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biosciences

## Launching the Next Generation Opioid Analgesics

## 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.

## 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** designations.



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



**Strong global patent estate**



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



**TAAP™**

Anti-abuse chemistry



**MPAR®**

Overdose protection

# Ensysce Battling Dueling Crises: Severe Pain vs Abuse/Overdose

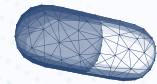
## — Pain is the Leading Cause of Doctor Visits



**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-slowng/index.html>



# How is the Ensysce Solution Different? TAAP™ & MPAR®: Chemical Safety Switches

## TAAP™

Trypsin-Activated Abuse Protection\*

### PROTECTIVE

Trypsin **URNS ON** RELEASE.

### CONTROLLABLE

Chemically engineered to control release.

### ANTI-ABUSE

Reduces abuse.

### PERFORMANCE

Improves product delivery.

## MPAR®

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

**URNS OFF** RELEASE only with overdose.

### SMART

Trypsin inhibitor and TAAP prodrug.

### COMBINATION

Platform based on trypsin control of activation and release.

### UNIQUE

MPAR® can provide overdose protection to other drug classes.

### MULTI-USE



\*For mechanism see appendix

# 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

# Market Opportunity – US

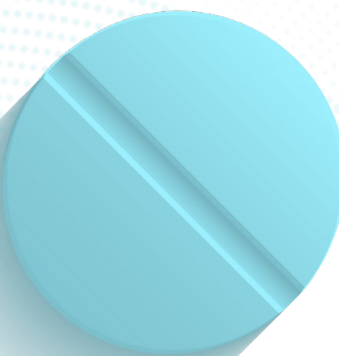
## US Pain Management Drugs Market \*

\$1.6 B



ACUTE

\$2.2 B



CHRONIC

## — 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.

# Diversified Pipeline

## Neuroscience and Respiratory Diseases

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



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**PF614** Strong Efficacy – Pain Management RE-Invented

**TAAP OXYCODONE**

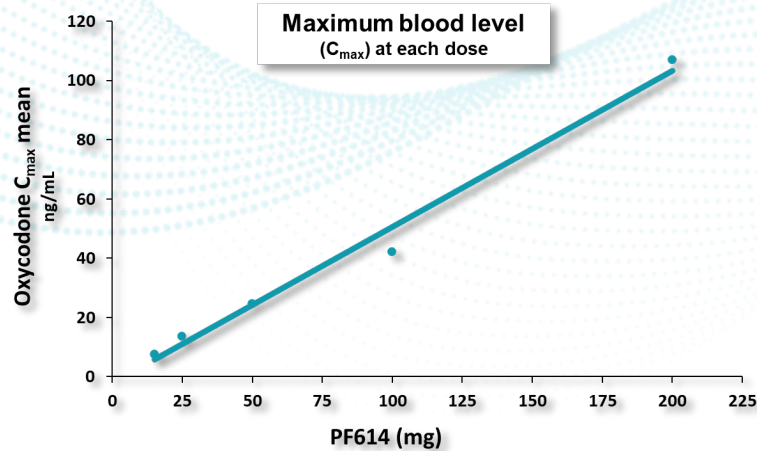
**Fast Track Designation**

**Grant by FDA January 2018**

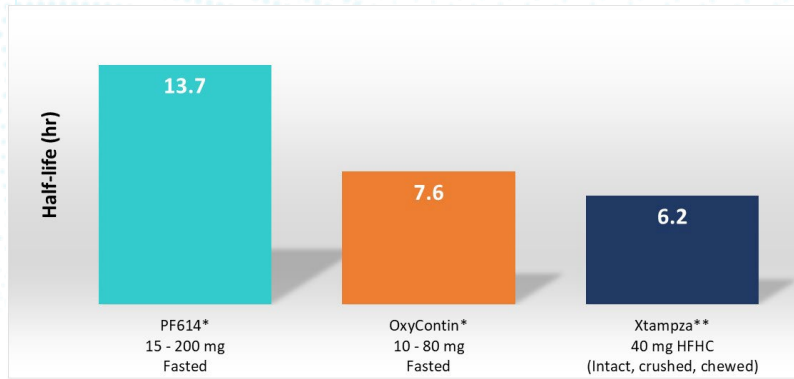
# PF614 – 12 hour pain relief/increased safety

