Ensysce™ biosciences

NASDAQ: ENSC

Improving Prescription Drug Safety Through Chemistry

Investor Presentation
May 17, 2022

Disclaimer

Ensysce's PF614 and nafamostat are currently in clinical and pre-clinical trials, 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 31, 2022.

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," 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 Overview

Committed to Stemming the Global Prescription Drug Abuse Epidemic

Ensysce™ biosciences

Who we are

Clinical-stage biotech company applying transformative chemistry to improve prescription drug safety and performance.

2 Core Technology Platforms

TAAP™
IMPROVED Trypsin Activated Anti-abuse chemistry

MPAR™
Combination Products for SMART Overdose protection

Mission

To use TAAP/MPAR to launch the Next Generation opioid products to reduce abuse and overdose while relieving suffering for people with severe pain and CNS disorders.

NASDAQ: ENSC

Share Price[1]	$0.67
Market Cap[1]	$23.2M
Shares Outstanding	34.6M
Nasdaq Listed	July 2021
Float	18.6M
Headquarters	La Jolla, CA

1) As of May 13, 2022

Ensysce Investment Summary

Ensysce™ biosciences

- **Clinical stage biotech company** using transformative trypsin-controlled chemistry to improve drug safety and performance.
- **Two highly novel technology platforms** that we believe can be applied to a large majority of prescription drugs, driving internal growth and external partnering opportunities.
- **Targeted therapy areas** focus on products with blockbuster potential in pain, ADHD and respiratory diseases.
- **Shortened development** with Fast Track and 505(b)(2) regulatory pathway, **de-risked with clinical data** that we believe shows that the technology works.
- **Lead product (PF614)** in Phase 2 trial – NCE with patent protection until mid 2030.
- **Strong global patent estate supported by over $100 M investment** covering composition of matter, pharmaceutical preparations and method of use.
- **Highly experienced management team** with broad biopharma background, from drug development to commercialization.

TAAP™

Anti-abuse chemistry

MPAR™

SMART Overdose protection

TAAP™ and MPAR™

Improving Drug Performance and Safety Through Chemistry

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TAAP™

IMPROVED Trypsin Activated Abuse Protection

ANTI-ABUSE	Reduce ability to tamper with drug product to abuse.
PROTECTIVE	Trypsin activated release only in small intestine.
CONTROLLABLE	Chemically able to provide immediate or extended release products.
IMPROVED	TAAP™ able to alter features that make a better drug product.

MPAR™

Multi-Pill Abuse Resistance: Combination Products for SMART Overdose Protection

SMART	Active only on overdose.
UNIQUE	Platform based on trypsin control of activation and release.
VAST APPLICABILITY	TAAP™ and MPAR™ can be applied to numerous drug classes.
COMBINATION	Ultra-potent trypsin inhibitor, nafamostat, added to TAAP products.

Addressing Opioid Abuse + Overdose

TAAP™ PLATFORM

Designed to Prevent
Drug Abuse

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Integrated Prodrug Technology Platform

Combining **anti-abuse** and **anti-overdose** technology to create new classes of prescription drugs that are designed to be powerful and safe for everyone

MPAR™ PLATFORM

Designed to Prevent
Overdose

Improving Pain reducing Abuse

Introducing the Next Generation of Opioids

3400 B.C.

Originally identified

1900s

Pharmaceuticals

Immediate release opioids

1990s

Abuse Deterrent Formulations (ADFs)

Physical formulation approach

Extended release claimed to reduce abuse and addiction

OxyContin and Xtampza

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TODAY

TAAP™ and MPAR™

Trypsin-Activated Chemical modification

designed 2-step activation

More Pain.

50M

People live with **chronic pain,** more than cancer, heart disease and diabetes, combined.

More Pain Killers.

153M

opioid prescriptions per year.[1]

More Abuse.

$560B

In healthcare costs and the loss of productivity due to abuse.

More Pain Killers That Kill.

222

deaths / day from opioid overdose. COVID catalyzing the rise of deaths in 2021.

1) CDC data for 2019

Market Opportunity

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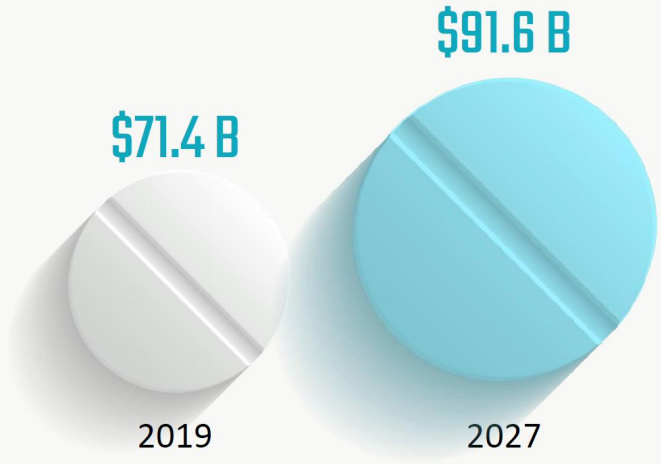
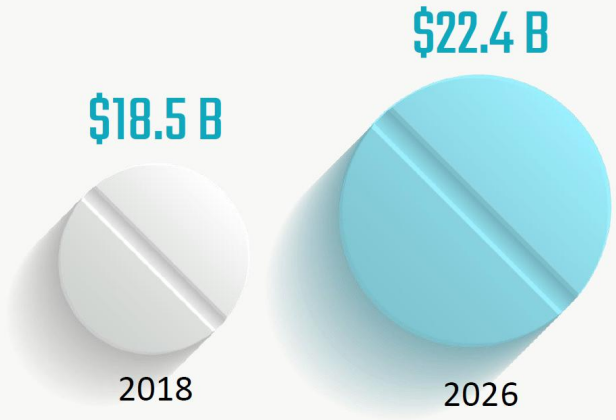
Global Pain Management Drugs Market



