Ensysce™ biosciences

Cy Biopharma

A New Era in Pain Therapeutics

NASDAQ: ENSC

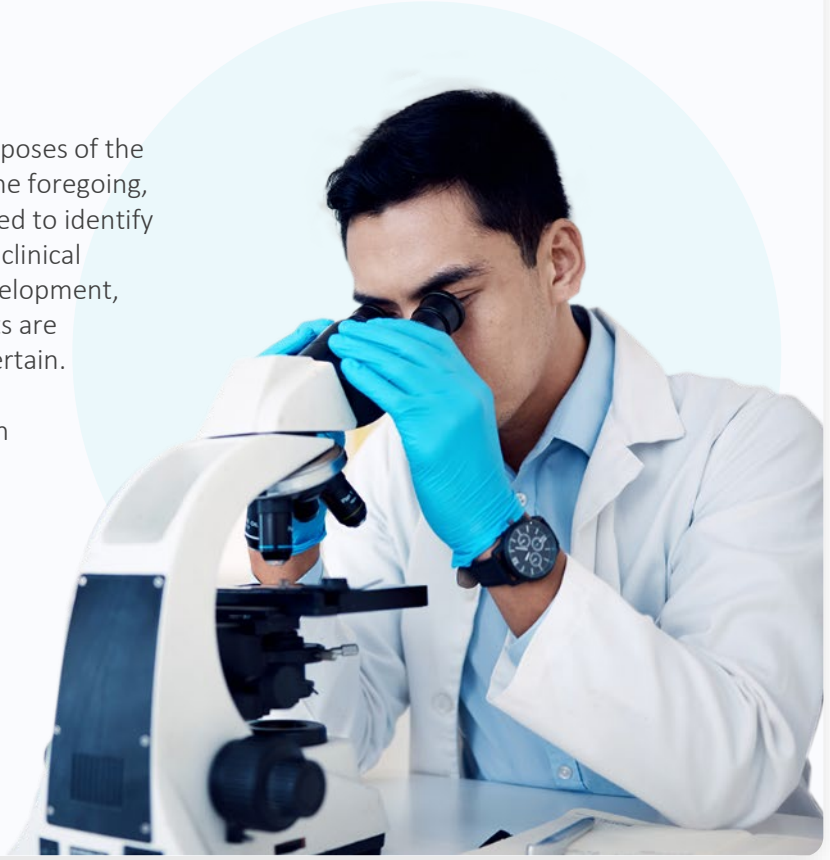
Investor Presentation Aug 2026

Disclaimer

Ensysce's PF614, PF614-MPAR and nafamostat are currently in clinical trials and pre-clinical studies. Cy's CY200 is in clinical developments. Accordingly, PF614, PF-614-MPAR and CY200 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, PF614-MPAR, Cy200, TAAP and MPAR are subject to the complete set of risks set forth in the Risk Factors disclosure found in the Company's most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission.

Forward Looking Statements

Statements contained in this presentation that are not purely historical may be deemed to be forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. Without limiting the foregoing, the use of words such as "may," "intends," "can," "might," "will," "expect," "plan," "believe" and other similar expressions are intended to identify forward-looking statements. The product candidates discussed are in clinic and not approved and there can be no assurance that the clinical programs will be successful in demonstrating safety and/or efficacy, that Ensysce will not encounter problems or delays in clinical development, or that any product candidate will ever receive regulatory approval or be successfully commercialized. All forward-looking statements are based on estimates and assumptions by Ensysce's management that, although Ensysce believes to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that Ensysce expected. In addition, Ensysce's business is subject to additional risks and uncertainties, including among others, the initiation and conduct of preclinical studies and clinical trials; the timing and availability of data from preclinical studies and clinical trials; expectations for regulatory submissions and approvals; potential safety concerns related to, or efficacy of, Ensysce's product candidates; the availability or commercial potential of product candidates; the ability of Ensysce to fund its continued operations, including its planned clinical trials; the dilutive effect of stock issuances from fundraising; and Ensysce's and its partners' ability to perform under their license, collaboration and manufacturing arrangements. These statements are also subject to a number of material risks and uncertainties that are described in Ensysce's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q. Any forward-looking statement speaks only as of the date on which it was made. Ensysce undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required under applicable law.



Ensysce Summary

Clinical-stage – 'Next generation opioids' - disrupting analgesia using transformative trypsin-controlled chemistry.

