2.4M
Nasdaq Listed	July 2021
Headquarters	La Jolla, CA

$3.1M **Cash**
as of 3/31/25

$10.6M **MPAR Grant Funding Available**
2025 to 2027

$5.3M **MPAR Grant Funding Awarded**
as of 6/1/25

NIH support

2018-2023 - $11 million

2024-2027 - $15 million

Award to advance overdose protection MPAR®

Two multi-year awards received to undertake the development of the overdose protection platform **MPAR®** (Multi-Pill Abuse Resistance).

NIDA grant

2019-2024 - $5 million

2025-2028 - $10 million

Award to advance TAAP/MPAR OUD

Multi-year award to undertake the pre-clinical and clinical development of TAAP and MPAR® for treatments of Opioid Use Disorder.

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TAAP™

Anti-abuse chemistry

MPAR®

Overdose protection

Ensysce™ biosciences

Investor Relations

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