## PF614 Clinical Data

### PF614 efficiently delivers oxycodone



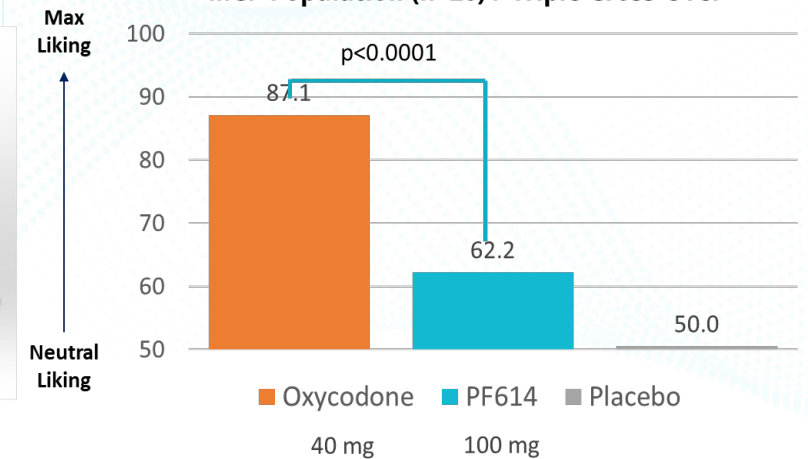
### Longer oxycodone half-life supports BID dosing



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

### Reduced nasal abuse potential

#### Drug Liking (at this moment) VAS MCP Population (n=26) / Triple Cross-Over



## PF614 Clinical Studies

**PF614-101: SAD Safety and PK**

**PF614-102: MAD and Bioequivalence to OxyContin**

**PF614-103: HAP Nasal PF614 vs crushed oxycodone**

**PF614-104: HAP oral PF614 vs oxycodone**

**PF614-201: Efficacy in Cold Pressor Study**

**PF614-301: Abdominoplasty PF614 vs placebo**



## PF614 for Severe Pain

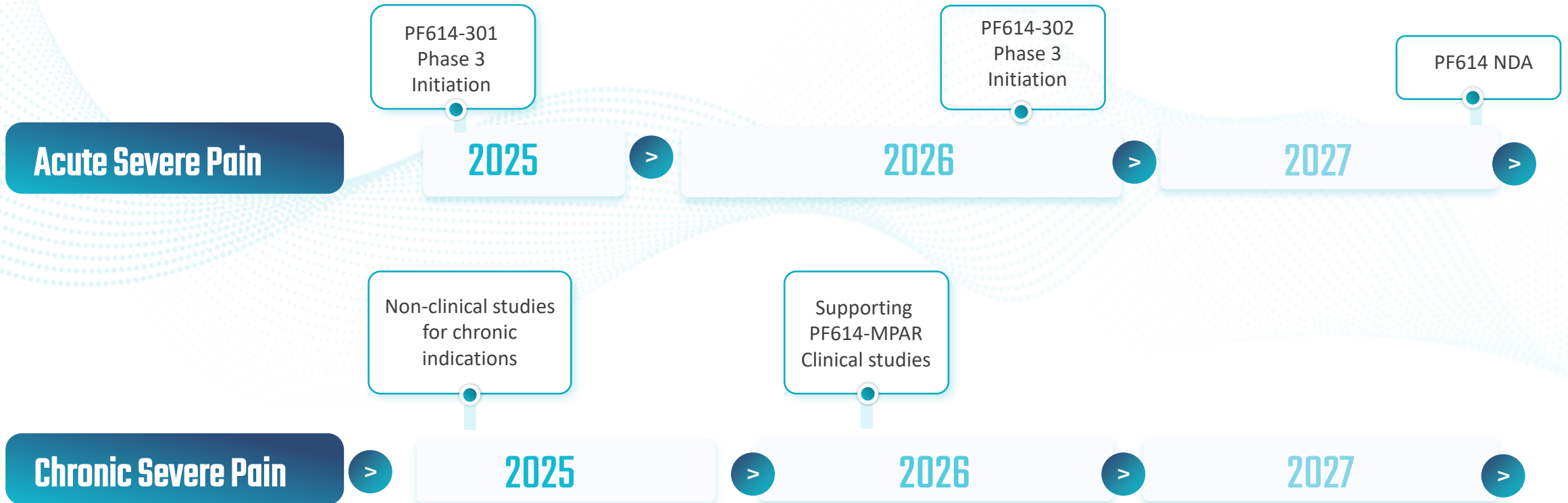
- Strong Efficacy –longer efficacy and increased safety
- Phase 3 Launched



2025/2026	DESCRIPTION	SIGNIFICANCE
<b>Regulatory</b>	Phase 3 Protocol reviewed	<b>FDA feedback on Pivotal study plans received</b>
<b>PF614-301</b>	Phase 3 study Abdominoplasty: Post-surgical pain initiated 2025	<b>Pivotal study leading to NDA*</b>
<b>PF614-302</b>	Open label study Bunionectomy: Post-surgical pain – to initiate 2026	<b>Study to support safety data base leading to NDA*</b>

