



Ensysce™
biosciences

**IMPROVING PRESCRIPTION DRUG SAFETY
THROUGH CHEMISTRY**

Noble Capital Markets Virtual Healthcare Conference
April 17, 2024

NASDAQ: ENSC

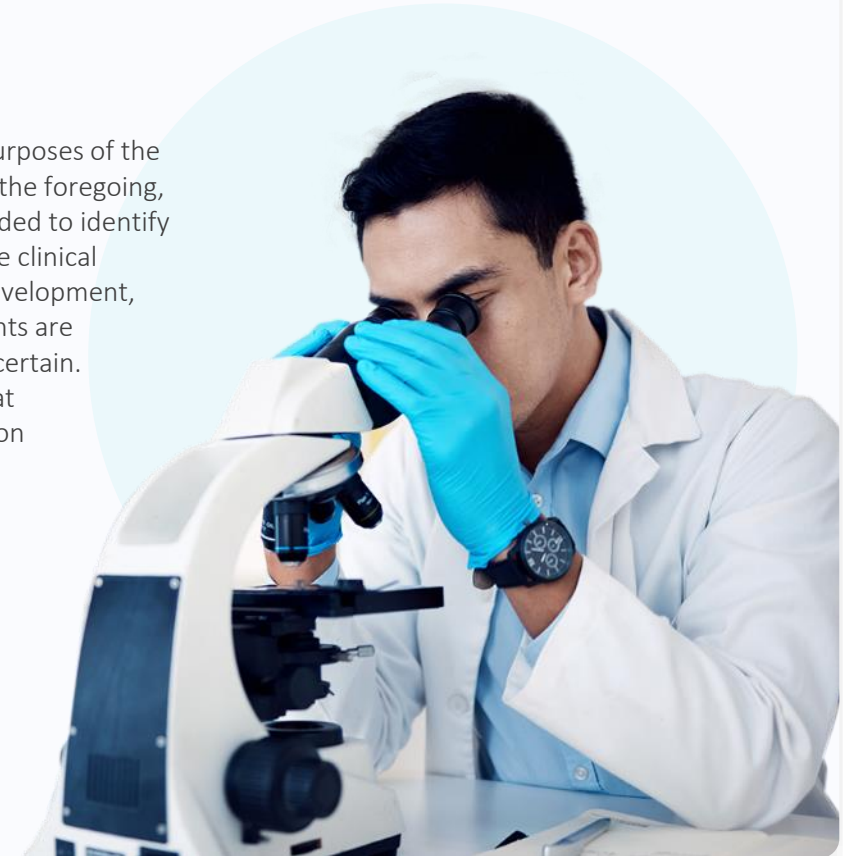
Investor Presentation April 2024

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 30, 2023.

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 Platform Technologies – Abuse and Overdose Protection

- Harnessing Trypsin Chemistry to Deliver Safer Oral Products

TWO CORE TECHNOLOGY PLATFORMS

TAAP™

Trypsin-Activated Abuse Protection

MPAR®

Multi-Pill Abuse Resistance:
Trypsin Inhibitor-Mediated Overdose Protection

...to deliver improved drug performance



PRODUCT BENEFITS

- > Safety: Drug only works via oral administration
- > Dosing: Product half-life can be tuned via design of prodrug linker
- > Same efficacy as TAAP version if patient takes drug as prescribed
- > Upon oral overdose, prodrug conversion to active drug is inhibited

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

Dueling Crises: Pain vs Abuse and Overdose

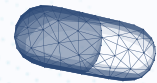
— Pain is the Leading Cause of Doctor Visits