Targeted therapy areas focus on products with blockbuster potential with **FAST TRACK** and **BREAKTHROUGH THERAPY** designations.

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

Strong global patent estate

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

Cy Summary

Clinical-stage - addressing the root cause of chronic pain through central nervous system modulation with new class of small molecule therapeutics.

New Approach – CY is undertaking the first study of its kind to develop a chronic pain therapy targeting the 5-HT2A serotonin receptor using a proprietary, naturally derived compound designed to reset maladaptive neural circuitry.

Targeted therapy areas - pain conditions with few or no effective options, starting with rare and orphan indications.

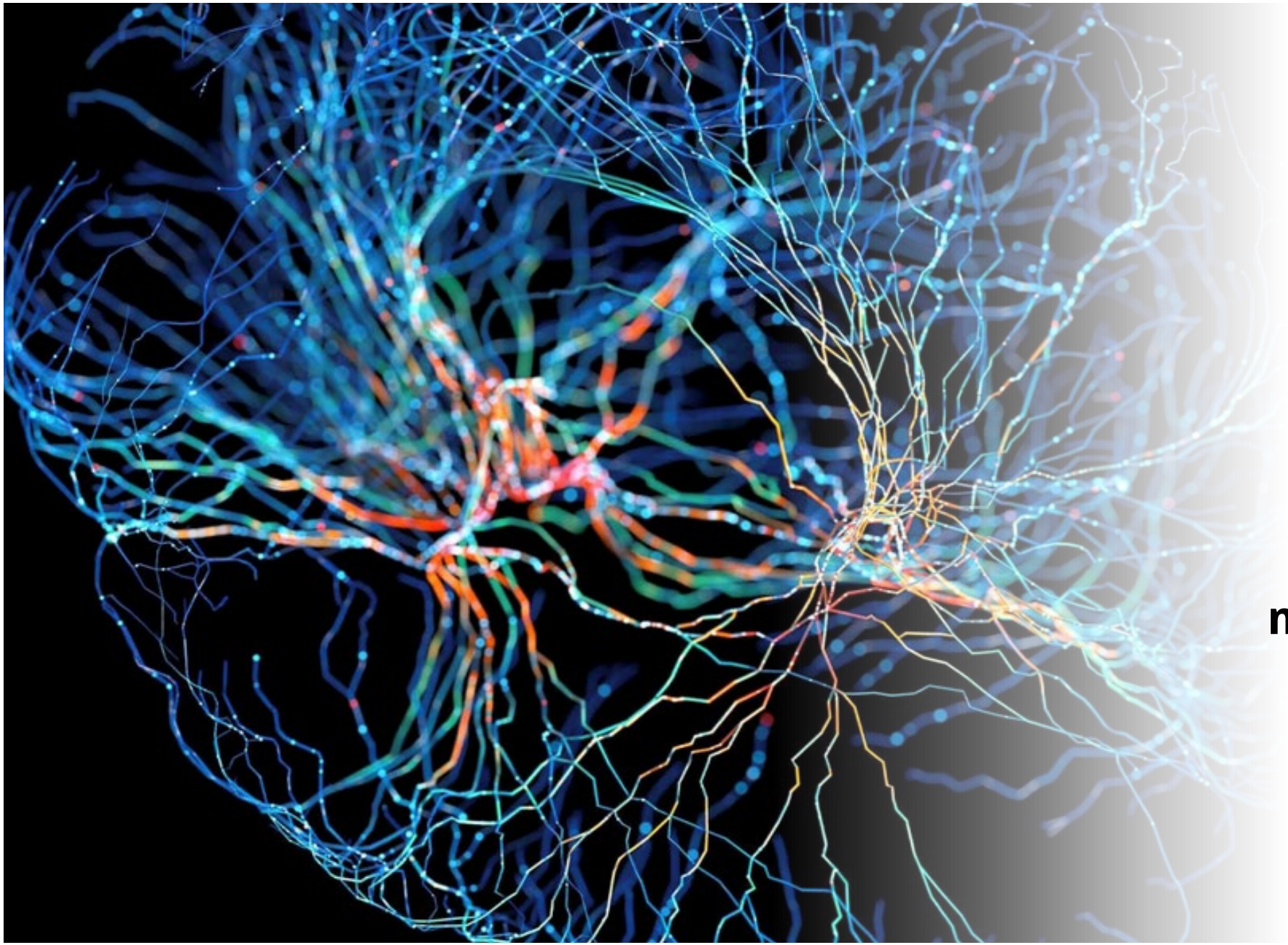
Lead Product - with **ORPHAN Drug Status for Regulatory acceleration, a** single-dose treatment with long-term durability.

