Ensysce™ biosciences

# IMPROVING PRESCRIPTION DRUG SAFETY THROUGH CHEMISTRY

**NASDAQ: ENSC**

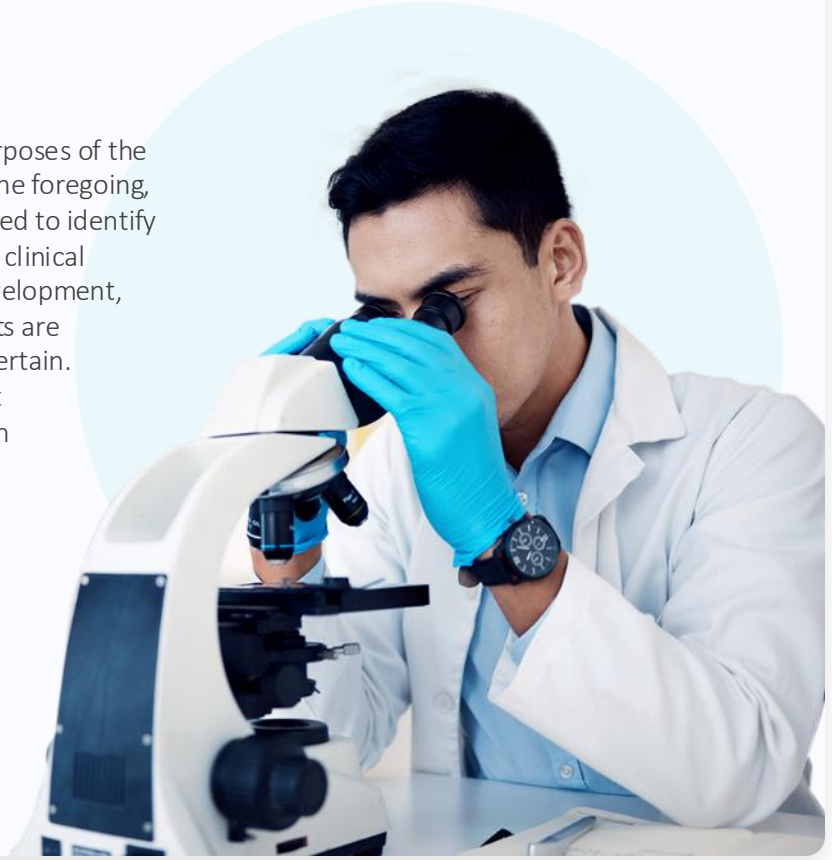
Investor Presentation September 2024

# 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



# 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

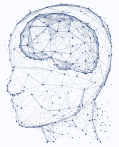
…to deliver improved drug performance.

## Immediate focus – severe pain

## Two Clinical Programs in Development

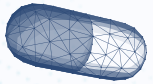
# Dueling Crises: Severe Pain vs Abuse/Overdose

## — 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.

# Lack of Innovation – Good News for Migraine Sufferers

## FDA Approved Analgesics 2014-2023

| YEAR | SPONSOR | DRUG NAME | INDICATION |
|---|---|---|---|
| 2023 | -- | -- | -- |
| 2022 | -- | -- | -- |
| 2021 | AbbVie | QULIPTA (atogepant) | Prevention of episodic migraine |
| 2020 | Trevena | OLINVYK (oliceridine) | Acute pain (i.v. opioid analgesic) |
| | Biohaven | NURTEC ODT (rimegepant) | Acute migraine |
| | Lundbeck | VYEPTI (eptinezumab) | Prevention of migraine |
| 2019 | Lilly | REYVOW (lasmiditan) | Acute migraine |
| | Allergan | UBREVLY (ubrogepant) | Acute migraine |
| | AbbVie | RINVOQ (upadacitinib) | Rheumatoid arthritis |
| 2018 | AbbVie | ORILISSA (elagolix) | Pain associated w/ endometriosis |
| | Lilly | OLUMIANT (baricitinib) | Rheumatoid arthritis |
| | Amgen | AIMOVIG (erenumab) | Prevention of migraine |
| | Teva | AJOVY (fremanezumab) | Prevention of migraine |
| | Lilly | EMGALITY (galcanezumab) | Prevention of migraine |
| 2017 | Sanofi-Aventis | KEVZARA (sarilumab) | Rheumatoid arthritis |
| 2016 | -- | -- | -- |
| 2015 | -- | -- | -- |
| 2014 | -- | -- | -- |