**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>



The Ensysce Solution to Severe Pain

— 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 2022

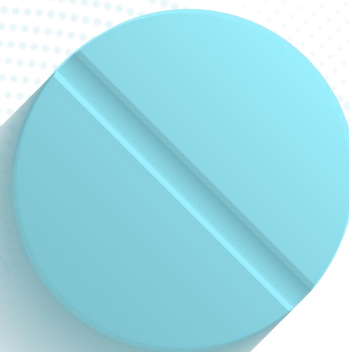
55% reduction in sales value 2016-2022

\$1.1 B



ACUTE

\$2.4 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

Pain Relief Delivery by TAAP

Two-Step Release Process



CHEMICAL MODIFICATION

Allowing either immediate or extended release



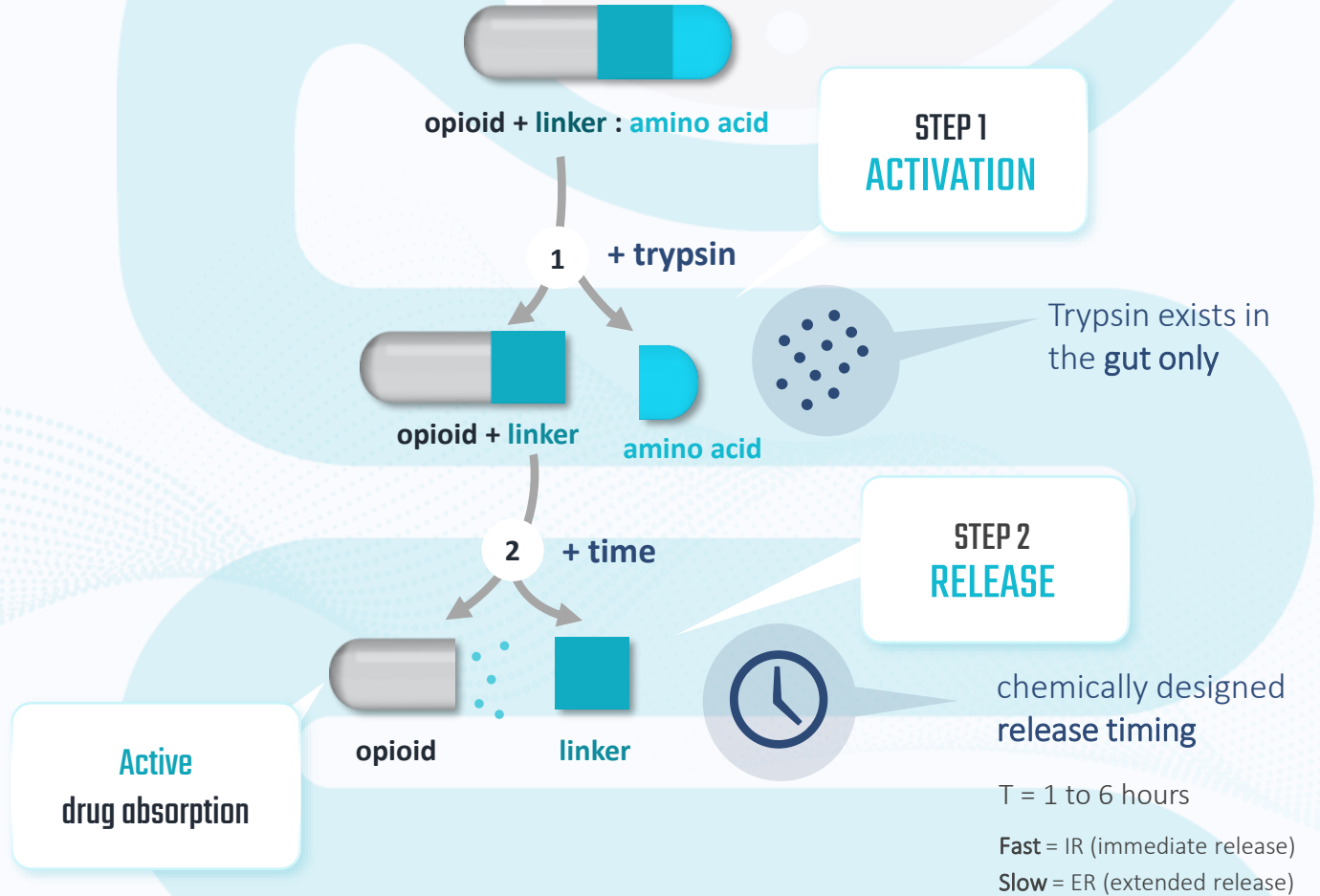
ONLY ACTIVATED BY TRYPSIN

Opioid not released by chewing, injecting or snorting



NOT ALTERED BY MANIPULATION

Difficult to extract opioid



PF614 for Severe Pain

— Strong Efficacy – Less Abuse



PF614

- **TAAP™ Prodrug**
 - > Delivers potent pain relief in clinically advantageous way
 - > Abuse Deterrence should qualify for drug label
- **Fast Track granted**
- **505(b)(2)**
 - > Clinical bioequivalence to OxyContin opens 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”

