2021 annual review

Ensysce™ biosciences

WE ARE THE SCIENCE BEHIND THE SOLUTION

Opioid abuse has been declared a public health emergency and every day hundreds of people are still dying in the United States after overdosing on opioids.

MARKET OPPORTUNITY

Global Pain Management Drugs Market

Global Opioids Market

$91.6 B - 2027
$71.4 B - 2019

$22.4 B - 2026
$18.5 B - 2018

Ensysce™ biosciences has the solution with its transformative TAAP™ and MPAR™ platforms to address the global need to reduce the economic and social burden of prescription drug abuse and overdose. Next Generation Opioids use Chemistry to Save Lives.

Ensysce Biosciences, San Diego, CA Founded in 2009, Ensysce, through >$100MM of research investment — including over $20MM of government support from the National Institute on Drug Abuse — has built a global IP portfolio (>100 patents in 25 countries) focused in three independent areas: improving abuse deterrence and preventing overdose from opioids, reducing abuse of ADHD agents, and altering the outcomes from respiratory illnesses.

Leveraging its Trypsin-Activated Abuse Protection (TAAP™) and Multi-Pill Abuse Resistance (MPAR™) platforms, the Company is developing a new class of powerful, tamper-proof opioids that prevent both drug abuse and overdoses. Ensysce's products are anticipated to provide safer options to treat severe pain and assist in preventing deaths caused by opioid abuse while reducing the human and economic cost. For more information on the Company's pipeline of clinical and preclinical agents please visit www.ensysce.com.

INTEGRATED TECHNOLOGY PLATFORMS TO REDUCE ABUSE AND OVERDOSE

Lead Products

PF614

PF614 MPAR™

PF614 TAAP

TRYPSIN-ACTIVATED ABUSE PROTECTION

Tamper-proof improved delivery platform

TAAP opioid

Ensysce is on a mission to launch the first new class of Opioids in decades — which protect against both abuse and overdose, something unique in the industry — while providing powerful relief for severe and chronic pain.

Trypsin-controlled chemistry to reduce abuse and control the delivery of pain-relieving opioids.

Step 1: Swallow drug to find Trypsin

Step 2: Timing chemically-controlled to release opioid for pain relief

Ensysce is striving to disrupt the pain care market using its two patented, first-in-class agents, PF614 and PF614-MPAR. Proprietary abuse-resistant prodrug technology TAAP™ is a highly novel approach to addressing abuse by snorting, extracting, injection, or chewing.

TAAP™ opioids have the potential to meet the medical needs of patients living with severe pain, while providing a solution to the national epidemic of prescription opioid abuse, limiting their use to oral administration.

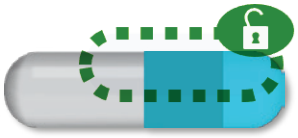
In addition, our unique Multi-Pill Abuse Resistant technology MPAR™ provides another layer of protection, reducing the possibility of oral overdose.

Together TAAP™ and MPAR™ may be designed to work in conjunction, both to overcome abuse and overdose — and ultimately — to save lives. **For more information scan the QR code below and see the science behind the solution.**

PF614
MPAR™

MULTI-
PILL ABUSE
RESISTANT

Smart anti-overdose platform



trypsin inhibitor

TAAP–enabled opioid

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

MPAR™ overdose protection reduces the opioid release as more product is consumed — accidentally or intentionally. This highly unique combination product may provide the ultimate safety to TAAP™ prescription drugs. It may be Ensysce's key to reducing deaths from drug overdoses.

EXTENSIVE PATENT PORTFOLIO

Patent-Issued Countries

$100B

Global Addressable Pain Market

TAAP™ and MPAR™ are covered by over **100 patents currently issued in 25 countries**, creating barriers to entry for new competitors globally.

Ensysce's technology is protected by a **suite of over 100 patents** issued in the U.S. and overseas (the UK, a majority of the EU, Australia, China, and others with a total of 25 countries).

DEAR SHAREHOLDERS,

As a fellow shareholder, I want to thank you for your support. 2021 was a transformational year for Ensysce, building the foundation for success in 2022 as we advance our mission to use our two technology platforms, TAAP™ (trypsin-activated abuse protection) and MPAR™ (multi-pill abuse resistant), to launch the next generation of opioid products with a focus on reducing abuse and overdose while relieving suffering for people with severe pain. We continue to make significant advancements across our clinical stage pipeline with a year of exciting milestones ahead, and I am looking forward to the continued journey.

First, for those less familiar with Ensysce, we are a clinical-stage biotech company, using transformative trypsin-controlled chemistry to improve drug safety and performance. By combining anti-abuse and anti-overdose technology, our goal is to create new classes of prescription drugs that are designed to be powerful and safe.