Ref.:
www.fda.gov/drugs/nda-and-bla-approvals/new-molecular-entity-nme-drug-and-new-biologic-approvals

# 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.

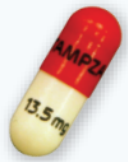

**Originally identified**

## 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

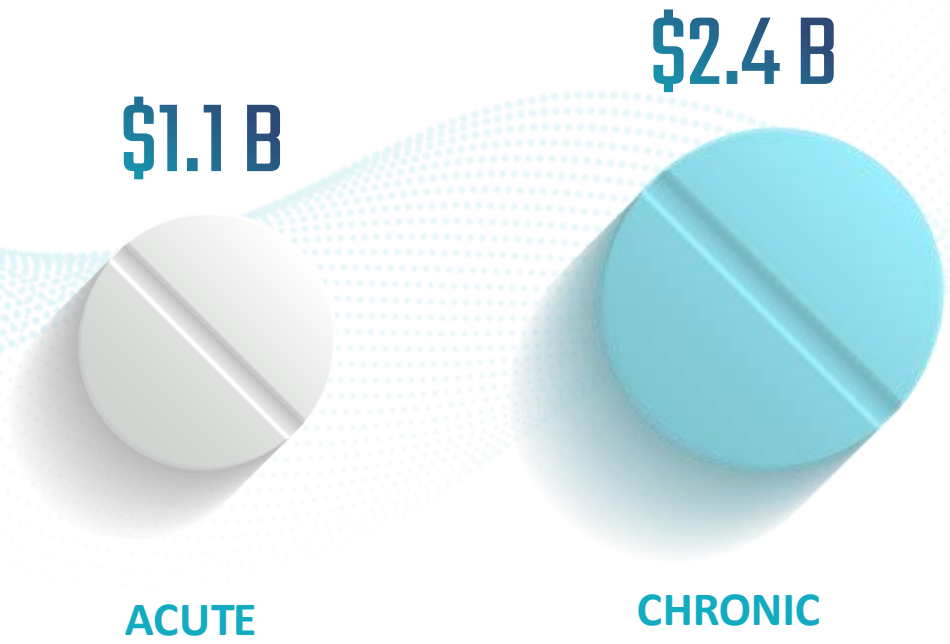
## Neuroscience and Respiratory Diseases

| 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

## LAUNCH STRATEGY

- **Launch PF614** for acute severe pain use
- **Launch PF614** for chronic pain use
- **Launch PF614-MPAR** for acute/ chronic use

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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]**

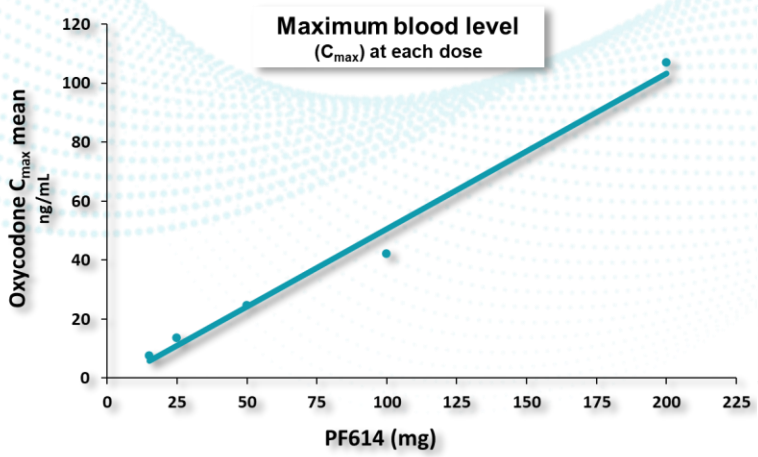
1) Clinical support; Potential 505(b)(2) path
2) Retaining Abuse Deterrence

