UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 18, 2023 (January 18, 2023)

Ensysce Biosciences, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-38306**	**82-2755287**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification Number)**

7946 Ivanhoe Avenue, Suite 201 **La Jolla, California** **(Address of principal executive offices)**	**92037** **(Zip Code)**

(858) 263-4196
Registrant's telephone number, including area code

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation to the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	**ENSC**	**The Nasdaq Stock Market LLC**
Warrants to purchase one share of Common Stock	**ENSCW**	**OTC Pink Open Market**

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On January 18, 2023, Ensysce Biosciences, Inc. delivered a presentation entitled "Improving Prescription Drug Safety Through Chemistry" to investors. A copy of the presentation is filed as Exhibit 99 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
99	Investor Presentation dated January 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: January 18, 2023

Ensysce Biosciences, Inc.

By: */s/ Lynn Kirkpatrick*
Name: Dr. Lynn Kirkpatrick
Title: President and Chief Executive Officer

Exhibit 99

Ensysce™ biosciences

NASDAQ: ENSC

Improving Prescription Drug Safety Through Chemistry

Investor Presentation

January 2023

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," "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 Overview – Platform Technology

Who we are

Clinical-stage biotech company with mission to improve drug safety to reduce abuse and overdose.

Using 2 Core Technology Platforms

TAAP™
Trypsin Activated Abuse Protection

MPAR™
Multi-Pill Abuse Resistance: Combination Products for Overdose Protection

Immediate Focus – Severe Pain

Delivering Next Generation opioid products

– strong efficacy with less abuse and overdose.

NASDAQ: ENSC

Shares Outstanding	2.8M
Shares Public Float	2.3M
Nasdaq Listed	July 2021
Headquarters	La Jolla, CA

As of November 7, 2022

TAAP™ and MPAR™

Improving Drug Performance and Safety Through Chemistry

Ensysce™ biosciences

TAAP™

Trypsin Activated Abuse Protection

ANTI-ABUSE	Reduce ability to tamper with drug product to abuse.
PROTECTIVE	Trypsin TURNS ON RELEASE only in small intestine.
CONTROLLABLE	Chemically able to provide immediate or extended-release products.
PERFORMANCE	TAAP™ to improve product delivery .

MPAR™

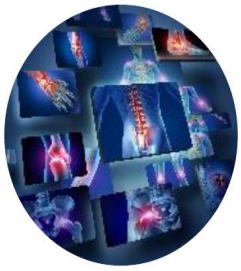
Multi-Pill Abuse Resistance: Combination Products for Overdose Protection

COMBINATION	Trypsin inhibitor, nafamostat, added to TAAP products.
SMART	TURNS OFF RELEASE only with overdose.
UNIQUE	Platform based on trypsin control of activation and release.
VAST APPLICABILITY	TAAP™ and MPAR™ can be applied to numerous drug classes.

Ensysce™ biosciences

Prescription Drug Abuse: a Health Crises in America

Pain & ADHD Drugs are Most Abused in America*



Pain

ADHD

Substance Abuse is the Nation's #1 Health Problem
– Department of Justice

107,000 Overdose Deaths in 2021
- National Institute for Health Care Management (NIHCM)

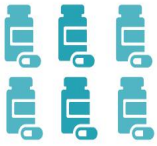
*HHS Publication No. PEP20-07-01-001 2020;
*https://www.aspenridgerecoverycenters.com/most-abused-prescription-drugs/

Dueling Crises: Pain vs Abuse and Overdose

Pain is a Leading Cause of Doctor Visits

35 Million Americans in Severe Pain

10 Million Misuse Opioids



153 million 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

The Ensysce Solution

The Next Generation of Opioids for Strong Pain Relief

Ensysce™ biosciences

- ✓ New class of opioid
- ✓ Low abuse – reassurance to patients
- ✓ Low overdose risk, 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

The Ensysce Difference

Ensysce™ biosciences

PF614
Bioequivalent to
OxyContin[1]