Global Opioids Market



1) Allied Market Research 2) Allied Market Research

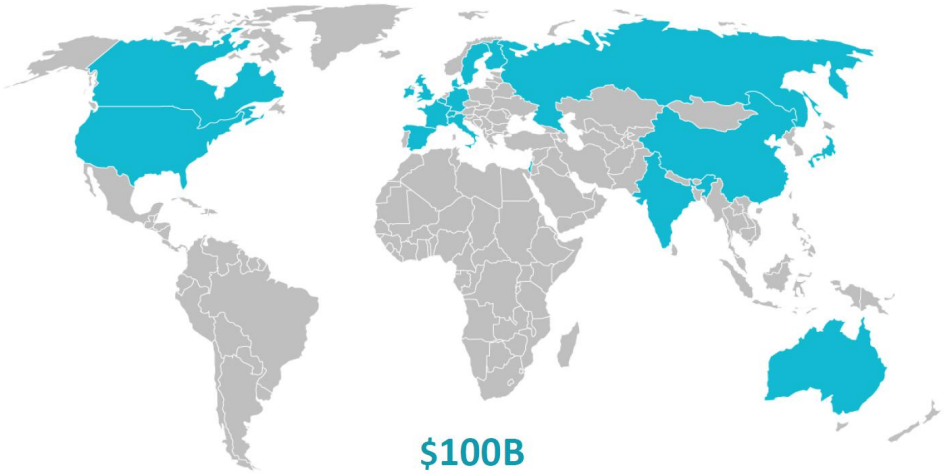
Extensive Patent Portfolio

Ensysce™ biosciences

Ensysce has over 100 patents currently issued in 25 countries, ensuring opportunity to address abuse globally

- Technology well-protected by a **suite of patents generated from over $100 million of research support**
- Patents provide protection to the **underlying molecules, pharmaceutical preparations and method of use** of both immediate and extended-release **TAAP/MPAR prodrugs**
- Substantial **patent pipeline** with a number of new products in development, a library of trade secrets and trademarks
- **Opportunity to partner globally**

Issued Patent Countries



$100B

Global Addressable Pain Market

Ensysce Innovation

TAAP™

TRYPSIN-
ACTIVATED
ABUSE
PROTECTION

IMPROVED TAMPER-PROOF DELIVERY PLATFORM

TAAP - 2-step verification mechanism to improve oral delivery, with release of active ingredient only in the small intestine with exposure to trypsin

TAAP chemical modification

TAAP is only activated by trypsin

TAAP not altered by manipulation

TAAP

Two-Step Release Process

Step 1: Swallow drug

- Following ingestion, the drug is activated only after exposure to trypsin, a digestive enzyme that is active only in the small intestine.

Step 2: Timing chemically controlled

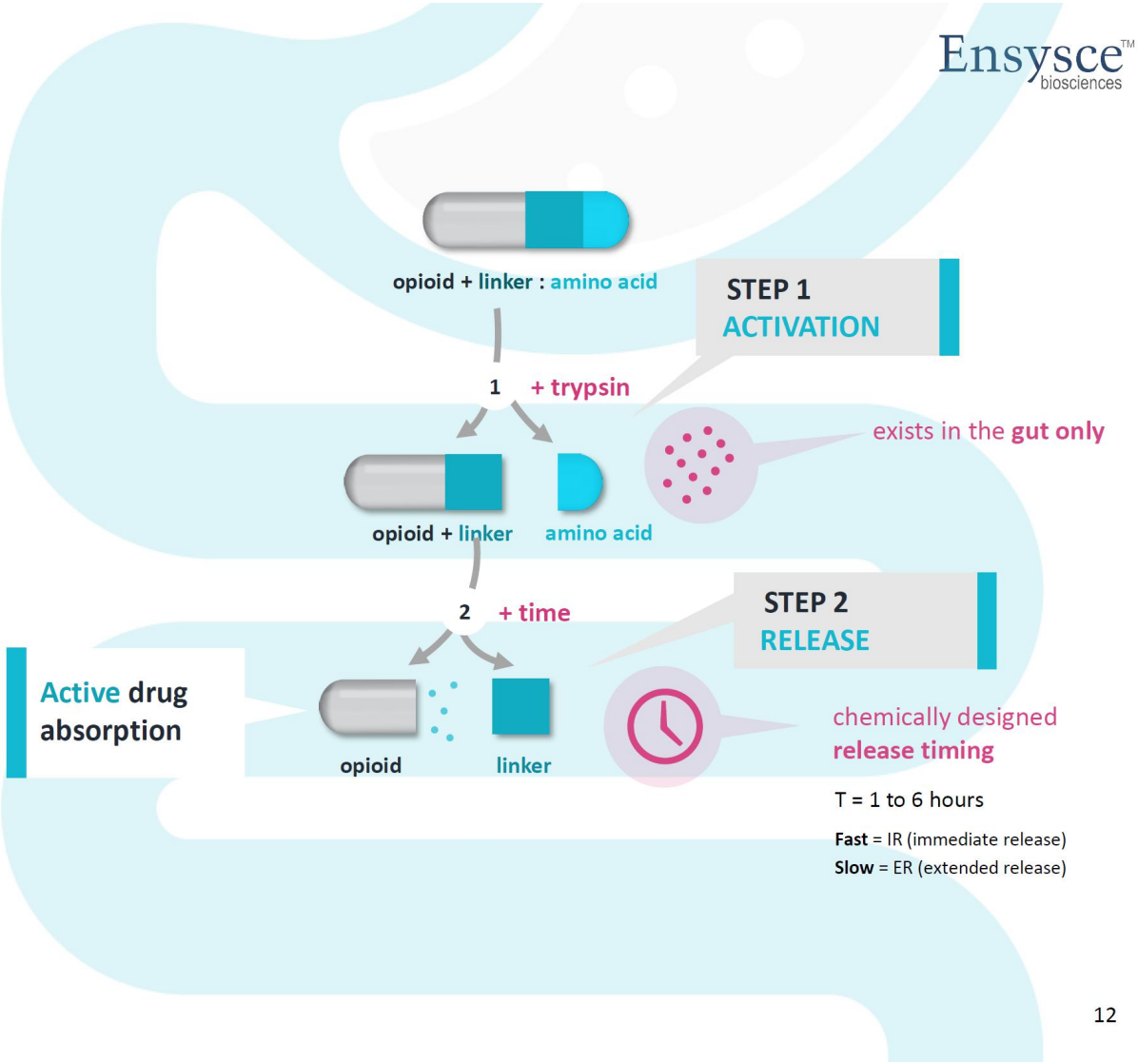
- A second step is required for full release of the active drug. The chemistry controls the rate of release, thereby making the Ensysce 2-step approach superior to other prodrug products.