- 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

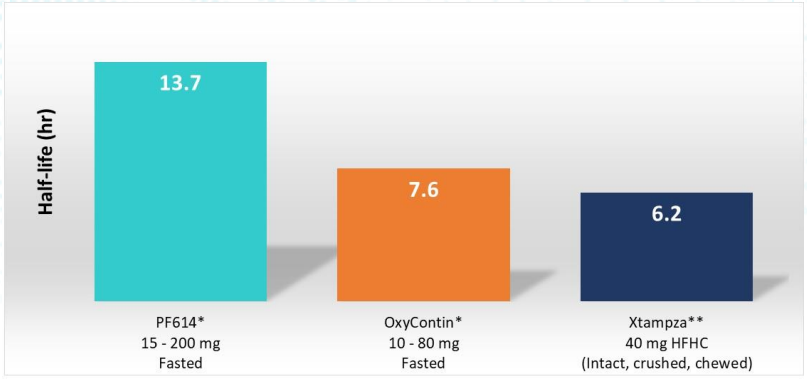
# PF614 – 12 hour pain relief/reduced abuse

## PF614 Clinical Data

### PF614 efficiently delivers oxycodone

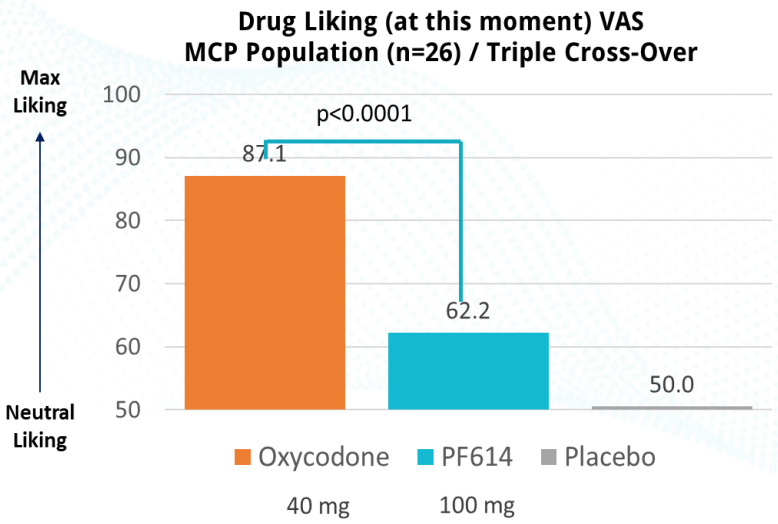



### Longer oxycodone half-life supports BID dosing




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

# Next Steps for PF614

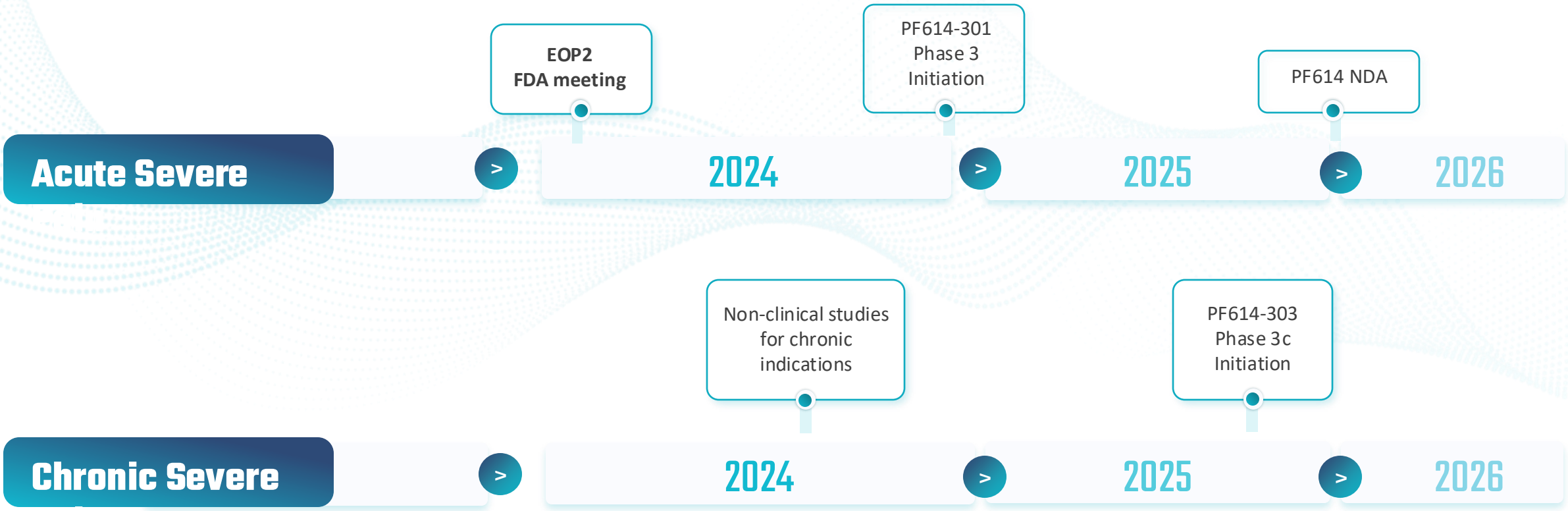