- Longer Pain Relief - True 12-hour Half-Life
- Ease of Swallowing - Can Dissolve in Water[2]
- Can Be Taken with or without Food[3]
- Difficult to Manipulate
- Blocks Opioid Release if Inhaled/ Injected
- Overdose Protection can be Added – Unique to Industry

1) Clinical support; Potential 505(b)(2) path
2) Retaining Abuse Deterrence
3) Compared to Xtampza

Diversified Pipeline

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

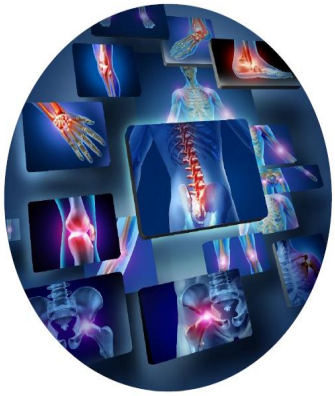

Ensysce™
biosciences
PF614 for severe pain - 'TAAP' oxycodone
10

PF614 for Severe Pain

Strong Efficacy – Less Abuse

Ensysce™ biosciences

PAIN



PF614

- ✓ TAAP™ Prodrug
  - Delivers potent pain relief – equivalent to Oxycontin with reduced abuse potential
- ✓ Fast Track granted
- ✓ 505(b)(2)
  - Shortened path to registration

RELIEF

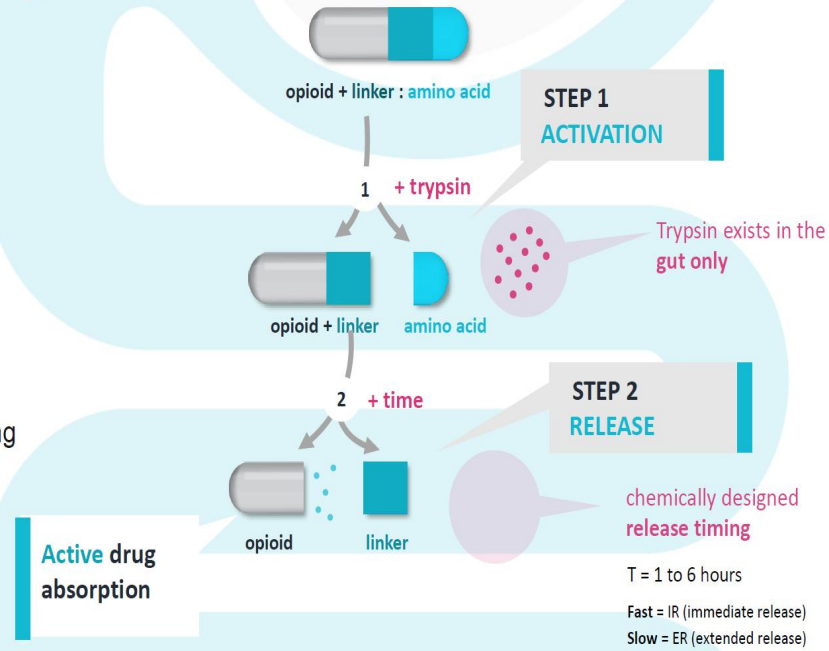
Pain Relief Delivery by TAAP

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 Delivery Profile

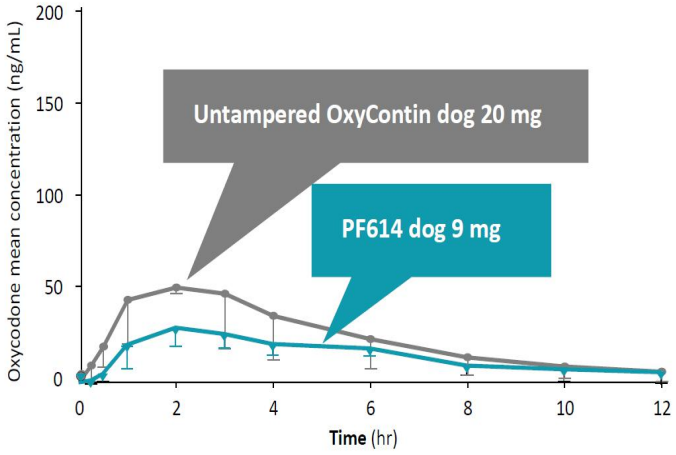
Equivalent to OxyContin

Ensysce™ biosciences

TAAP™ Preclinical Data

- PF614 chemically releases oxycodone with the same extended release (ER) profile as OxyContin
- The same release profile demonstrates that PF614 will achieve similar pain relief as OxyContin