Real 12-hour half-life for twice daily dosing

No food effect

Can dissolve in water for easy dosing

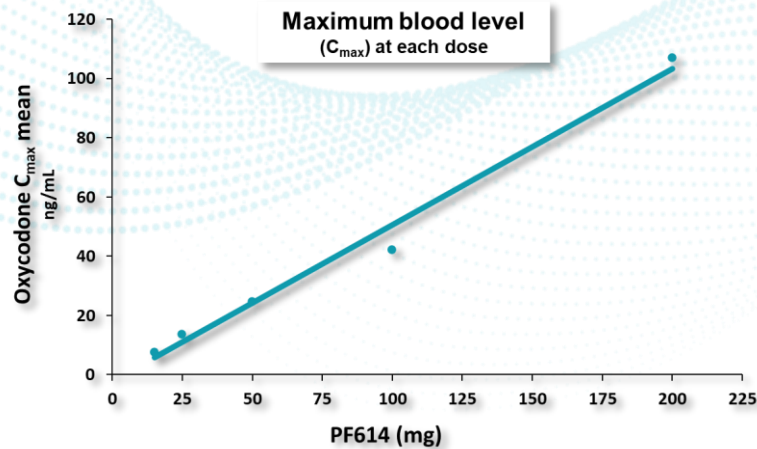
Can “Switch on” to start activation

Can “Switch off” to stop overdose

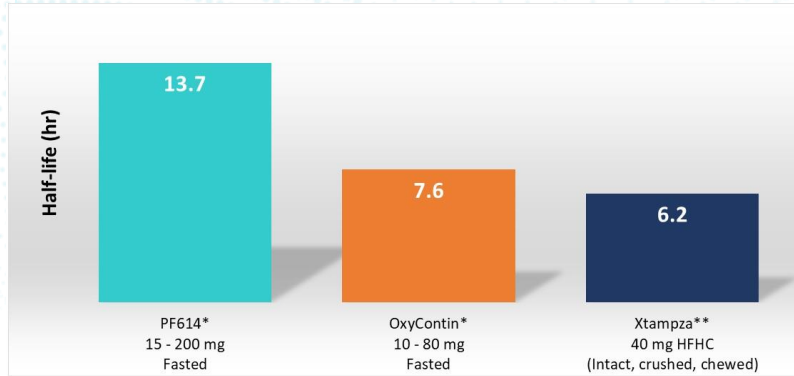
PF614 – 12 hour pain relief/reduced abuse

PF614 Clinical Data

PF614 efficiently delivers oxycodone



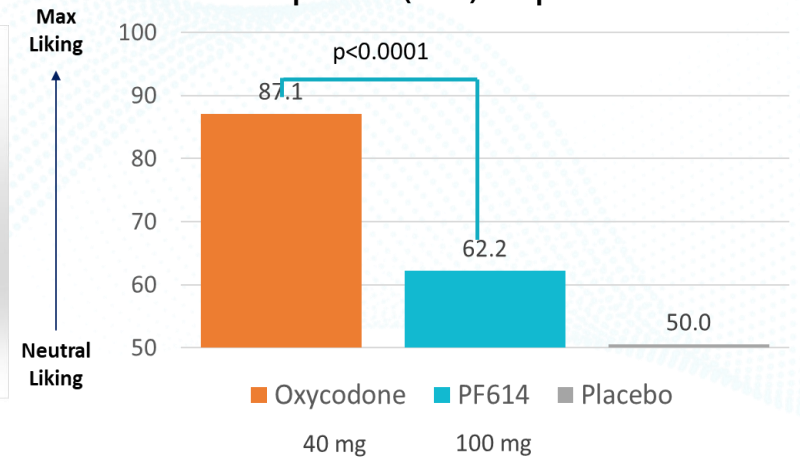
Longer oxycodone half-life supports BID dosing



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

Reduced nasal abuse potential

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



Clinical Milestones



COMPLETED STUDIES 2022-2023

SIGNIFICANCE

PF614-102

Multi-ascending dose and Bioequivalence study
Positive bioequivalence data between PF614 and OxyContin