Protects from:

Chewing

Crushing and snorting

Crushing and injecting

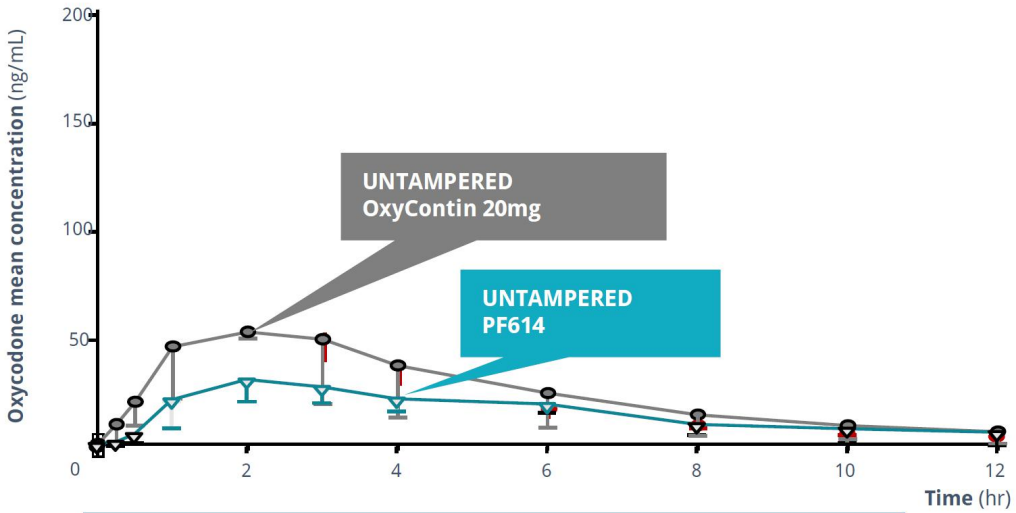


PF614: TAAP delayed release oxycodone prodrug
Release kinetics cannot be altered

- **Unlike OxyContin**, Ensysce's opioid PF614, even when crushed, has no altered release kinetics

- In Phase I studies have been able to **dose match** PF614 to marketed OxyContin dose units.

Pre-clinical Blood Concentration of Opioid Vs. Time (dog)



Pre-clinical data in dogs comparing Ensysce's opioid against current opioid OxyContin ***demonstrated that Ensysce can prevent opioid abuse*** *while OxyContin cannot*

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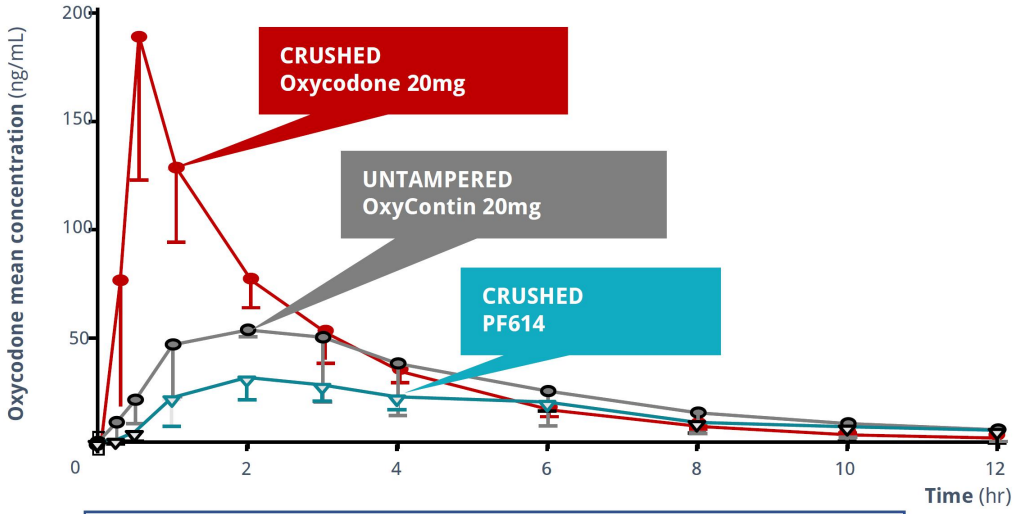

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MPAR™

MULTI-
PILL
ABUSE
RESISTANT

SMART ANTI-OVERDOSE PLATFORM

MPAR™ is a smart anti-overdose platform that is designed **to** protect patients from overdosing when it is combined with TAAP opioids.

MPAR™ is only triggered by an overdose

MPAR™ inhibits trypsin activation step

Using a prescribed dose gives pain relief

MPAR™ Mechanism of Action

Combination Product With Dose-Triggered Trypsin Inhibition

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MPAR™ Combination Product Legend:

TAAP–enabled opioid | Trypsin Inhibitor

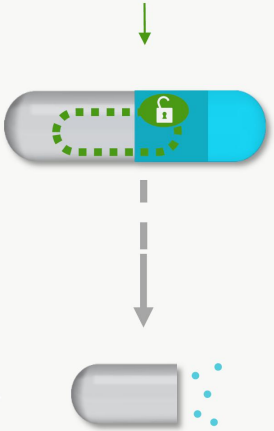
PRESCRIBED DOSE

No Interference when **normal** dose taken;
Low dose of trypsin inhibitor (nafamostat) does not affect release of the opioid

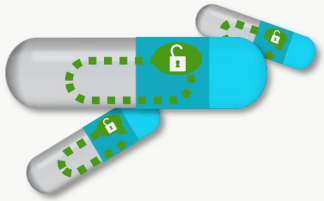
Trypsin activation releases free and active drug product

SUB-THRESHOLD

trypsin inhibitor



DOSE THRESHOLD

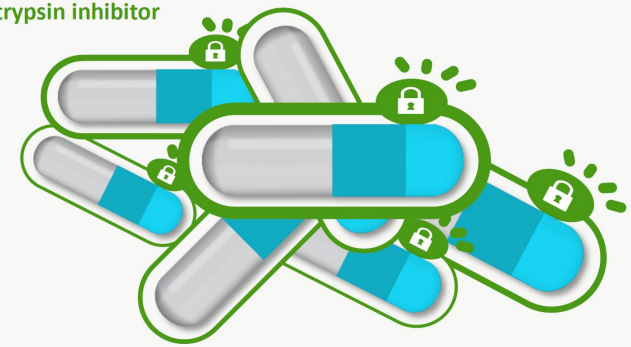


ACCIDENTAL OVERDOSE

A higher amount of MPAR /more nafamostat begins to inhibit trypsin activity, limiting opioid release