Diversified Pipeline

Neuroscience and Pain

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
PF8001	ADHD - Immediate release	TAAP-Dexamphetamine			
PF8026	ADHD - Extended release	TAAP-Dexamphetamine			
PF9001	Opioid Use Disorder	TAAP-Methadone			
CY200/201	Complex Regional Pain Syndrome				FDA Orphan Drug Designation
CY30X/40X	Partial 5HT2a agonism/high 5HT1a activity				

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



CY200

Neural Reset

A new class for pain

Serotonergic modulation of neural networks

FDA Orphan Drug Designation 2026

*ischysogenic/ From Greek *ischys* ‘strength’ + genic ‘producing, giving rise to’

CY Therapy Overview

- **Mechanisms of Action**
  hypothesized for psychedelics in chronic pain[1]

- **Botanical extract**
  may confer greater size & durability of the effect[2]

- **Two oral formulations**
  CY200 – Oral capsule
  CY201 – Oral liquid
  - potential composition of matter & distribution advantages

- **Planned trial designs aligned**
  with regulatory and international consensus guidance for psychedelic and CRPS clinical research

  - FDA Pain; EMA Psychedelics Workshop 2024; COMPACT
    (Core Outcome Measurement set for complex regional Pain syndrome Clinical Studies)
  - IRB submission (USA)
  - Phase 2 single dose study in London (IRAS submission)
  - Phase 3 (USA, Europe, Australia)

1. Whelan, A and Johnson, MI (2018) Lysergic acid diethylamide (LSD) and Psilocybin for the Management of Patients with Persistent Pain: A Potential Role? Pain Management, 8 (3). ISSN 1758-1869 DOI: https://doi.org/10.2217/pmt-2017-0068
2. Shahar O, Botvinnik A et al. Effect of chemically synthesized psilocybin and psychedelicmushroom extract on molecular and metabolic profiles in mouse brain. Molecular Psychiatry (2024) 29:2059 – 2073

CY200 Mechanisms of action

Multi-tryptamine therapy - Neural Reset

5HT2 Activation improves Pain/ Mood

Synaptic remodeling

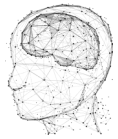
Reduced central sensitization

Reduced pain chronification

1. Weiss F, Magnesa A, et al. Psychedelic-induced neural plasticity: A comprehensive review and a discussion of clinical implications. Brain Sci. 2025;15:117. doi: 10.3390/brainsci15020117.
2. Laabi S, LeMmon C, et al. Deciphering psilocybin: Cytotoxicity, anti-inflammatory effects, and mechanistic insights. Int. Immunopharmacol. 2024;130:111753. doi: 10.1016/j.intimp.2024.111753.
3. Natoli S, Cuomo A, et al. Psilocybin and Chronic Pain: A New Perspective for Future PainTherapists? Med. Sci. 2025, 13, 277. https://doi.org/10.3390/medsci13040277.
4. Hammo, A., Wisser, S. & Cichon, J. Single-dose psilocybin rapidly and sustainably relieves allodynia and anxiodepressive-like behaviors in mouse models of chronic pain.Nat Neurosci 28, 2285–2295 (2025). https://doi.org/10.1038/s41593-025-02068-0