## Preparation for Phase 3

| 2024 | 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**

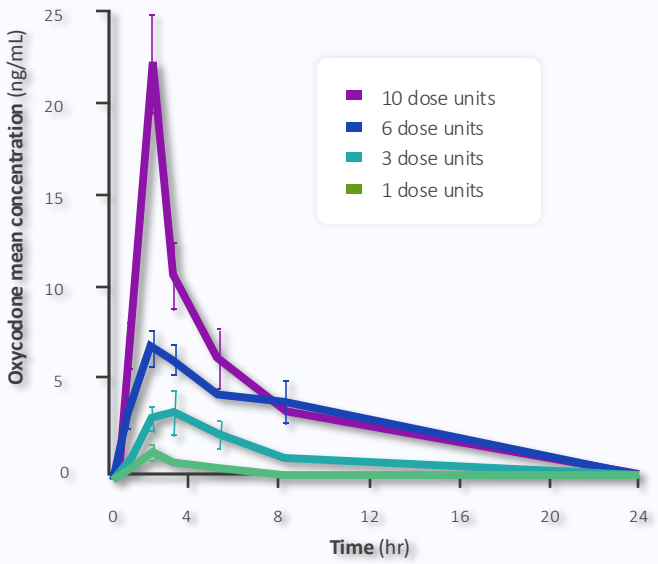
Grant by FDA January 2024

# PF614-MPAR Pre-Clinical Data

## — Blocks Activation of PF614 and Oxycodone Release if Overdosed

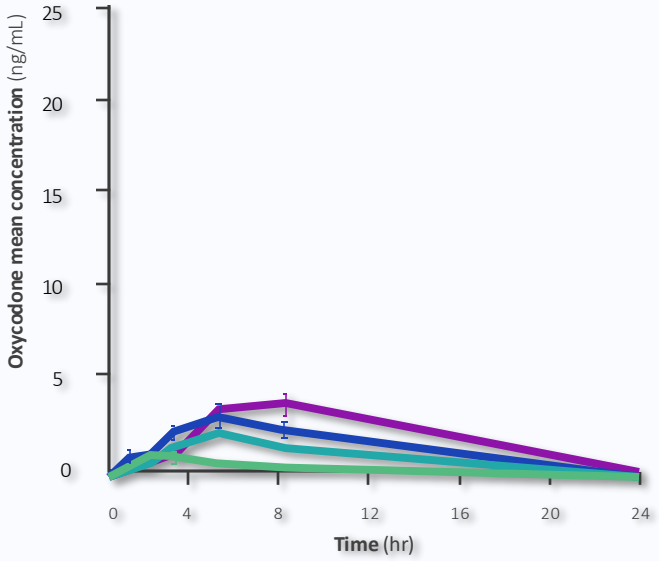
### Oxycodone levels *without* MPAR®

PF614 without nafamostat




### Oxycodone levels *with* MPAR®

PF614 with nafamostat

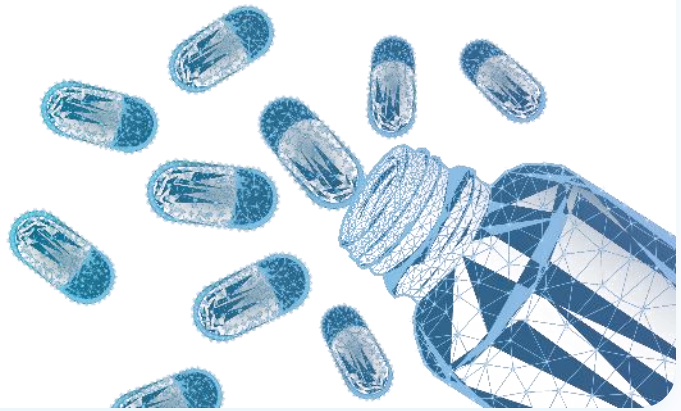