ABOVE THRESHOLD

trypsin inhibitor



EXCESS MPAR DOSE

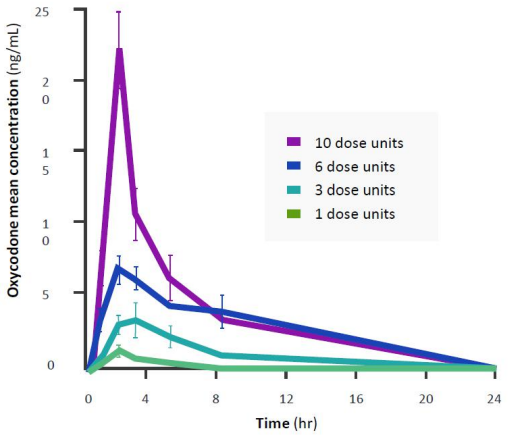
Trypsin Activation blocked / overdose averted

PF614-MPAR™

Blocks activation of PF614 and Oxycodone Release if Overdosed

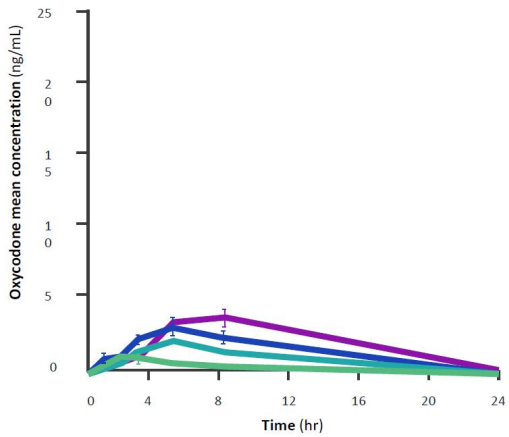
Without MPAR™

PF614 without TI nafamostat



With MPAR™

PF614 with TI nafamostat



TAAP + MPAR™: PRECLINICAL DATA

in rats n=4 / dose

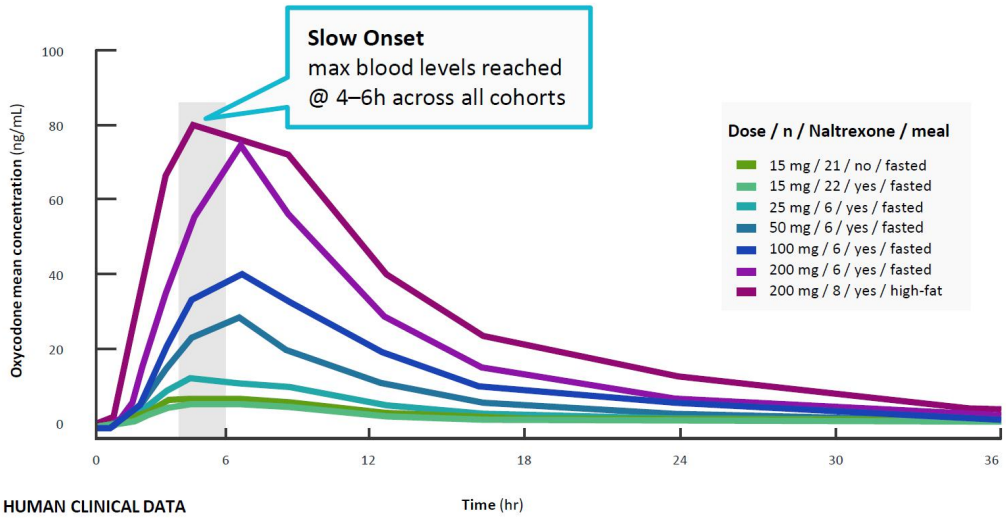
- Combination product of PF614 with an ultrapotent trypsin inhibitor, nafamostat
- Taken at prescribed doses there is no change in oxycodone release from PF614
- With increasing dose unit administration, increasing amounts of nafamostat blocks trypsin activation of PF614 and prevents opioid overdose
- PF614-MPAR™ entered Phase 1 clinical trial in December 2021
- Data expected H2 2022

PF614-101

Designed for Safer, More Efficient & Longer-Lasting Pain Relief

Ensysce™ biosciences

Oxycodone Concentration in Blood vs. Time following **PF614** administered **as** oral solution



TAAP: HUMAN CLINICAL DATA

PF614-101 Phase 1

- PF614 provides slow onset with maximum blood concentration reached at 4 to 6 hr after swallowing;

Good Safety Profile

- PF614 has shown no unexpected adverse events in Phase I

Efficient conversion to oxycodone

- PF614 is effectively converted to Oxycodone after it is swallowed providing **dose equivalency in a ratio of 2.5:1 PR614:OxyContin.**

PF614 LONGER LASTING COMPARED TO OXYCONTIN

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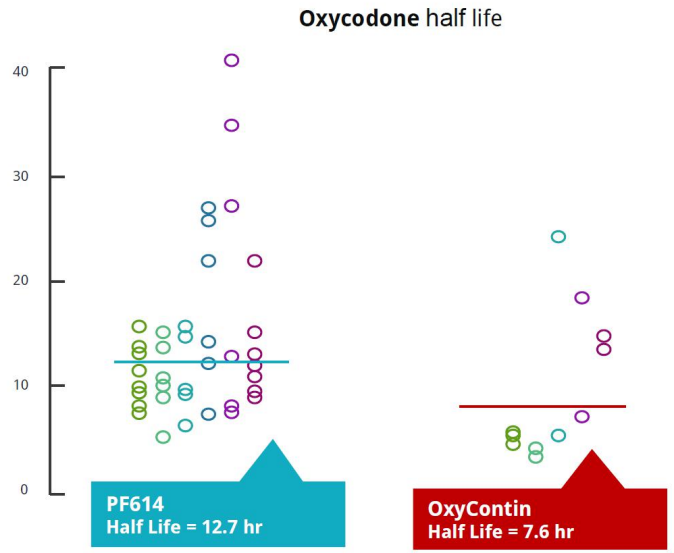

TAAP™: CLINICAL DATA

Dose (PF614 / OxyContin)
- 15 mg / 10 mg
- 25 mg / 10 mg
- 50 mg / 20 mg
- 100 mg / 50 mg
- 200 mg / 80 mg
- 200 mg / --

PF614-101Phase 1

- Ensysce's opioid **PF614's half-life is 12.7 hours**, versus OxyContin's 7.6 hours
- As a result, Ensysce's PF614 is more convenient for the patient, since PF614 needs to be taken only **twice-a-day**, in contrast to OxyContin (which some patients end up taking **three times per day**)

PF614
Clinical Status

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- **PF614-102**
  - Multi-ascending dose/Bioequivalence study in healthy volunteers; MAD Data reported 05/05/22; BE data expected Q2 2022.
- **PF614-103**
  - Human abuse liability study via intranasal administration. Study initiation Q2 2022. Data expected Q3 2022.
- **PF614-104**
  - Human abuse liability study via oral administration. Study initiation expected Q3 2022. Data expected Q1 20 23.
- **PF614-MPAR-101**
  - PF614 administered alone or in combination with nafamostat; Cohort 1 data reported 05/05/22; Full data expected Q4 2022.