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

## - Development Pathway for Acute and Chronic Pain Indications



**Bold text: Completed**

Non-bold text: Planned studies



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**PF614-MPAR**    **Powerful Analgesia + Overdose protection**  
**TAAP Oxycodone combination product**

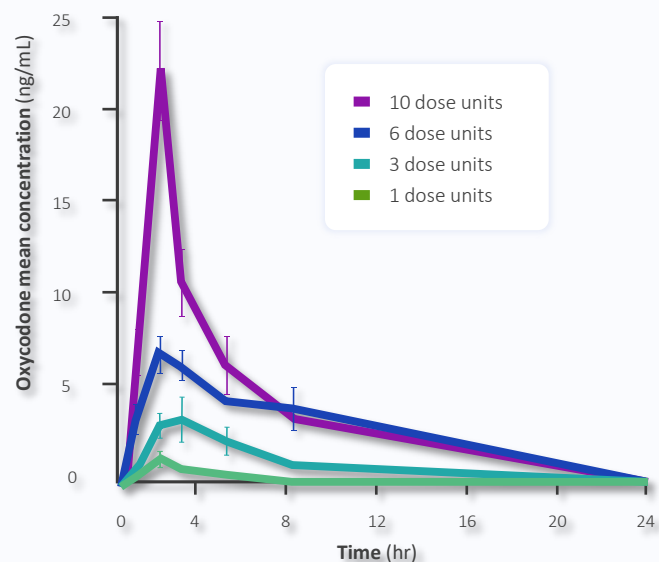
**Breakthrough Therapy Designation**  
**Grant by FDA January 2024**