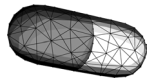
The Problem

CRPS – Refractory Severe Chronic Pain



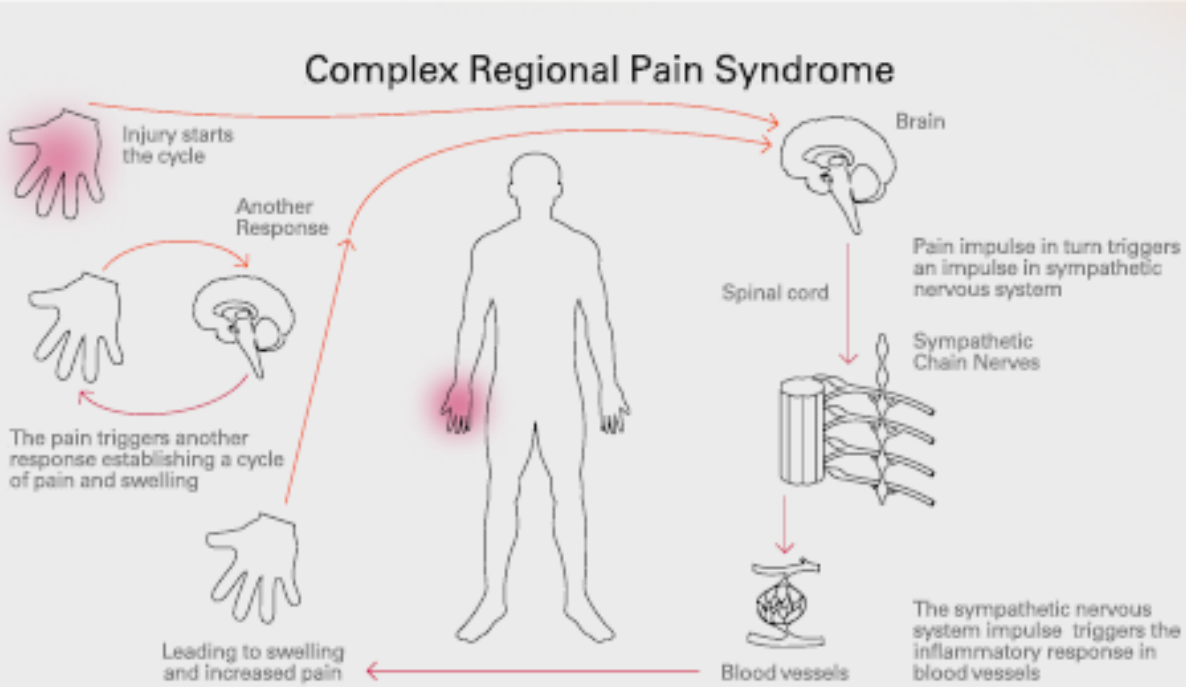
200,000
Americans with CRPS[2-4]

30%
Of sufferers unable to work[3]



No approved therapy

Current treatment options - **$30,000-150,000**[1]



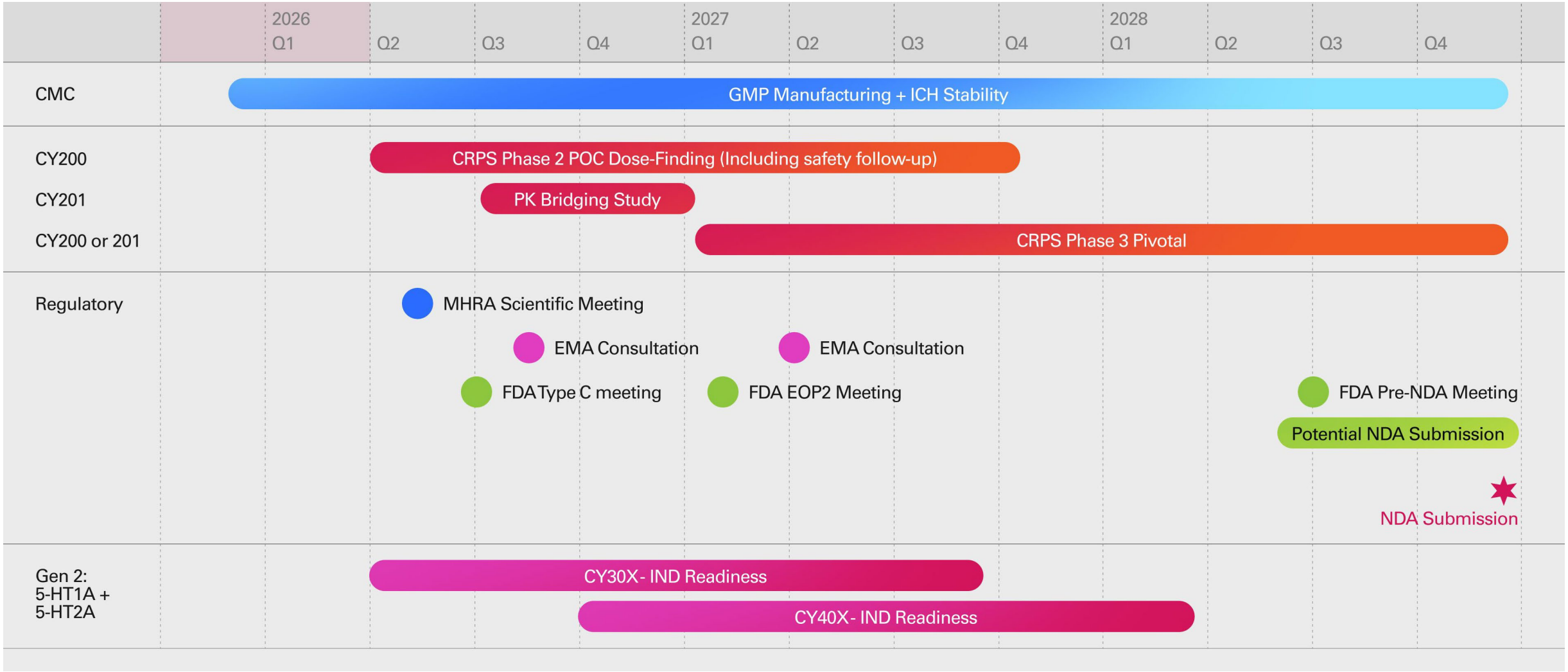
1. Financial impact of spinal cord stimulation on the healthcare budget: a comparative analysis of costs in Canada and the United States. Journal of Pain and Symptom Management. 2009;37(4):668–676. doi: 10.1016/j.jpainsymman.2008.04.007 PMID: 19558289 and supporting letter from Dr. Krishnan Chakravarthy (President of American Society of Pain & Neuroscience), Cy Biopharma Support Letter 12162025 16.Dec.2025.pdf
2. Elsharydah A, Loo NH, Minhajuddin A, Kandil ES. Complex regional pain syndrome type 1 predictors—epidemiological perspective from a national database analysis. J Clin Anesth.2017;39:34-37
3. Ferraro M C, O'Connell N E et al. Complex regional pain syndrome: advances in epidemiology, pathophysiology, diagnosis, and treatment.The Lancet Neurology. 2024.23,5; 522-33https://doi.org/10.1016/S1474-4422(24)00076-0
4. Lima et al. Complex Regional Pain Syndrome: Diagnosis, Pathophysiology, and Treatment Approaches. Cureus. 2024 Dec 24;16(12):e76324. doi: 10.7759/cureus.76324. PMID: 39850174; PMCID: PMC11756781.

