



Ensysce™
biosciences

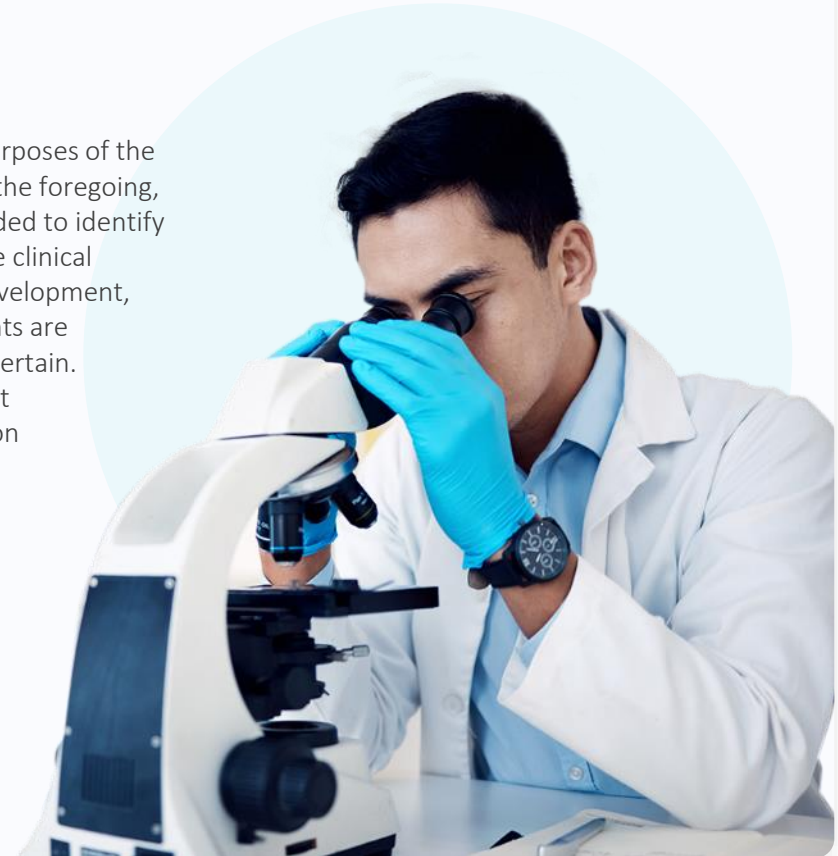
**IMPROVING PRESCRIPTION DRUG SAFETY
THROUGH CHEMISTRY**

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



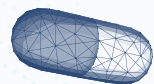
35
Million

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-slowng/index.html>



Supply Crisis for Pain Sufferers

N 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



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 **URNS 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