Blood Concentration of Opioid Vs. Time



Ref: Kirkpatrick DL et al., J Opioid Manag 2017;13(1):39-49

PF614 Cannot be Manipulated to Change Delivery

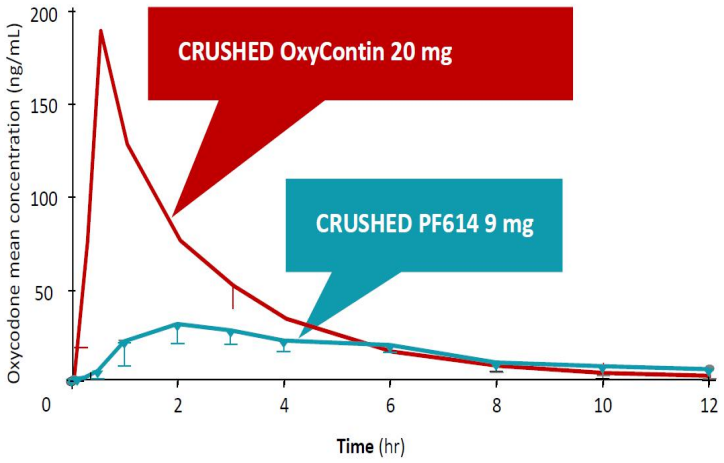
PF614 Release Profile Does Not Change

Ensysce™ biosciences

TAAP™ Preclinical Data

- **PF614**, even when crushed, releases oxycodone slowly in the blood, thereby reducing the large Cmax which leads to reduced 'drug liking'.
- The study demonstrated the significant difference between the manipulated PF614 versus manipulated (crushed) **OxyContin**

Blood Concentration of Opioid Vs. Time



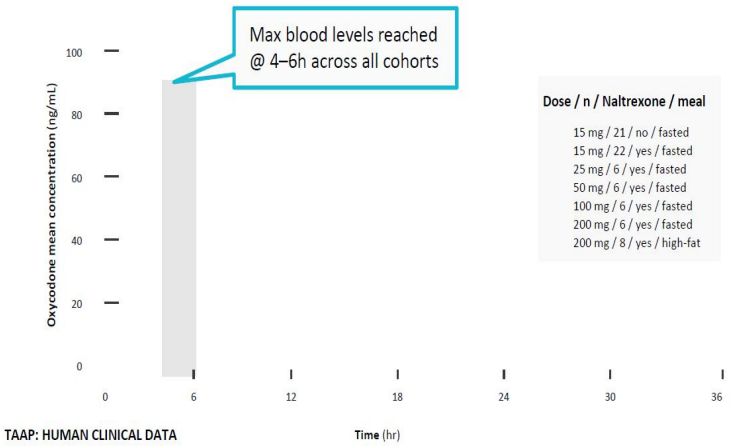
Ref: Kirkpatrick DL et al., J Opioid Manag 2017;13(1):39-49

PF614-101 Clinical Data

Designed for Longer-Lasting Pain Relief

Ensysce™ biosciences

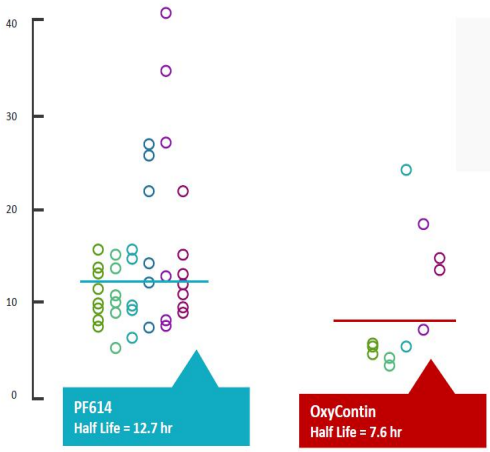
Oxycodone Concentration in Blood vs. Time following PF614 administered as oral solution