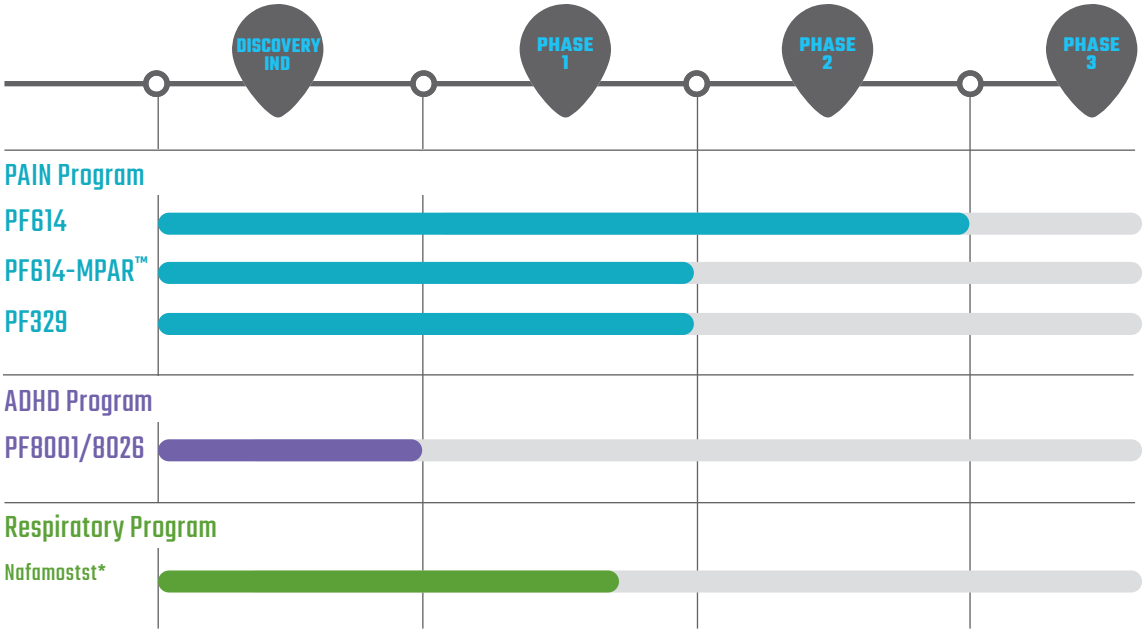
While we are currently focused on applying our chemistry to opioids to combat the ongoing opioid crisis, our platforms have the unique ability to be applied to a large majority of prescription drugs, driving unlimited opportunity for our platforms. To provide further context, the global pain management drug market is $91.6 billion, with the global opioids market at $22.4 billion. We have over 100 patents issued in 25 countries, supported by over $100 million in investments covering composition of matter, pharmaceutical preparations, and methods of use. The runway is truly limitless.

Turning to the year's achievements, in early 2021 we received FDA allowance for an Investigational New Drug (IND) application for PF614-MPAR™, a two-step extended-release oxycodone prodrug which is designed to provide not only abuse deterrence but also overdose protection properties with both TAAP™ and MPAR™. TAAP™ chemical modification inactivates the active ingredient in Ensysce's opioid products including PF614 and provides abuse deterrence, resistance to manipulation and other forms of recreational drug abuse, while providing a high degree of pain relief for those in severe pain. MPAR™ is a smart anti-overdose platform that is designed to protect patients from overdosing when it is combined with TAAP™ opioids.

In July, we were honored to receive the 3rd year funding of a multi-year grant from the National Institute on Drug Abuse (NIDA). This award provided $2.8 million to initiate a Phase 1 study of the first MPAR™ overdose protection product in the U.S., PF614-MPAR™. This brings the total support from NIDA to $8.0 million. An additional $2.8 million award for year four is pending. The award further confirmed the importance of our TAAP™ and MPAR™ technology, with this recognition by the National Institutes of Health through NIDA.

Clinically, we are pushing forward with the evaluation of our lead candidate, PF614, the TAAP-oxycodone prodrug we have designed to compete with OxyContin in the marketplace. The first cohort of subjects were enrolled in September, in the second clinical study of our next generation opioid PF614 conducted by Matthew Johnston, MD, PRA Health Sciences, Salt Lake City, Utah. The study, a two-part multiple-ascending oral dose (MAD)/Bioequivalence (BE) trial is built on the safety and pharmacokinetic results of the initial Phase 1 study, and has the potential to lead to an understanding of how PF614 compares to currently available commercial products. This study will demonstrate how PF614 compares to OxyContin, and importantly, may support the use of the 505(b)(2) regulatory path to registration. The 505(b)(2) path which can be advantageous because

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

"WHILE WE ARE CURRENTLY FOCUSED ON APPLYING OUR CHEMISTRY TO OPIOIDS TO COMBAT THE ONGOING OPIOID CRISIS, OUR PLATFORMS HAVE THE UNIQUE ABILITY TO BE APPLIED TO A LARGE MAJORITY OF PRESCRIPTION DRUGS, DRIVING UNLIMITED OPPORTUNITY FOR OUR PLATFORMS."

it may lead to a faster route to approval without the need for duplication of previously conducted studies, is being used by this highly innovative approach to reduce opioid abuse. In January, we successfully completed the MAD Part A of the study which evaluated three dose levels of PF614 delivered orally, twice daily for five days to groups of healthy subjects. Separate study participants received OxyContin at three comparable dose levels. Following completion of each cohort, a positive review from the trial's independent Safety Review Committee allowed the trial to proceed to the next dose level. Following completion of Part A, we initiated the BE Part B of the trial which recently concluded the clinical portion at the end of March. We are continuing to analyze the data from this trial and expect full results to be reported by the end of 2Q 2022.