URNS 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

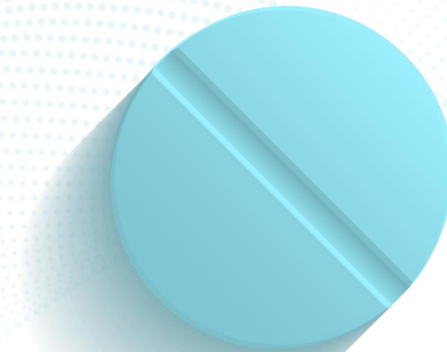
US Pain Management Drugs Market

\$1.6 B



ACUTE

\$2.2 B



CHRONIC

— 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 OxyContin¹

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

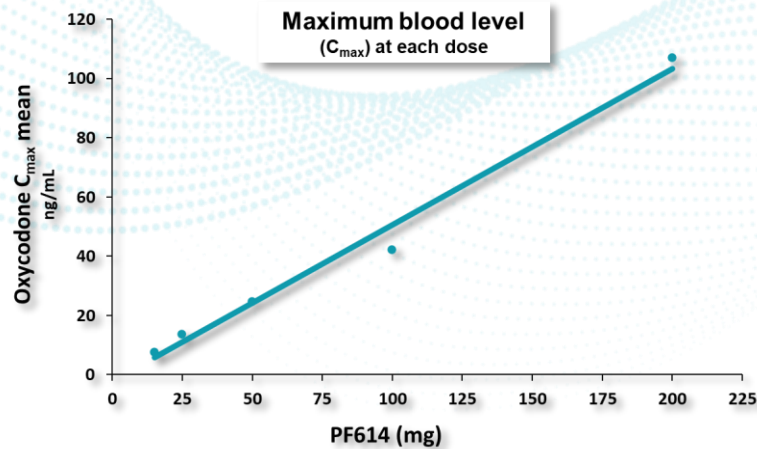
Can “Switch on” to start activation

Can “Switch off” to stop overdose

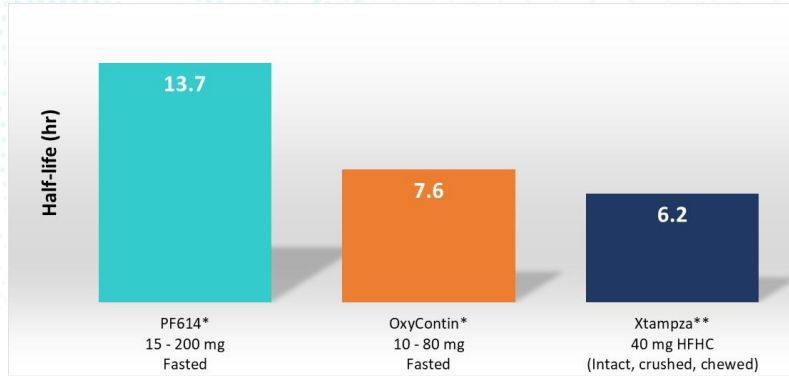
PF614 – 12 hour pain relief/reduced abuse

PF614 Clinical Data

PF614 efficiently delivers oxycodone



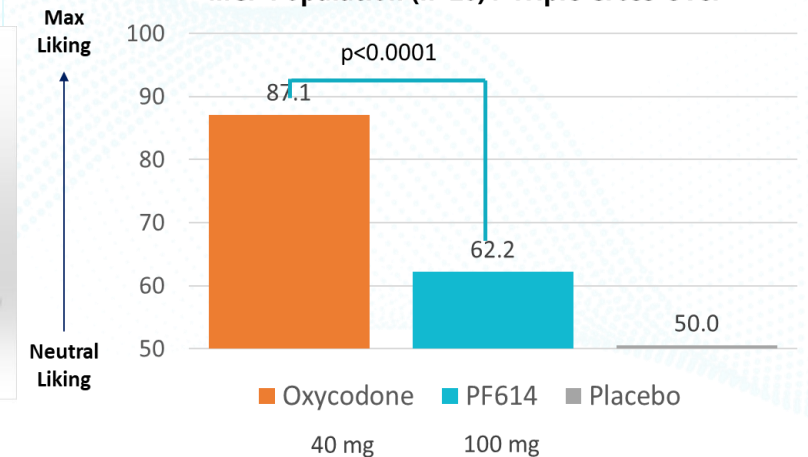
Longer oxycodone half-life supports BID dosing



* From PF614-101, Phase 1 SAD trial
** From Application208090Orig1s000 CDER pg 11