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

— Initiate Phase 3

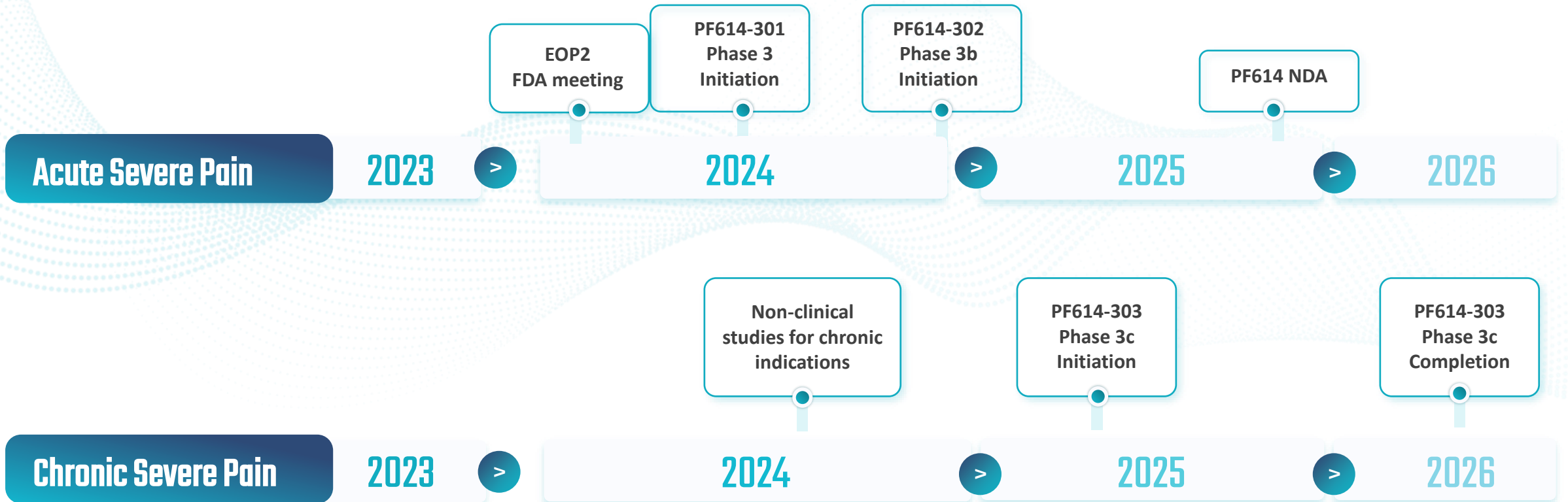


2024	DESCRIPTION	SIGNIFICANCE
Regulatory	End of Phase 2 meeting held to discuss Phase 3 plans for initial Acute Pain indication	FDA input into non-clinical, CMC and pivotal trials leading to NDA*
PF614-301	Phase 3 study Abdominoplasty: Post-surgical pain	Pivotal study leading to NDA
PF614-302	Phase 3 study Bunionectomy: 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





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PF614-MPAR

TAAP Oxycodone with overdose protection

Breakthrough Therapy Designation Grant by FDA

PF614-MPAR for Severe Pain with added overdose protection

— Strong Efficacy – Less Abuse and Reduced Overdose Potential



PF614-MPAR

- **Opioid with Oral Overdose Protection**
 - > Sub-active levels of trypsin inhibitor provides SMART overdose protection
- **Breakthrough Therapy designation**
- **Development Supported by NIDA**
 - > Clinical bioequivalence: development timeline follow PF614