Latest Clinical data in CRPS

Cy Biopharma sponsored studies generated clinical data used for FDA orphan drug designation as well as independent academic work.

- ✓ **Innovative POC – observational study ongoing**
- ✓ **Observed effect in a POC subject - > 2.5 months**
- ✓ **Doses well tolerated - up to 50mg per dose**
- ✓ **Study designs - mirrored UCSD and NYU**

CY200/201 Development Plan



CY Differentiated NCE Pipeline

Next generation NCEs planned CY30X/40X

- Novel molecule library with attractive receptor activation profiles
- Differentiated by partial 5-HT2A agonism, high 5-HT1A activity, low 5-HT2B risk and balanced 5-HT2C and 5-HT6/7 engagement[1]
- May increase social stress resilience[2], descending pain control[3] and increased neuroplasticity
- The 5-HT1A receptor is postulated to be involved in pain control pathways, such as descending modulation, where its activation may contribute to the inhibition of nociceptive transmission and modulation of pain.[3]

1. SYGPRJ [13145-CYBI-001] Report.pdf Updated 19 Jun 2025 by Rudi Prihandoko, Sygnature Discovery
2. Mineur,Y., Einstein, E., Bentham, M. et al. Expression of the 5-HT1A Serotonin Receptor in the Hippocampus Is Required for Social Stress Resilience and the Antidepressant-Like Effects Induced by the Nicotinic Partial Agonist Cytisine. Neuropsychopharmacol 40, 938–946 (2015). https://doi.org/10.1038/npp.2014.269
3. Millan MJ. Descending control of pain. Prog Neurobiol. 2002;66(6):355–474.

ENSC
Advancing Safer Prescription Medicines Using Chemical Safety Switches

- **Government funding from National Institute on Drug Abuse & FDA Breakthrough Therapy designation**
- Mission to develop differentiated medicines that improve the safety of prescription drug therapy.
- Proprietary MPAR® (Multi-Pill Abuse Resistance) platform designed to reduce the risk of oral overdose from multiple-tablet ingestion.
- Lead clinical programs leverage MPAR® to address significant unmet needs in pain management.
- Platform approach with potential application across multiple prescription drug products.
- Complements Cy Biopharma's pipeline by broadening the combined company's innovative CNS and pain-focused portfolio.