TAAP: HUMAN CLINICAL DATA

Oxycodone half life

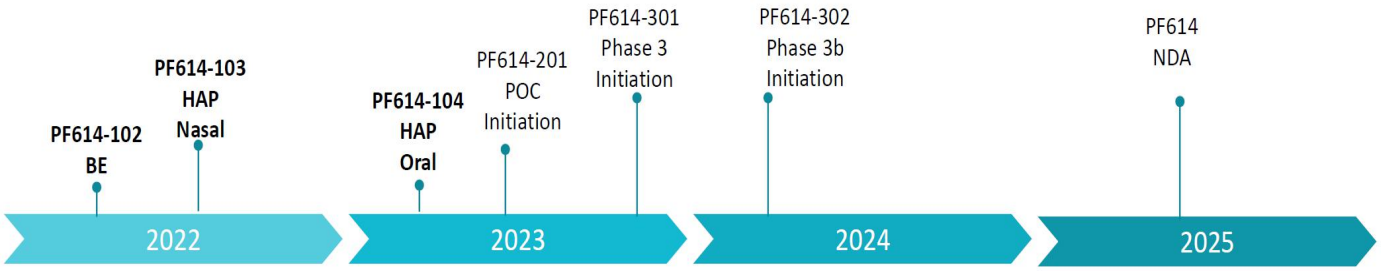
TAAP™: CLINICAL DATA



PF614 provides good safety profile, efficient conversion to oxycodone and longer half-life than OxyContin.

PF614 Development Plans

Clinical Development for Acute Pain Setting – update study numbers



POC Proof of concept study exploring onset of PF614 pain relief

Phase 3 Phase 3 efficacy studies in soft tissue and bony tissue surgeries

Bold text: Completed and current studies
Non-bold text: Planned studies


Ensysce™
biosciences
PF614-MPAR
TAAP oxycodone with
overdose protection

MPAR™ Mechanism of Action

Combination Product With Dose-Triggered Overdose Protection

Ensysce™ biosciences

MPAR™ Combination Product Legend:

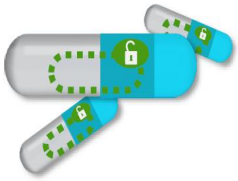
TAAP–enabled opioid | Trypsin Inhibitor

PRESCRIBED DOSE

Delivers pain relief as needed

Trypsin activation releases free and active drug product

DOSE THRESHOLD



ACCIDENTAL OVERDOSE

MPAR™ begins to inhibit trypsin, 'turning off' activation of TAAP and limiting opioid release.