PF614

Clinical studies in progress

NEW DATA: PF614-102 MAD/BE

Multi-Ascending Dose Study

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A Phase 1b, Randomized, 2-Part Single-Center Study to Evaluate the Pharmacokinetics and Safety of Multiple-Ascending Oral Doses of PF614 and the Food Effect and Bioavailability/Bioequivalence of Single Oral Doses of PF614 Relative to OxyContin in Healthy Adult Subjects

The primary objectives of the study are:
To assess the safety, tolerability and pharmacokinetics of intact prodrug, PF614, as well as oxycodone,

Administration
Oral twice daily (BID) doses for 5 days to groups of healthy adult subjects, naltrexone blocked

3 Ascending Dose Cohorts

PF614	50 mg	n = 6	OxyContin	20 mg	n = 2
PF614	100 mg	n = 6	OxyContin	40 mg	n = 2
PF614	200 mg	n = 6	OxyContin	80 mg	n = 2

NEW DATA: PF614-102 MAD

PF614 and OxyContin produce identical Adverse Events

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Table of Adverse Events

	PF614 50 mg n=6 n (%)	OxyContin 20 mg n=2 n (%)	PF614 100 mg n=6 n (%)	OxyContin 40 mg n=2 n (%)	PF614 200 mg n=6 n (%)	OxyContin 80 mg n=2 n (%)
Total subjects with at least 1 TEAE*	2 (33.3)	1 (50.0)	1 (16.7)	1 (50.0)	6 (100.0)	2 (100.0)

* **Treatment Emergent Adverse Events**: Vertigo, Photophobia, Nausea, Constipation, Diarrhea, Vomiting Urinary Tract infection, Tooth fracture, Decreased appetite, Dizziness, Headache, Depressed mood, Rhinorrhoea, Dermatitis

NEW DATA: PF614-102 MAD

PK of oxycodone release from PF614 or OxyContin

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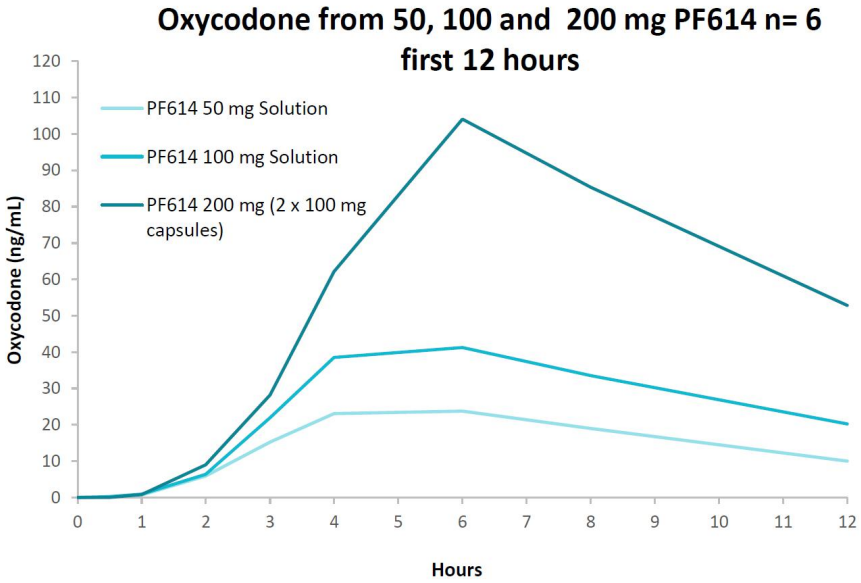

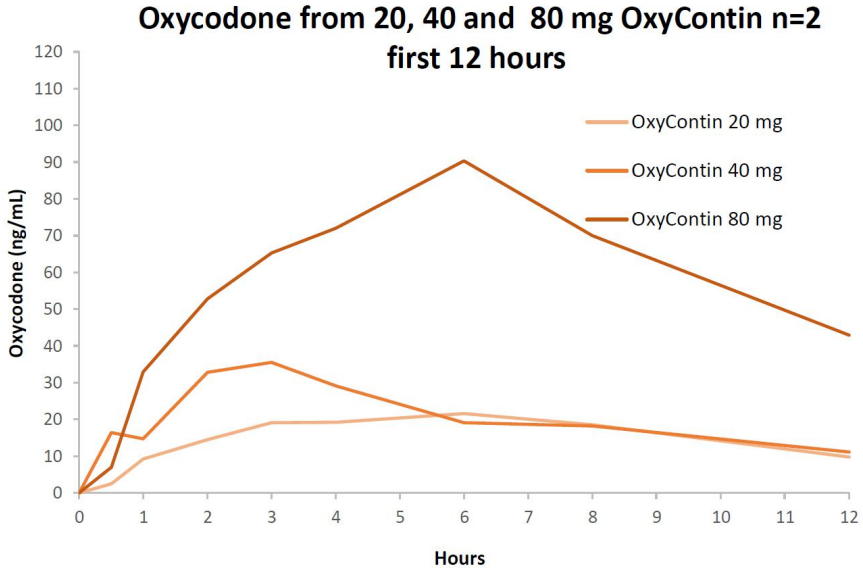

NEW DATA: PF614-102 MAD

Oxycodone from OxyContin or PF614 C_{max}

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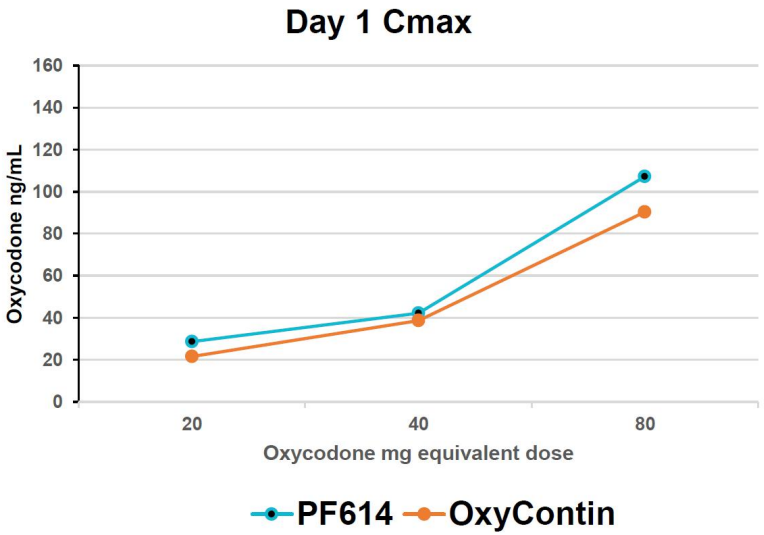