TAAP™ & MPAR®: Chemical Safety Switches

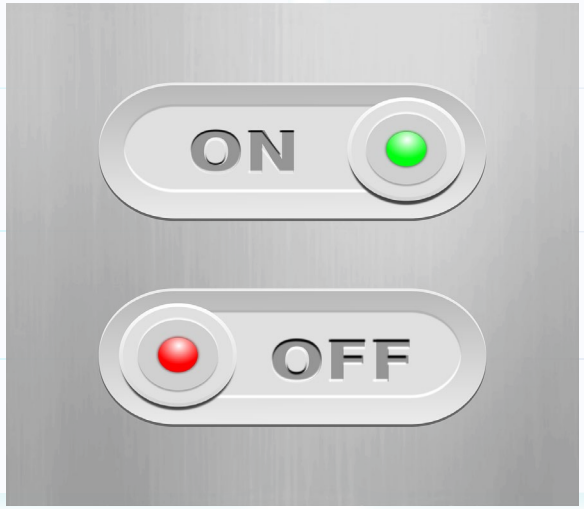
TAAP™

Trypsin-Activated Abuse Protection*

MPAR®

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

PROTECTIVE	Trypsin **TURNS ON RELEASE.**		**TURNS OFF RELEASE** only with overdose.	**SMART**
CONTROLLABLE	Chemically engineered to control release.		Trypsin inhibitor and TAAP prodrug.	**COMBINATION**
ANTI-ABUSE	Reduces abuse.		Platform based on trypsin control of activation and release.	**UNIQUE**
PERFORMANCE	Improves product delivery.		MPAR® can provide overdose protection to other drug classes.	**MULTI-USE**