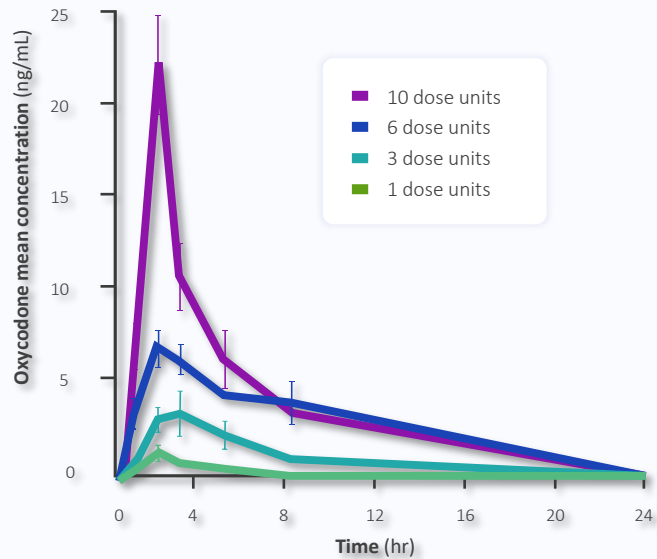


PF614-MPAR Pre-Clinical Data

— Blocks Activation of PF614 and Oxycodone Release if Overdosed

Oxycodone levels *without* MPAR®

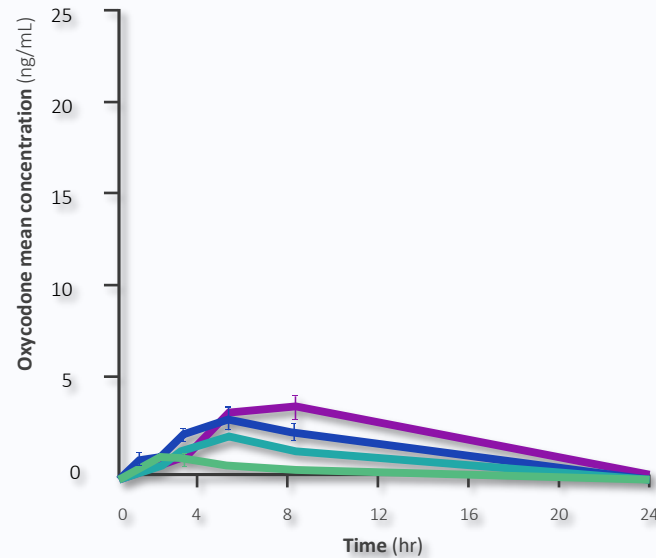
PF614 without nafamostat



TAAP + MPAR™: PRECLINICAL DATA

Oxycodone levels *with* MPAR®

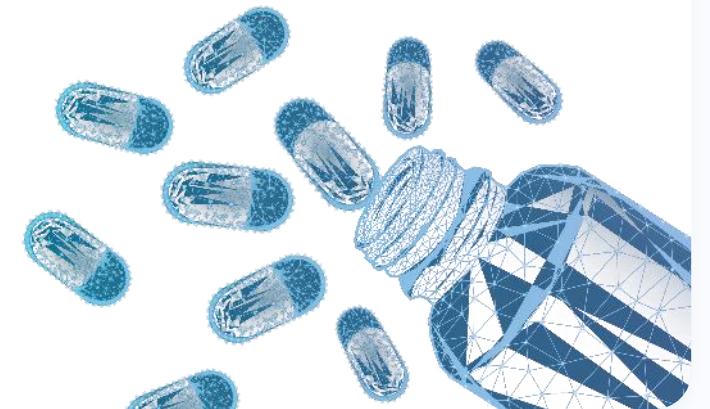
PF614 with nafamostat



in rats n=4 / dose

PRE-CLINICAL MPAR SUPPORT DATA

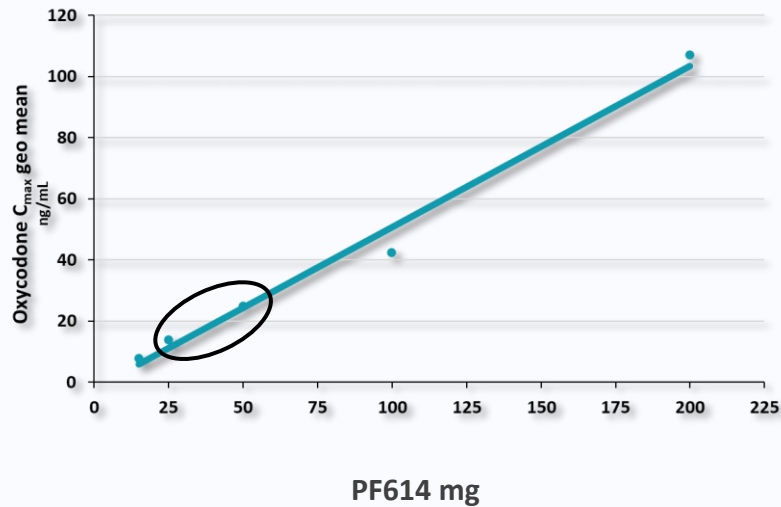
- > Combination product of PF614 with an ultrapotent trypsin inhibitor, nafamostat
- > Taken at prescribed doses there is no change in oxycodone release from PF614
- > With increasing dose unit administration, increasing amounts of nafamostat blocks trypsin release of oxycodone and prevents opioid overdose