EXCESS DOSE

EXCESS MPAR DOSE

Trypsin Activation blocked / overdose averted

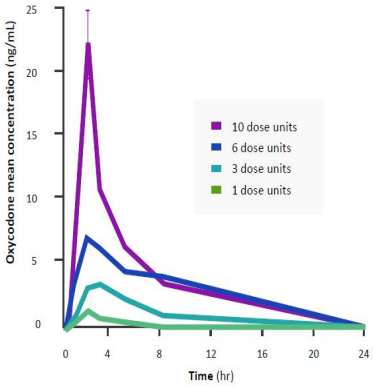
MPAR™ is only triggered by an overdose

PF614-MPAR™

Blocks Activation of PF614 and Oxycodone Release if Overdosed

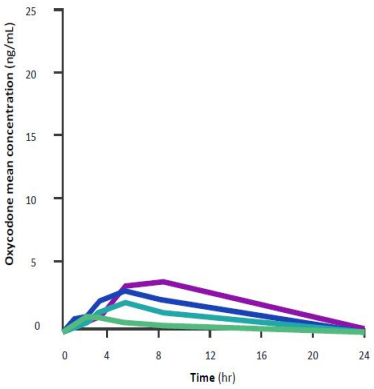
Without MPAR™

PF614 without nafamostat



With MPAR™

PF614 with nafamostat



TAAP + MPAR™: PRECLINICAL DATA

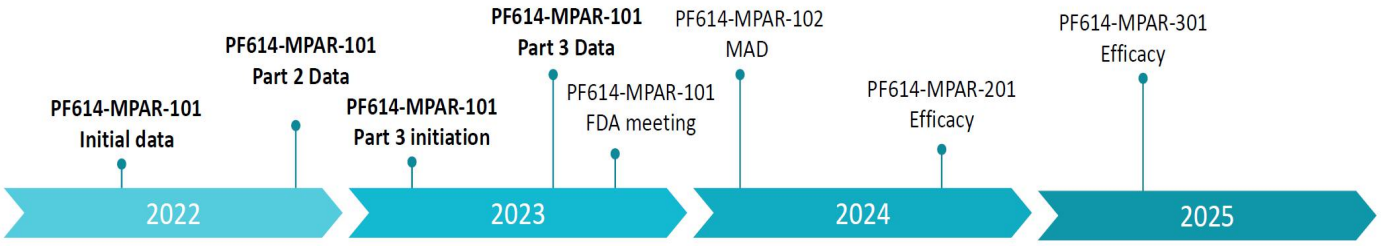
in rats n=4 / dose

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 activation of PF614 and prevents opioid overdose
- PF614-MPAR™ entered Phase 1 clinical trial in December 2021
- **Human Data demonstrating overdose protection reported in May 2022**

PF614-MPAR Development Plans

Clinical Development for Overdose Protection – look at study numbers



Bold text: Current Studies
Non-bold text: Planned studies

Milestones 2022-2023

STUDY	OUTCOME	SIGNIFICANCE
PF614-102	Bioequivalence study **Positive bioequivalence data: July 2022**	**505(b)(2) Regulatory path possible**
PF614-103	*Nasal* Human Abuse Potential (HAP) study **Positive topline data reported Nov 2022**	**Abuse-deterrent labeling possible**
PF614-MPAR-101	PF614 nafamostat combination **Positive PK data to define drug product**	**First overdose-protected prescription opioid**
PF614-104	*Oral* Human abuse potential study **Study recruitment completed Dec 2022**	**Abuse-deterrent labeling possible; data expected H1 2023**

Opportunities with TAAP™

Improving Drug Delivery Through Collaborations

Ensysce™ biosciences

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.

Cash Resources

$4.5M
Cash
as of 9/30/22*

$5.9M
Grant Funding Available
as of 9/30/22

$4.1M
Financing Gross Proceeds
12/07/22*

NIH support

2018

Ensysce received $11+M to progress MPAR™

Final year of four-year award received to undertake the **pre-clinical and clinical development** of the 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.

*Additional cash proceeds required in Q1 2023

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
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
Tufts University
Roche

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

3DMS
JSR
endo
GE
Wharton

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

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

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 Highlights

- **Clinical-stage biotech company -** transformative trypsin-controlled chemistry.
- **Two highly novel technology platforms** to control delivery of prescription drugs.
- **Targeted therapy areas** focus on products with blockbuster potential.
- **Shortened development** with Fast Track and 505(b)(2) regulatory pathway, **de-risked with positive clinical data showing the technology works**.
- **Lead product (PF614)** in Phase 2 trial – New Chemical Entity (NCE)
- **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