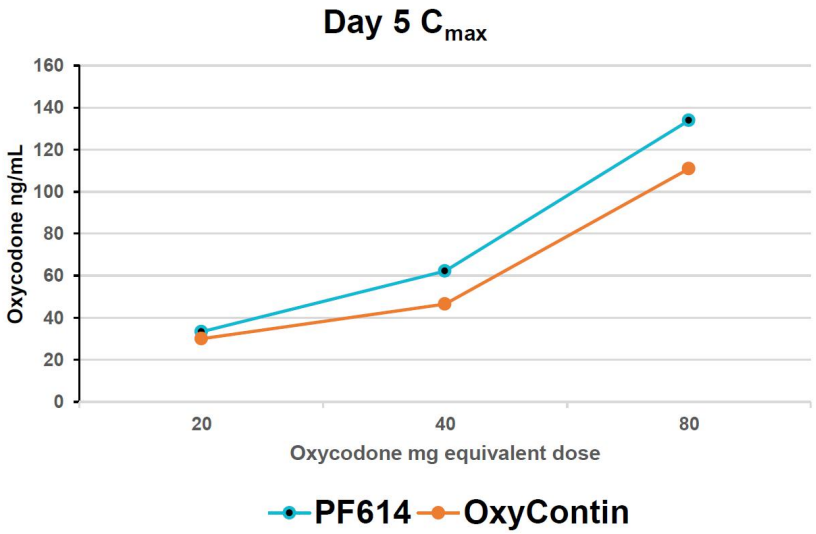

NEW DATA: PF614-102 MAD

Oxycodone from OxyContin or PF614 AUC_{0-t}

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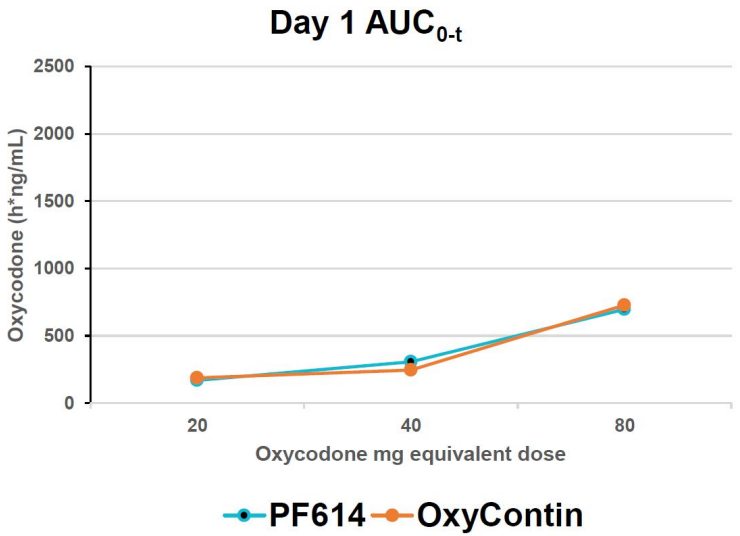

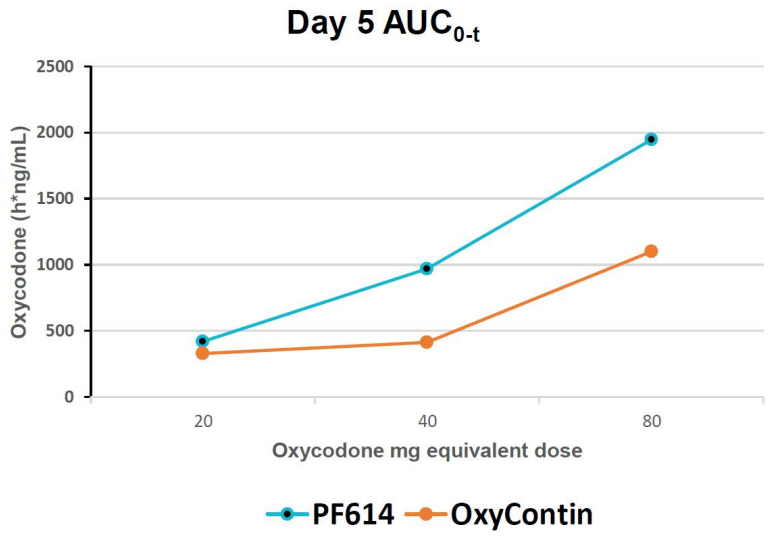

NEW DATA: PF614-102 MAD

Oxycodone from OxyContin or PF614 AUC_{0-t}

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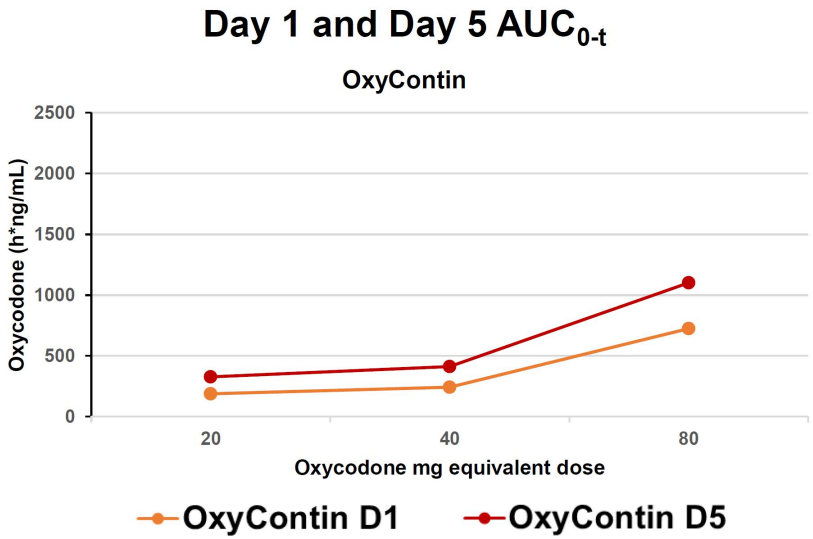