Our robust intellectual property (IP) continued to evolve in 2021, highlighted by a Notice of Allowance from the patent office for a patent entitled Compositions Comprising Enzyme-Cleavable Amphetamine Prodrugs and Inhibitors Thereof, providing us with another possibility to build our pipeline of products for ADHD indications.

Notably, during the year we entered the public markets and commenced trading on the Nasdaq Capital Market through a special purpose acquisition company (SPAC) business combination, a milestone that provided the opportunity to progress our clinical programs. We believe that a Nasdaq listing will help to expand our potential shareholder base, improve liquidity, elevate our public profile within the industry, and ultimately enhance shareholder value. A subsequent $15.0 million convertible note financing strengthened our balance sheet and provided us with additional and necessary proceeds to continue the advancement of our lead clinical trial programs.

Importantly, we further deepened our executive management bench with multiple strategic additions in 2021. Our new Chief Financial Officer, David Humphrey, brings over 20 years of experience with development-stage companies as they progress toward product commercialization. Linda Pestano, PhD, our new Chief Development Officer, has worked throughout her career to guide the development of novel therapeutics to improve patient outcomes and quality of life. Our outreach and industry expertise were also strengthened by the addition of David J. Kovacs, VP Public Policy, who has extensive experience shaping policy and setting strategy for disruptive companies in pharmaceutical and technology sectors, and David Tanzer, our newly-appointed VP Strategic Development, an accomplished business executive specializing in helping companies with innovative IP and technology maximize their potential.

Looking ahead, we are well-positioned to execute across our clinical stage pipeline. As mentioned above, we expect data from our BE study in the second quarter of the year to position PF614 as our first commercial candidate. Additional clinical trials to evaluate PF614 are in the process of being initiated, including two human abuse liability (HAL) studies that are key for gaining abuse-deterrent labeling. We have a management team committed to our mission and an advancing patent portfolio with additional pipeline candidates. An enhanced balance sheet and public company status will help to provide us with some of the capital necessary to continue advancement of our lead clinical trial programs. Taken together, we are proud of our 2021 accomplishments and progress toward providing safer options for doctors, and their patients who experience severe pain. Thank you to all our shareholders, partners, and staff for your support on our journey. I look forward to another exceptional year at Ensysce.

Lynn Kirkpatrick

D. Lynn Kirkpatrick, PhD

Chief Executive Officer

Ensysce™ biosciences

STOCKHOLDER INFORMATION

www.ensysce.com
NASDAQ: ENSC

Corporate Headquarters
Ensysce Biosciences
7946 Ivanhoe Avenue
Suite 201
La Jolla, CA, 92037, United States
(858) 263-4196
Info@Ensysce.com

SEC Form 10-K
A copy of Ensysce's Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission is available at sec.gov and upon request.

Transfer Agent
To keep your contact information current and for stockholder questions regarding lost stock certificates, address changes, and changes of ownership or names in which the shares are held, direct inquiries to:

Continental Stock Transfer & Trust
1 State Street, 30th Floor
New York, NY 10004-1561
Phone: (212) 509-4000
Email: cstmail@continentalstock.com
Continentalstock.com

Independent Accountant
Mayer Hoffman McCann PC
13500 Evening Creek Drive N
Suite 450
San Diego, CA 92128

Market Information
Our common stock trades on the Nasdaq Capital Market under the symbol "ENSC."

CLINICAL ADVISORY BOARD

Dr. Richard Dart
Dr. Dart is the Director of the Rocky Mountain Poison and Drug Center and specializes in emergency medicine and toxicology.

Dr. Jeffrey Gudin
Dr. Gudin is listed Faculty, Department of Anesthesiology and Pain Management at University of Miami, Miller School of Medicine.

Dr. William Schmidt
Dr. Schmidt has over 25 years of pharma industry experience, with special emphasis on discovery and development of novel analgesic and narcotic antagonist drugs.

Dr. Lynn Webster
Dr. Webster has dedicated more than three decades to becoming an expert in the field of pain management.

BOARD OF DIRECTORS

Dr. Bob Gower
Chairman of the Board
Experienced Executive and Entrepreneur

Dr. Lynn Kirkpatrick, PhD
Chief Executive Officer
Career focused on novel drug discovery and development

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 University

Steve Martin
Experienced Senior Executive and Chief Financial Officer

Lee Rauch
Experienced CEO and Strategy Advisor

Dr. Curtis Rosebraugh
Experienced in extensive FDA drug approvals

Forward-Looking Statements
Statements contained in this 2021 Annual Shareholder Letter 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 our 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 current reports on Form 8-K, which are available, free of charge, at the SEC's website at www.sec.gov. 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.