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


Ensysce™
biosciences
Appendix
28


Ensysce™
biosciences
PF614
Data Updates
29

PF614-102 MAD/BE

Multi-Ascending Dose Study

Ensysce™ biosciences

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,

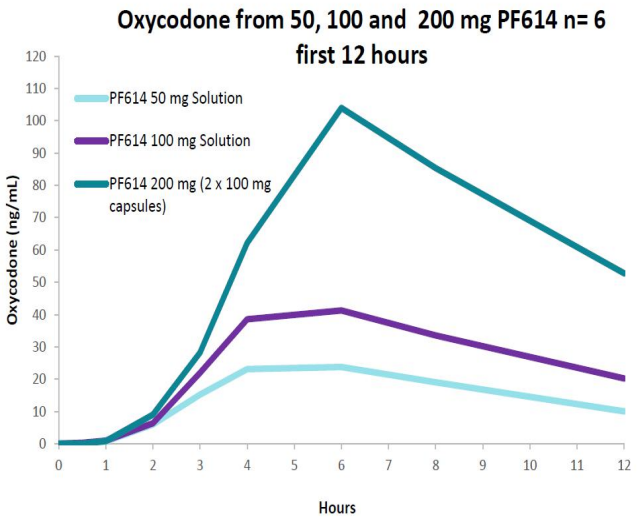
Administration

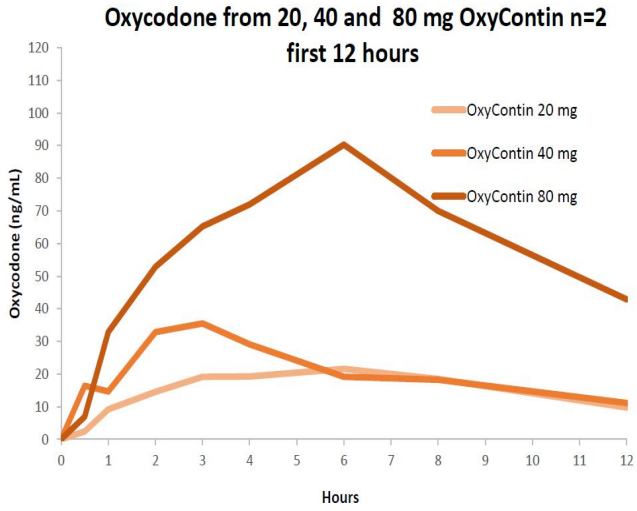
MAD: Oral twice daily (BID) doses for 5 days to groups of healthy adult subjects, naltrexone blocked randomized 3:1 PF614 to OxyContin. N=24

BE: Single oral dose of PF614 100 mg or OxyContin 40 mg under fasted and fed (high fat meal) conditions. N=60 to complete 4 conditions.

PF614-102 MAD

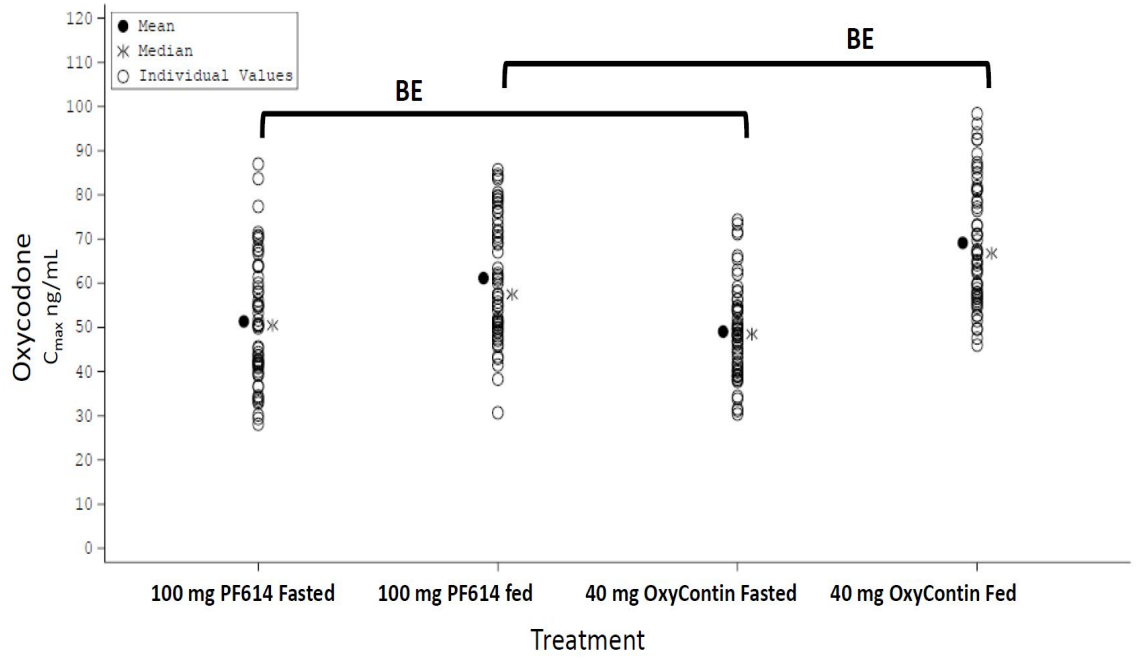
Pharmacokinetics (PK): oxycodone release from PF614 or OxyContin