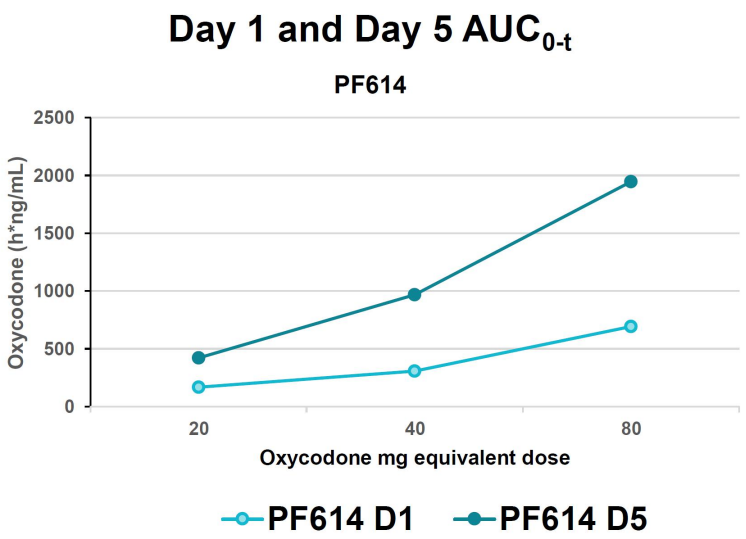

NEW DATA: PF614-MPAR-101

PF614 (25 mg) with and without nafamostat (10 mg)

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A Single Dose Study to Evaluate the Pharmacokinetics of Oxycodone and PF614 when PF614 Solution is Co Administered with Nafamostat, as an Immediate Release Solution and/or Extended Release (ER) Capsule Formulations in Healthy Subjects

The primary objectives of the study are:
To assess the pharmacokinetics (PK) of oxycodone, when PF614 solution is administered alone and with nafamostat as an immediate-release (IR) solution and/or extended-release (ER) capsule prototypes

Administration
Single oral dose of PF614 (25 mg) with or without Nafamostat IR/ER or a combination (10 mg total) to groups of healthy adult subjects

Cohort 1

PF614 25 mg n = 8

PF614 25 mg and nafamostat 10 mg n = 6

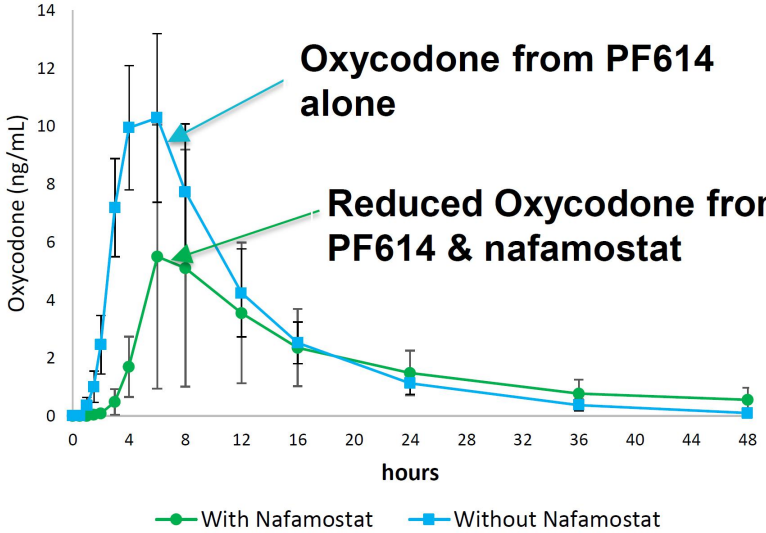
NEW DATA: PF614-MPAR-101

PF614 (25 mg) with and without nafamostat (10 mg)

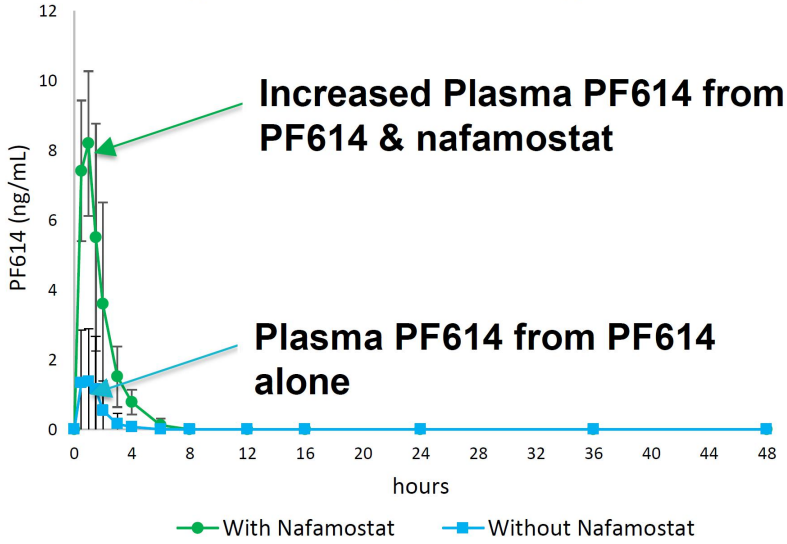
Ensysce™ biosciences

First Demonstration of Human Overdose Protection:

Average Systemic **Oxycodone** after
25 mg Oral PF614 with/without 10 mg Nafamostat



Average Systemic **PF614** after
25 mg Oral PF614 with/without 10 mg Nafamostat



NEXT STEPS: Optimization of PF614 + nafamostat combination product = **MPAR**

CASH RESOURCES

$8.4M
Cash
as of 3/31/22

$4.1M
Grant Funding
as of 3/31/22

$2.8M
New Grant Funding
Expected in July

NIH support

2018

NIDA awarded Ensysce up to $12M grant to progress MPAR™

Four-year award to undertake the **pre-clinical and clinical development** of the company's opioid overdose protection platform MPAR™ (Multi Pill Abuse Resistance).

NIDA grant

2019

NIDA awarded Ensysce up to $15M grant to progress TAAP/MPAR™ for OUD

Five-year award to undertake the **pre-clinical and clinical development** of the company's TAAP and MPAR™ for treatments of Opioid Use Disorder.

Lead Product PF614

Advantages over Abuse-Deterrent Formulations: OxyContin

PF614 Properties

- True abuse deterrence
- Not susceptible to chewing
- Not susceptible to extraction/injection
- Two-step oral activation
- Chemistry modifications, not just a simple coating or reformulation
- Real 12-hour pain control for a true twice-a-day product
- New chemical entity with no generic equivalent

ADF Opioids

ADF opioids fall short, offering abuse deterrence without the additional benefits of PF614

PF614: Development Plans

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✓ **505(b)(2) Regulatory Path**

- Helps avoid unnecessary duplication of studies already performed on a previously approved drug if bioequivalence can be demonstrated, reducing time and cost for development.