in rats n=4 / dose

TAAP + MPAR™: PRECLINICAL DATA

### PRE-CLINICAL MPAR SUPPORT DATA

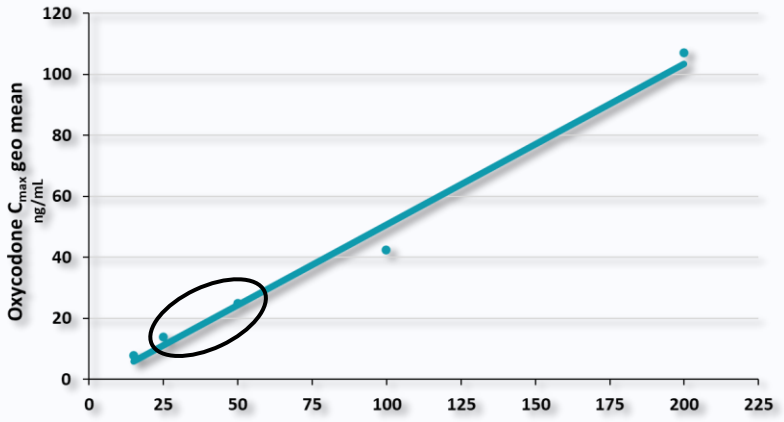
- Combination product of PF614 with an ultrapotent trypsin inhibitor, nafamostat
- Taken at prescribed doses there is no change in oxycodone release from PF614
- With increasing dose unit administration, increasing amounts of nafamostat blocks trypsin release of oxycodone and prevents opioid overdose