PF614-MPAR Pain Relief with Overdose Protection

Phase 1 Clinical Study Demonstrating Overdose Protection

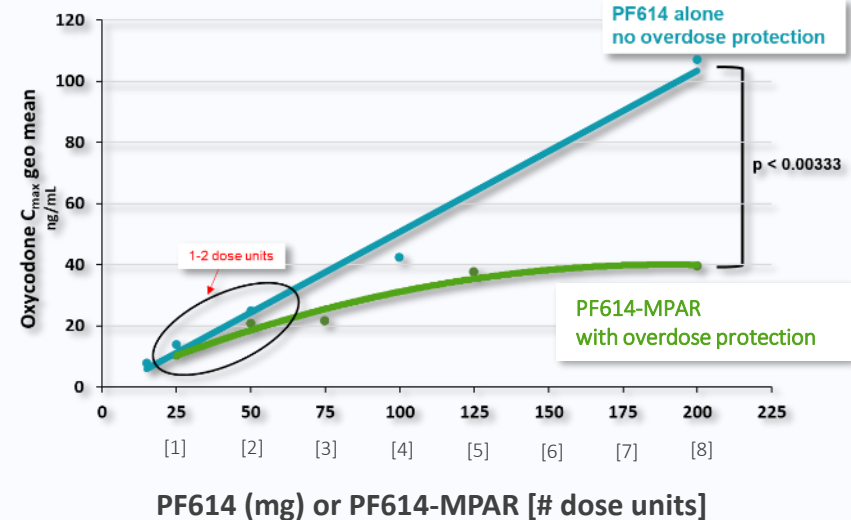
PF614 alone no MPAR® overdose protection



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 2022-2023

SIGNIFICANCE

PF614-MPAR-101 Part A:

PF614 and nafamostat
Positive PK data to define drug product

Identified PF614 / nafamostat combination product 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

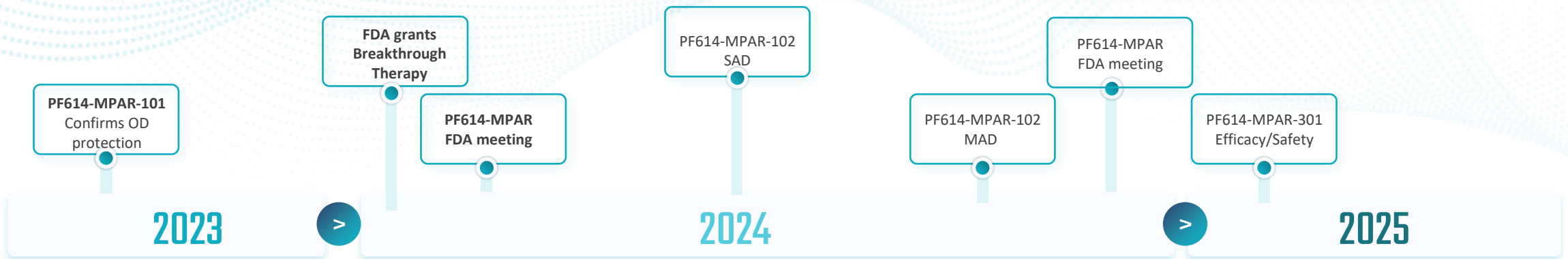
Breakthrough Therapy Designation

Granted by FDA January 2024

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

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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	7.3M
As of March 8, 2024	Shares Public Float	7.2M
	Nasdaq Listed	July 2021
	Headquarters	La Jolla, CA

\$1.1M Cash*
as of 12/31/23

\$2.2M Grant Funding Available
as of 12/31/23

\$2.1M Warrant Exercises
January 2024

\$4.7M Financing Gross Proceeds
February 2024

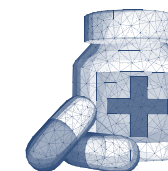


NIH support

2018-2023

Ensysce received \$11M+ to advance MPAR®

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



NIDA grant

2019-2024

NIDA awarded Ensysce up to \$15M grant to advance TAAP/MPAR® for OUD

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

*Additional cash proceeds required in second half of 2024

Ensysce Summary



Clinical-stage company - transformative trypsin-controlled chemistry.



Targeted therapy areas focus on products with blockbuster potential.



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



Shortened development timeline with Fast Track and 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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APPENDIX



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TAAP™ and MPAR®





Expanded Opportunities



Drug Development Opportunities with TAAP™

— Improving Drug Delivery and Lifecycle Management

TAAP™ CHEMICAL 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

The IDEAL Analgesic for severe pain



Efficacy = oxycodone

Slow to reach blood levels – not “liked”

Real 12-hour half-life

Not easy to snort/ inject

“Switches on” to start activation

“Switches off” to stop overdose

Can dissolve in water for easy dosing

No food effect