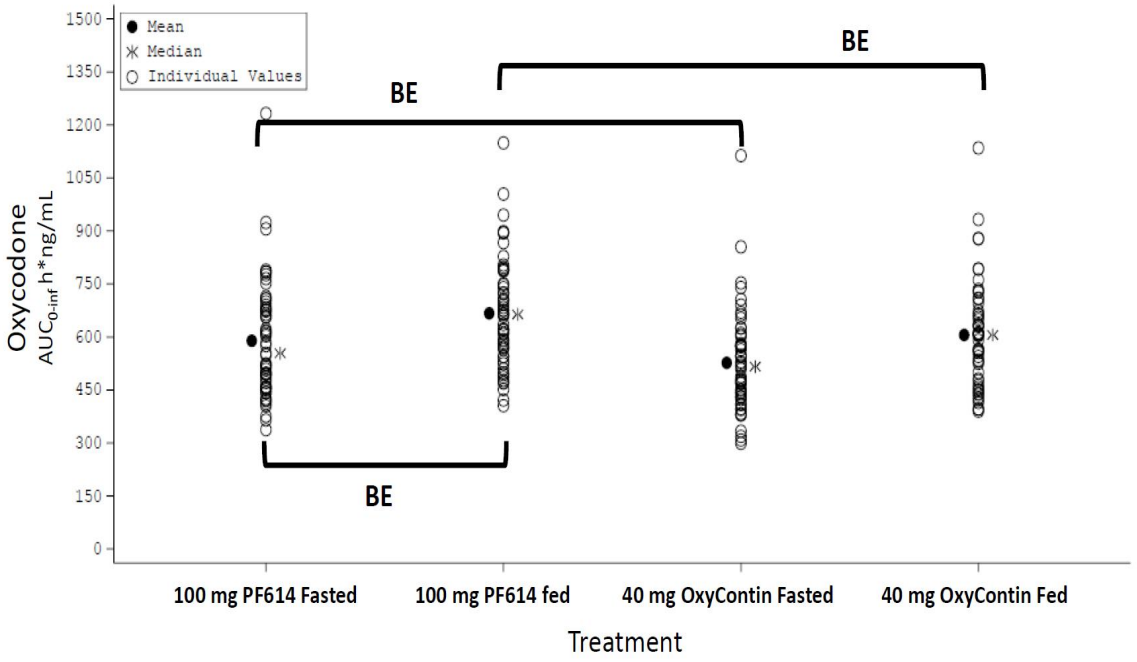
PF614-102 BE

PK: Oxycodone from OxyContin or PF614 C_{max} Fasted or Fed



PF614-102 BE

PK: Oxycodone from OxyContin or PF614 AUC_{0-inf} Fasted or Fed



PF614-102

SAFETY: PF614 and OxyContin produce similar Adverse Events

Part A: 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)

Part B: Table of Adverse Events

	PF614 fasted 100 mg n=58 n (%)	OxyContin fasted 40 mg n=59 n (%)	PF614 fed 100 mg n=58 n (%)	OxyContin fed 40 mg n=58 n (%)
Total subjects with at least 1 TEAE*	14 (24.1)	12 (20.3)	12 (20.7)	9 (15.9)