Reduced nasal abuse potential

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



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

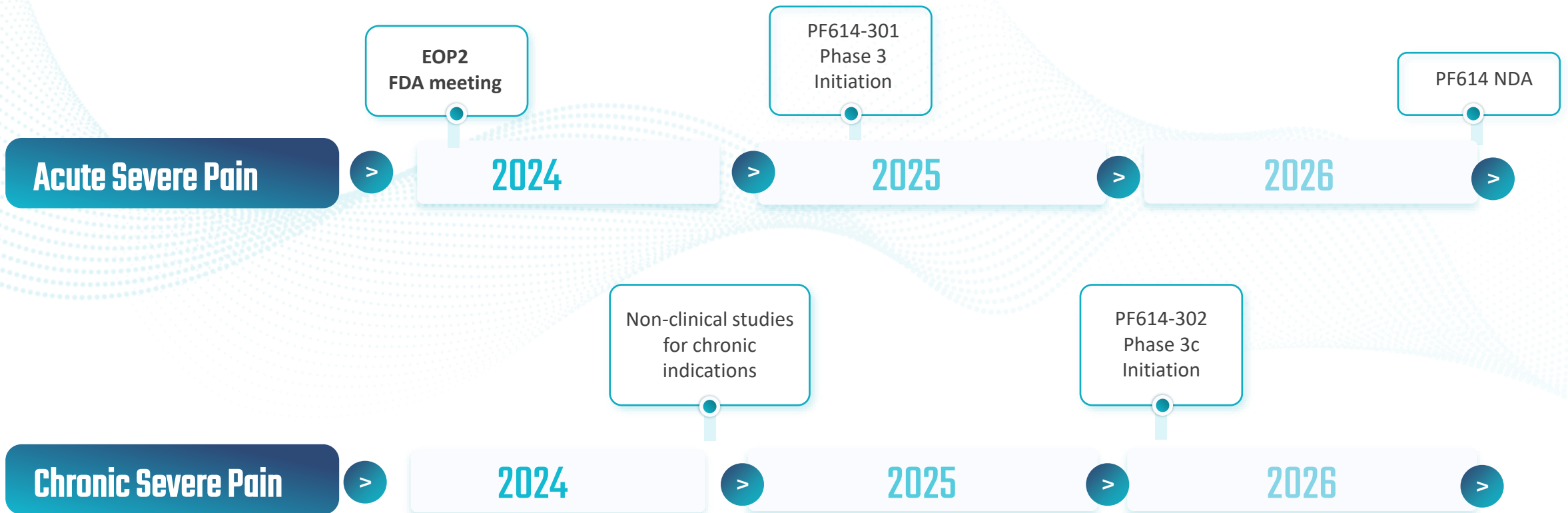


2024	DESCRIPTION	SIGNIFICANCE
Regulatory	End of Phase 2 meeting held to discuss Phase 3 plans for Acute Pain indication	FDA input into non-clinical, CMC and pivotal trials leading to NDA*
PF614-301	Phase 3 study Abdominoplasty: Post-surgical pain	Pivotal study leading to NDA