# PF614-MPAR Pain Relief with Overdose Protection

## — Phase 1 Clinical Study Demonstrating Overdose Protection

### PF614 alone no MPAR® overdose protection

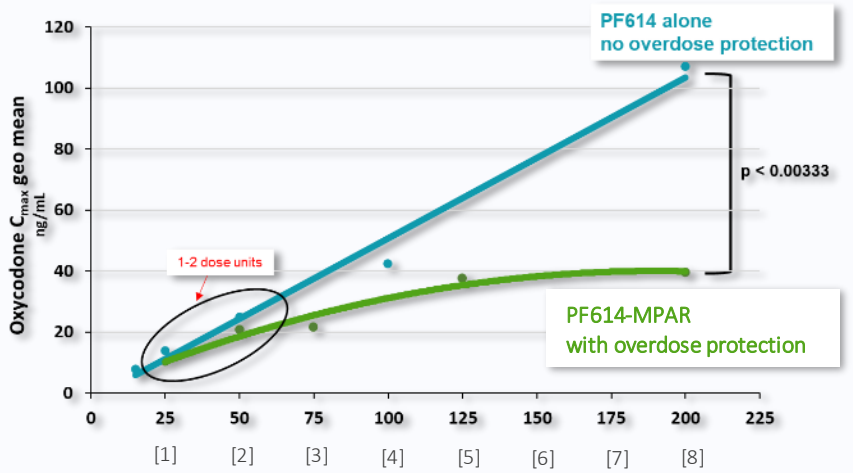



**PF614 mg**

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

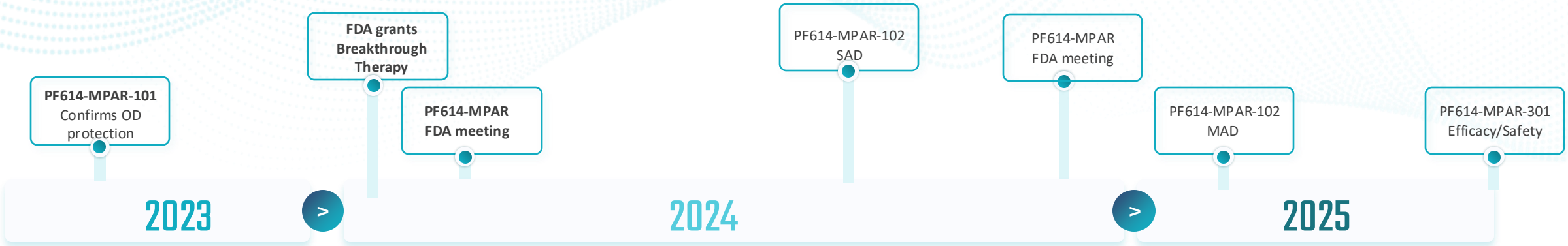
# Clinical Milestones

| COMPLETED STUDIES | SIGNIFICANCE |
| --- | --- |
| **PF614-MPAR-101 Part A:**<br>PF614 and nafamostat<br>Positive PK data to define drug product | **Optimized PF614 / nafamostat combination for 25 mg dose unit** |
| **PF614-MPAR-101 Part B**<br>*Escalating 25 mg PF614-MPAR dose units*<br>Confirmation of overdose protection | **First demonstration of overdose protection for a prescription opioid** |
| **PF614-MPAR**<br>Breakthrough Therapy Designation | Granted by FDA |

# PF614-MPAR Development Plans

## — Clinical Development for Overdose Protection

| 2024 | OUTCOME | SIGNIFICANCE |
|---|---|---|
| **PF614-MPAR** | Meeting held with FDA to discuss development plans | Outline path to commercialization |
| **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 |




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

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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

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# 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 August 30, 2024

| | |
|---|---|
| Shares Outstanding | 12.4M |
| Shares Public Float | 12.2M |
| Nasdaq Listed | July 2021 |
| Headquarters | La Jolla, CA |

**$1.0M** **Cash**
as of 6/30/24

**$1.9M** **OUD Grant Funding Available**
as of 6/30/24

**$5.1M** **Financing Gross Proceeds**
August 2024

## NIH grant – MPAR

2018-2023 - $11 million
**2024-2027 - $14 million**

**NIH awards to advance MPAR® overdose protection**

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

## NIH grant – OUD

2019-2024 - $5 million
2024-2028 - $10 million

**NIH 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.

# Ensysce Summary

**Clinical-stage company** - transformative trypsin-controlled chemistry.

**Targeted therapy areas** focus on products with blockbuster potential with FAST TRACK AND BREAKTHROUGH THERAPY DESIGNATION.

**Lead Product with demonstrated efficacy, reduced clinical risk,** and positive data showing **reduced abuse potential.**

**Shortened development timeline** with 505(b)(2) regulatory pathway, **de-risked** with **positive clinical data** showing the technology works.

**Strong global patent estate**

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

## TAAP™

Anti-abuse chemistry

## MPAR®

Overdose protection

Ensysce™ biosciences

# Investor Relations


## SHANNON DEVINE

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