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


Ensysce™
biosciences
PF614-MPAR
Data Updates
35

PF614-MPAR-101

MPAR CLINICAL DATA: PF614 (25 mg) with and without nafamostat (10 mg)

Ensysce™ biosciences

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

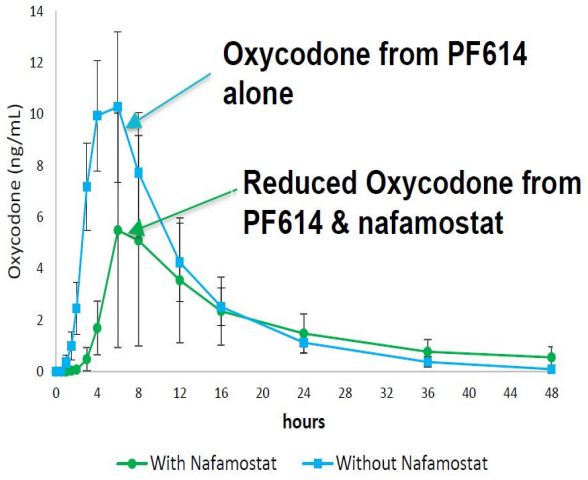
PF614-MPAR-101

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

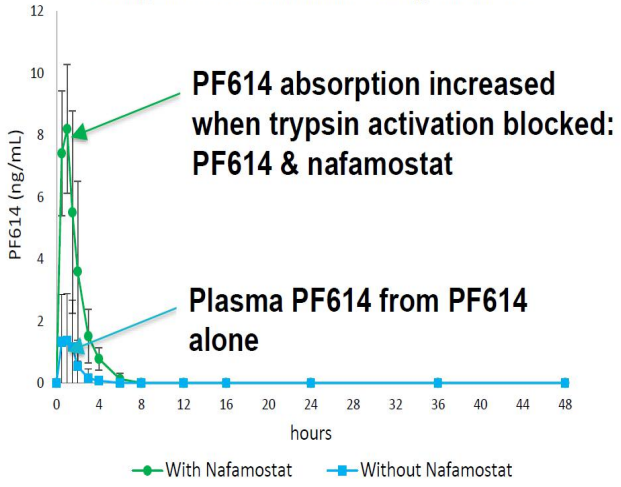
Ensysce™ biosciences

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



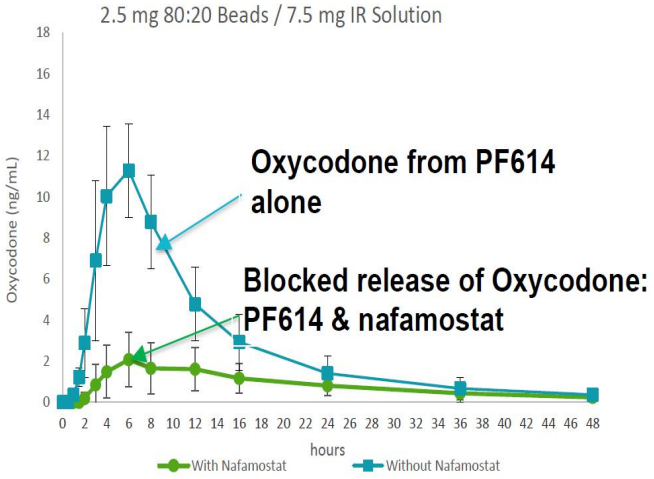
NEXT STEPS: Optimization of PF614 + nafamostat combination product = **MPAR**

PF614-MPAR-101

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

Improved Overdose Protection with Formulated Nafamostat:

Average Systemic **Oxycodone** after
25 mg Oral PF614 with or without Nafamostat
2.5 mg 80:20 Beads / 7.5 mg IR Solution



Average Systemic **PF614** after
25 mg Oral PF614 with or without Nafamostat
2.5 mg 80:20 Beads / 7.5 mg IR Solution