*For mechanism see appendix

Ensysce™ biosciences

Cy Biopharma

PF614-MPAR

Powerful Analgesia + Overdose protection

TAAP Oxycodone combination product

Breakthrough Therapy Designation

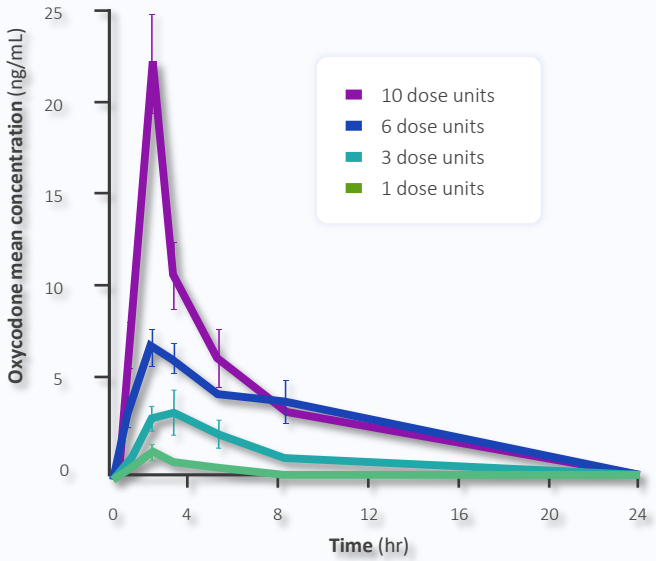
Grant by FDA January 2024

PF614-MPAR Pre-Clinical Data

— Blocks Activation of PF614 and Oxycodone Release if Overdosed

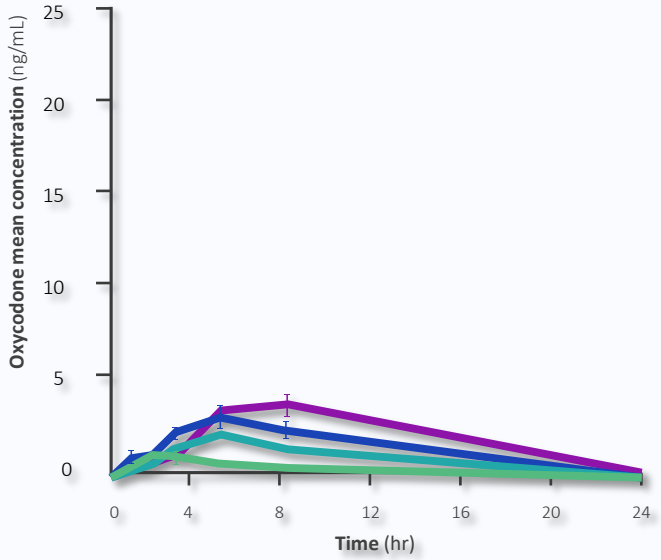
Oxycodone levels *without* MPAR®

PF614 without nafamostat



Oxycodone levels *with* MPAR®

PF614 with nafamostat

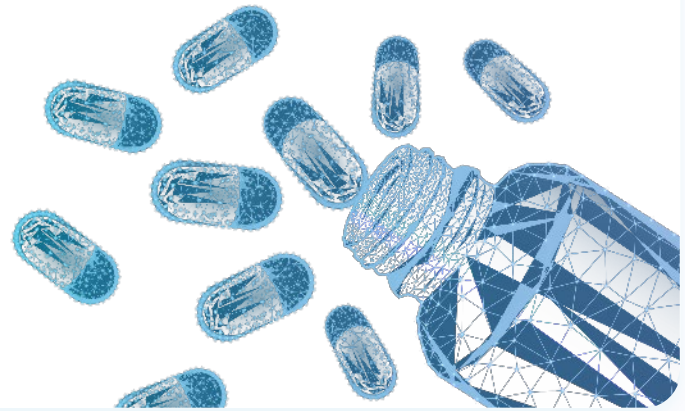


TAAP + MPAR™: PRECLINICAL DATA

in rats n=4 / dose

PRE-CLINICAL MPAR SUPPORT DATA

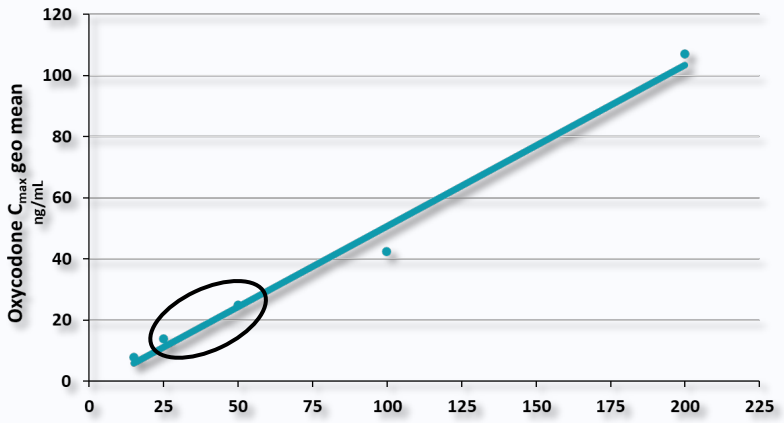
- Combination product of PF614 with an ultrapotent trypsin inhibitor, nafamostat
- Taken at prescribed doses there is no change in oxycodone release from PF614
- With increasing dose unit administration, increasing amounts of nafamostat blocks trypsin release of oxycodone and prevents opioid overdose



PF614-MPAR Pain Relief with Overdose Protection

— Clinical Data Demonstrating Oral Overdose Protection Achievable

PF614 alone no MPAR® overdose protection

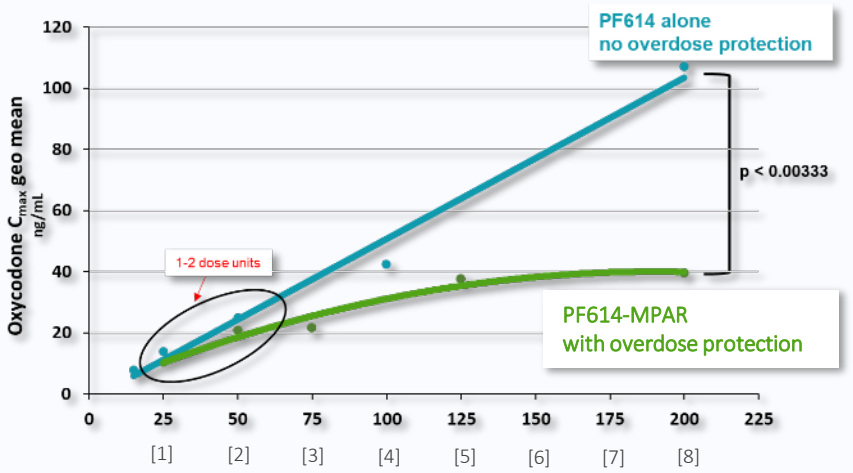


PF614 mg

PF614 alone (Phase 1SAD-MAD studies)