*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

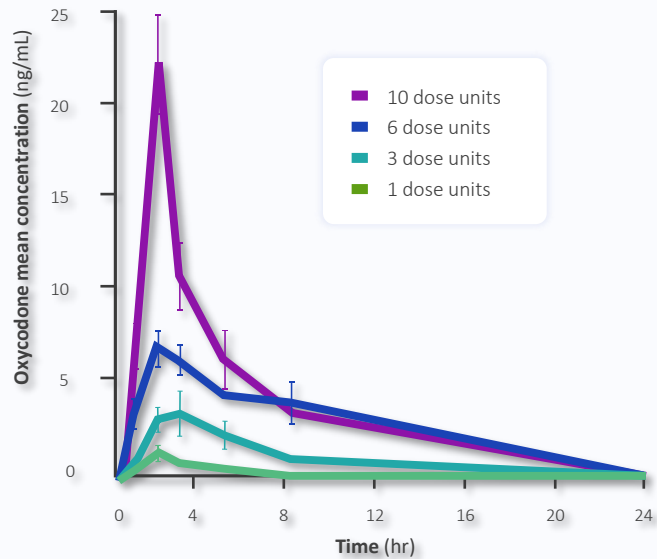
Grant by FDA January 2024

PF614-MPAR Pre-Clinical Data

— Blocks Activation of PF614 and Oxycodone Release if Overdosed

Oxycodone levels *without* MPAR®

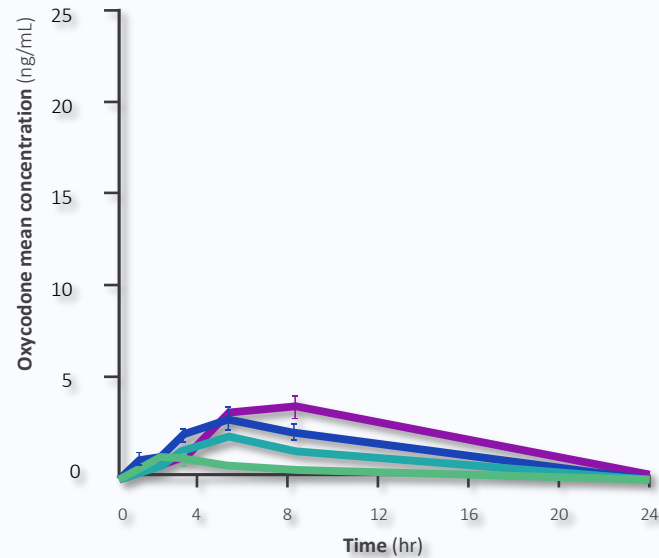
PF614 without nafamostat



TAAP + MPAR™: PRECLINICAL DATA

Oxycodone levels *with* MPAR®

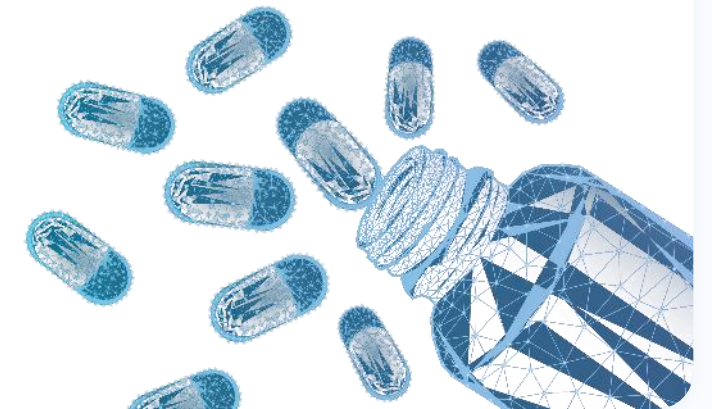
PF614 with nafamostat



in rats n=4 / dose

PRE-CLINICAL MPAR SUPPORT DATA

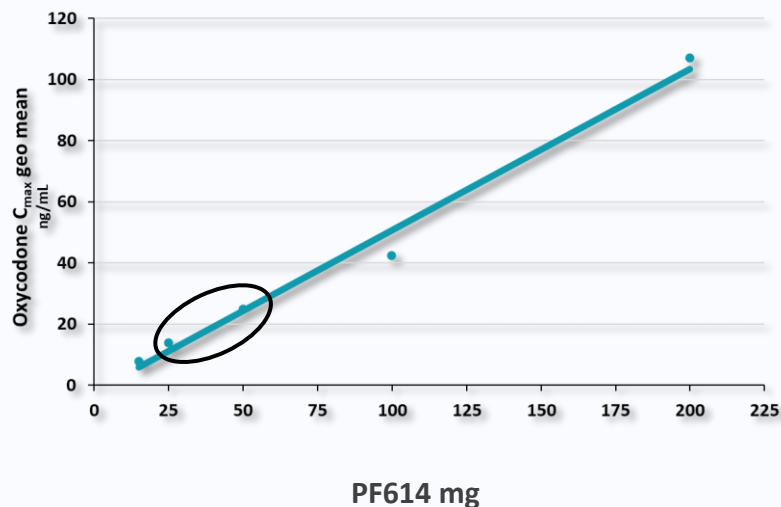
- > Combination product of PF614 with an ultrapotent trypsin inhibitor, nafamostat
- > Taken at prescribed doses there is no change in oxycodone release from PF614
- > With increasing dose unit administration, increasing amounts of nafamostat blocks trypsin release of oxycodone and prevents opioid overdose



PF614-MPAR Pain Relief with Overdose Protection

Phase 1 Clinical Study Demonstrating Overdose Protection

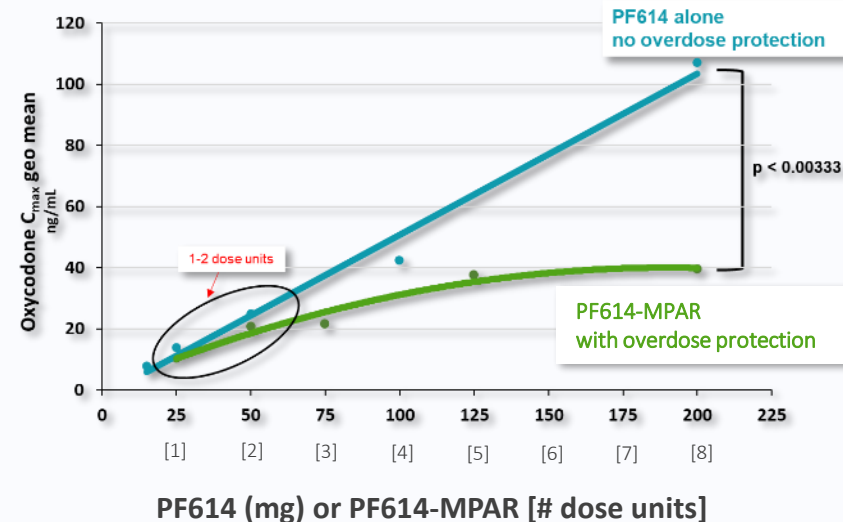
PF614 alone no MPAR® overdose protection



PF614 alone (SAD-MAD studies)

Linear dose increase after each dose

PF614-MPAR 25 mg with MPAR® overdose protection



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:

PF614 and nafamostat
Positive PK data to define drug product

Optimized PF614 / nafamostat combination for 25 mg dose unit

PF614-MPAR-101 Part B

Escalating 25 mg PF614-MPAR dose units
Confirmation of overdose protection

First demonstration of overdose protection for a prescription opioid

PF614-MPAR

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



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



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

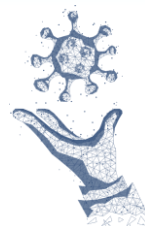
Experienced CEO and Strategy Advisor

Cash Resources

NASDAQ: ENSC	Shares Outstanding	1.3M
As of December 6, 2024	Shares Public Float	1.1M
	Nasdaq Listed	July 2021
	Headquarters	La Jolla, CA

\$4.2M Cash
as of 9/30/24

\$13.6M MPAR Grant
Funding Available
as of 9/30/24

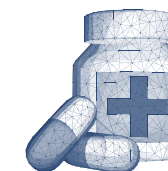


NIH support

2018-2023 - \$11 million
2024-2027 - \$14 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
2024-2028 - \$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.

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



Investor Relations

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