# PF614-MPAR Pre-Clinical Data

— Blocks Activation of PF614 and Oxycodone Release if Overdosed

## Oxycodone levels *without* MPAR®

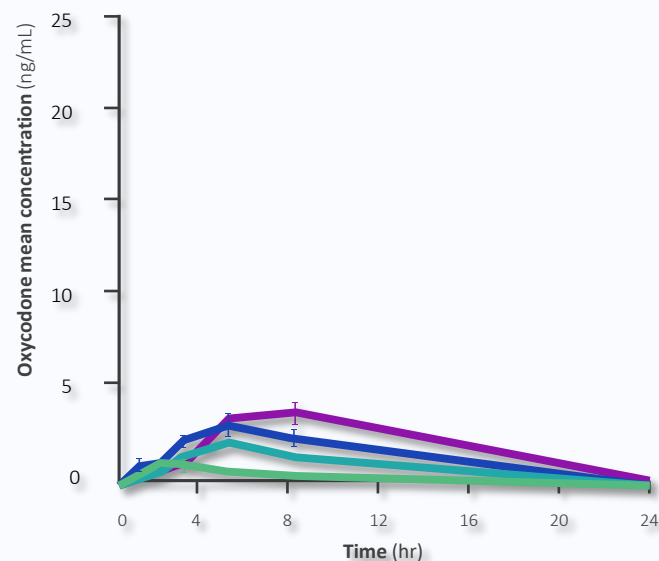
PF614 without nafamostat



TAAP + MPAR™: PRECLINICAL DATA

## Oxycodone levels *with* MPAR®

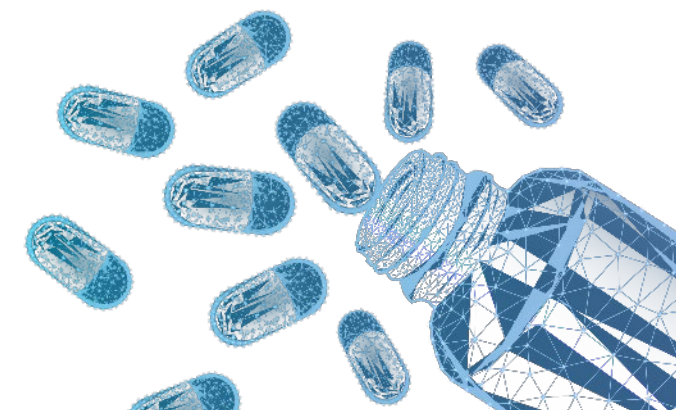
PF614 with nafamostat



in rats n=4 / dose

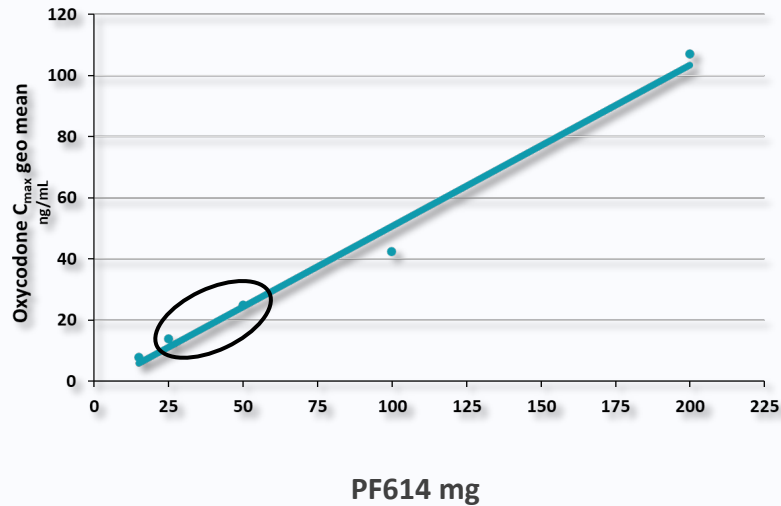
## PRE-CLINICAL MPAR SUPPORT DATA

- > 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



## Phase 1 Clinical Study Demonstrating Overdose Protection

PF614 alone no MPAR® overdose protection

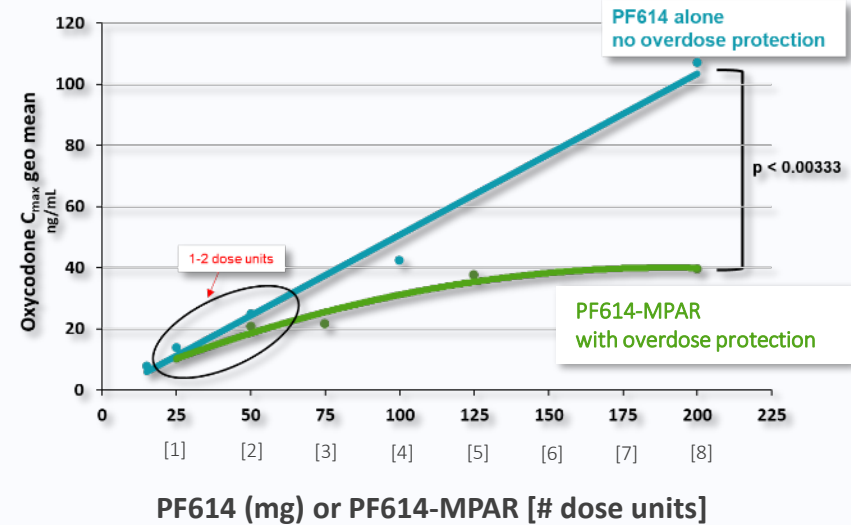


PF614 alone (SAD-MAD studies)

Linear dose increase after each dose

Goal to deliver two doses up to twice daily

PF614-MPAR 25 mg with MPAR® overdose protection



PF614 + nafamostat (PF614-MPAR study)

MPAR- Reduced activation after two dose units

Trypsin controlled opioid release



## — Clinical Development for Overdose Protection

2025/2026	OUTCOME	SIGNIFICANCE
<b>PF614-MPAR-102</b>	Continue Phase 1b SAD 100 mg dose followed by MAD	Confirm overdose protection followed by MAD study to support Type B FDA meeting
<b>PF614-MPAR</b>	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

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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 us to obtain new patents and extend market positions, revitalize approved medications and repurpose approved medications for the benefit of patients and care givers. *Specifically, Ensysce has used to develop a highly novel product for OUD.*



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



**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



**GEOFF BIRKETT**  
Chief Commercial Officer

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



**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



**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



**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



## 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



**William Chang**

Entrepreneur, Realty Company & Movie executive



**Steve Martin**

Experienced Senior Executive and Chief Financial Officer



**Dr. Adam Levin**

Academic and clinical orthopedic surgeon at Johns Hopkins Univ.

# Cash Resources

## NASDAQ: ENSC

As of April 2, 2026

Shares Outstanding	9.3M
Shares Public Float	9.3M
Nasdaq Listed	July 2021
Headquarters	La Jolla, CA

**\$4.3M**

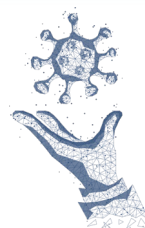
**Cash**  
as of 12/31/25

**\$2.0M**

**Equity Financing**  
April 2026

**\$7.4M**

**MPAR Grant**  
**Funding Available**  
Jan 2026 to May 2027

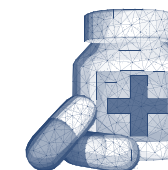


## NIH support

2018-2023 - \$11 million  
2024-2027 - \$15 million

### Awards to advance overdose protection

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

### 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



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**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** 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



# Investor Relations

**SHANNON DEVINE**

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