✓ **FDA FAST TRACK**

- Allowing rolling NDA submission and more access to discussions with agency

✓ **Clinical Development**

- Completion of BE Study 06/22; Data H1 2022
- Human Abuse liability study (nasal) initiation 05/17/22; Data Q3 2022
- Human Abuse liability study (oral) initiation Q1 2023
- Phase 3 plans in discussions with the FDA

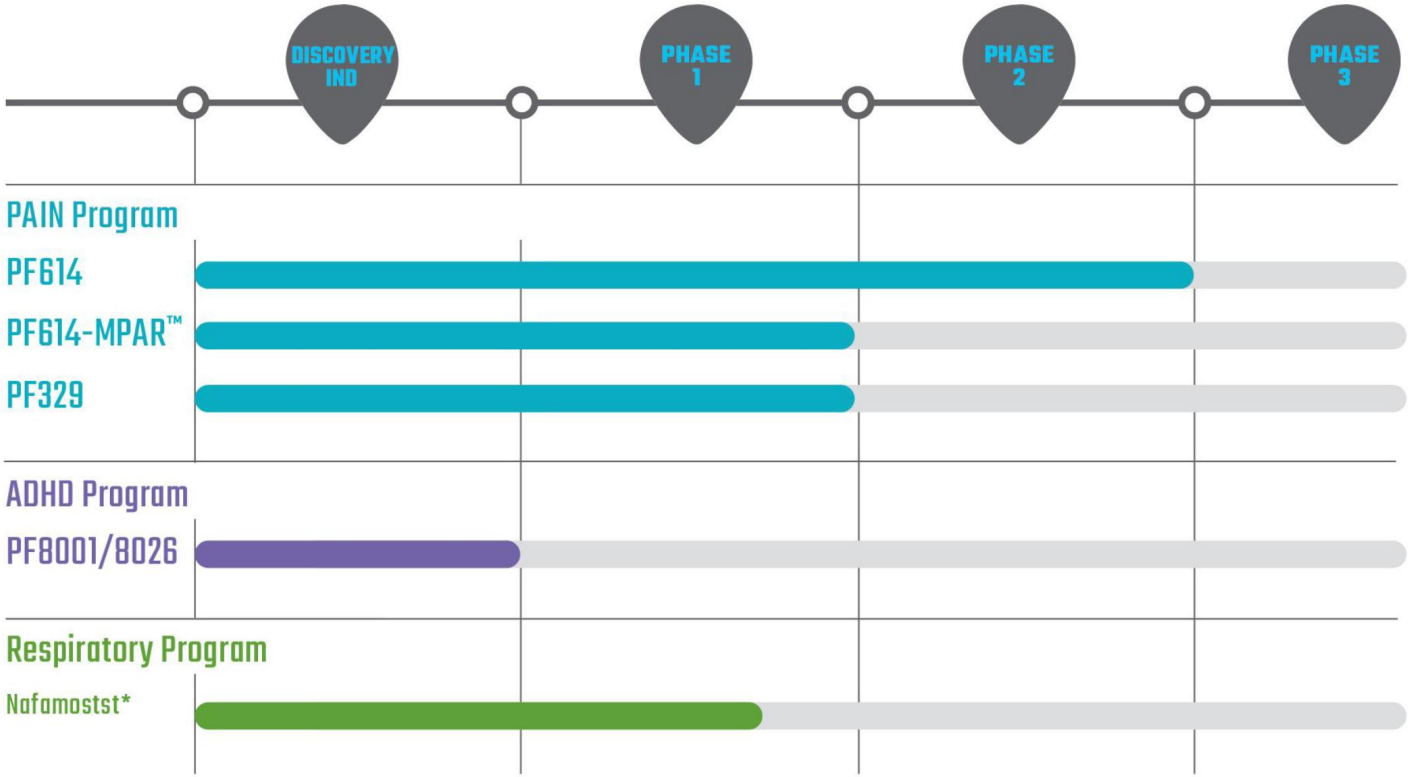
✓ **CMC and Non-clinical studies ongoing**

- In parallel with clinical development

PF614

A Next Generation Opioid For Severe Pain

Diversified Pipeline



TAAP and MPAR™ platforms with 50(b)(2) regulatory development path
*Nafamostat in develpment for MPAR, infections and respiratory dseases
HAL: Human Abuse Liability clinical study

Management Team

Highly Motivated, Experienced Team with Proven Record

Ensysce™ biosciences

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
ACTIV 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
Roche
Tufts University

Nily Osman, MD
Chief Medical Officer

- Board certified neurologist and headache/pain specialist
- Over 10 years of pharma industry experience creating and delivering complex medical affairs and clinical development plans within multiple therapeutic areas including orphan disease indication.

DUPONT
Adolor
CrystalGenomics
UCSF

Richard Wright, MBA
Chief Business Officer

- Background in Intellectual Property monetization, banking, venture capital
- Co-founder of an immunology biotech company, later sold to private equity

BDMS
JSR
endo
GE
Wharton University of Pennsylvania

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

BIOMIRA
ONCOTHYREON
CASCADIAN THERAPEUTICS
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

Ensysce Investment Summary

Ensysce™ biosciences

- **Clinical stage biotech company** using transformative trypsin-controlled chemistry to improve drug safety and performance.
- **Two highly novel technology platforms** that we believe can be applied to a large majority of prescription drugs, driving internal growth and external partnering opportunities.
- **Targeted therapy areas** focus on products with blockbuster potential in pain, ADHD and respiratory diseases.
- **Shortened development** with Fast Track and 505(b)(2) regulatory pathway, **de-risked with clinical data** that we believe shows that the technology works.
- **Lead product (PF614)** in Phase 2 trial – NCE with patent protection until mid 2030.
- **Strong global patent estate supported by over $100 M investment** covering composition of matter, pharmaceutical preparations and method of use.
- **Highly experienced management team** with broad biopharma background, from drug development to commercialization.

TAAP™

Anti-abuse chemistry

MPAR™

SMART Overdose protection

Ensysce™ biosciences

7946 Ivanhoe Avenue, Ste 201, La Jolla, CA 92037

Investor Relations

Shannon Devine
MZ North America
203-741-8811
ENSC@mzgroup.us

www.ensysce.com