Linear dose increase after each dose

PF614-MPAR 25 mg with MPAR® overdose protection



PF614 (mg) or PF614-MPAR [# dose units]

PF614 + nafamostat (PF614-MPAR-101 study)

MPAR- Reduced activation after two dose units

FDA Breakthrough Therapy Designation

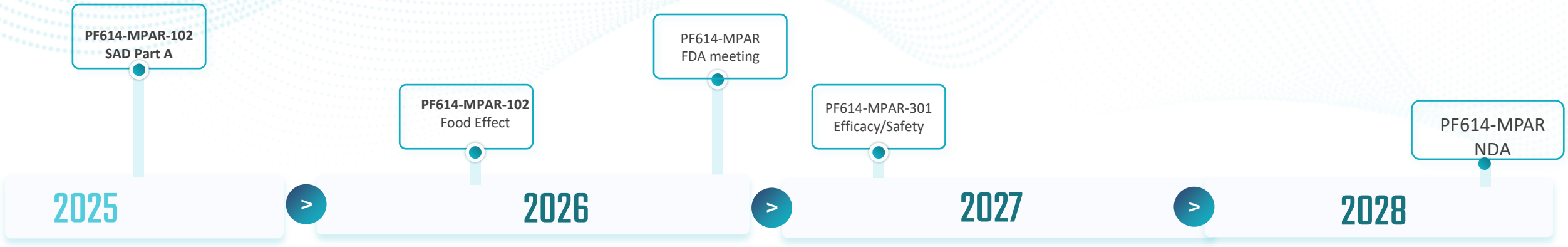
Goal to deliver two doses up to twice daily

Trypsin controlled opioid release

PF614-MPAR Development Plans

— Clinical Development for Overdose Protection

2026	OUTCOME	SIGNIFICANCE
PF614-MPAR-102	Continue Phase 1b SAD 100 mg dose and food effect	Confirm overdose protection followed by MAD study to support Type B FDA meeting
PF614-MPAR regulatory	FDA to discuss 'Overdose Protection' labeling	Outline path to commercialization



Bold text: Completed
Non-bold text: Planned studies
OD: Overdose
SAD: Single Ascending dose study

Ensysce™ biosciences

Cy Biopharma

TAAP™ and MPAR®

Expanded Opportunities

Drug Development Opportunities with TAAP™

Improving Drug Delivery and Lifecycle Management

TAAP™ MODIFICATION ATTRIBUTES

- Reaches the gastrointestinal tract/epithelial cells intact
- Chemistry controlled GI delivery for 'Immediate' or 'Extended-Release'
- Improves aqueous solubility
- Enhances the drug's permeation through the epithelial lining

OPPORTUNITY

Our TAAP™ platform enables new chemical entity (NCE) solutions that allow us to obtain new patents and extend market positions, revitalize approved medications and repurpose approved medications for the benefit of patients and care givers. *Specifically, Ensysce has used to develop a highly novel product for OUD.*

Possible oral delivery of injectable drugs

Enhance activity of drugs on GI tract

Extend half-life to improve dosing

Ensysce™ biosciences

Cy Biopharma

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

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 ACTIVX Biosciences pwc

JAMES MORRISON

Chief Operating Officer

- Founder and CEO of Cy Biopharma
- Patient Advocate
- Former analyst, energy trader and principal of BGC
- Bachelor of Civil Law, Oxford

Trafigura bgc

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 Roche

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

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

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, former Director of Rocky Mountain Poison and Drug Center, specializes in emergency medicine toxicology.

DR. WILLIAM SCHMIDT

Over 25 years of pharma industry experience, with special emphasis on novel analgesic and narcotic antagonist drugs

DR. RICHARD LANGFORD

Past President of British Pain Society and current practicing physician at the London Clinic

Board of Directors

Business, Finance, Healthcare & Regulatory Expertise

Dr. Lynn Kirkpatrick

Career focused on novel drug discovery and development

Dr. Bob Gower

Seasoned Executive and Entrepreneur

William Chang

Entrepreneur, Realty Company & Movie executive

JAMES MORRISON

Seasoned Finance Executive and Entrepreneur

Steve Martin

Experienced Senior Executive and Chief Financial Officer

Dr. Adam Levin

Academic and clinical orthopedic surgeon at Johns Hopkins Univ.

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Investor Relations

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