January 5, 2026

Ensysce Biosciences Issues Annual Shareholder Letter

- ***PF614-301 Phase 3 Trial Enrollment Underway, Advancing Toward Market Launch***
- ***FDA Aligned with ENSC Manufacturing Path for PF614, Enabling Commercial Scale Up***
- ***MPAR® Patent Protection Extended Through 2042***
- ***Up to $20 Million in Funding Secured to Advance Late-Stage Programs***

SAN DIEGO, CALIFORNIA / ACCESS Newswire / January 5, 2026 /Ensysce Biosciences, Inc. (NASDAQ:ENSC) ("Ensysce" or "Company"), a clinical-stage pharmaceutical company developing innovative solutions for severe pain relief while reducing the potential for opioid abuse and overdose, today issued its 2025 annual letter to shareholders from Chief Executive Officer, Dr. Lynn Kirkpatrick.

Dear Fellow Shareholders,

2025 was a year of meaningful execution and strategic advancement for Ensysce. I would like to thank our shareholders for your continued support as we advance our mission to deliver safer, more responsible opioid analgesics without compromising access to effective pain relief. Over the past year, we made substantial progress across clinical development, regulatory alignment, intellectual property, and financing- strongly positioning the Company for 2026 and beyond.

Our efforts in 2025 were centered on advancing our clinical programs built on Ensysce's proprietary TAAP™ (Trypsin-Activated Abuse Protection) and MPAR® (Multi-Pill Abuse Resistance) technology platforms. Together, these platforms are designed to fundamentally improve the safety profile of opioid medications by addressing both abuse and overdose risk while preserving therapeutic efficacy.

TAAP™ Program Update: PF614

Our lead clinical candidate, PF614, is an extended-release oxycodone analgesic incorporating TAAP™ technology. PF614 potentially represents a new class of opioid and is designed to activate only when swallowed and exposed to trypsin in the small intestine, rendering it highly resistant to tampering and reducing the potential for abuse through non-oral routes of administration.

In July 2025, we reached a major milestone with the initiation of our pivotal PF614-301 Phase 3 clinical trial, titled *"A Multicenter, Randomized, Double-Blind, Placebo- and Active-*

Controlled Study to Evaluate the Efficacy and Safety of PF614 for the Treatment of Moderate to Severe Pain Following Abdominoplasty." This study is designed to assess PF614's ability to deliver effective post-surgical pain relief via steady analgesia, while addressing key safety concerns associated with traditional opioids.

To ensure rigorous trial execution, we partnered with Rho, Inc., a leading contract research organization (CRO) with extensive experience in central nervous system (CNS) and pain studies. On December 9, 2025, we initiated subject enrollment at two clinical sites, with additional sites expected to follow. We anticipate providing enrollment and progress updates during the first half of 2026 as we advance our Phase 3 program.

Importantly, in November 2025 we received highly constructive written feedback from the U.S. Food and Drug Administration (FDA) regarding our commercial manufacturing strategy for PF614. The Agency agreed with our proposed regulatory starting materials, drug substance specifications, and overall chemistry, manufacturing and controls (CMC) approach. This alignment provides a clear and direct path to commercial-scale manufacturing. We have initiated drug substance manufacturing activities with Purisys, LLC, a subsidiary of Noramco, and are working closely with our drug product manufacturing partner, Galephar, to support NDA registration readiness.

MPAR® Program Update: PF614-MPAR

Our second clinical candidate, PF614-MPAR, combines PF614 with our proprietary MPAR® overdose protection technology. PF614-MPAR is engineered to "switch off" opioid release in an overdose scenario, offering a potentially life-saving advance for patients who require opioid-strength analgesia. We believe PF614-MPAR is the only oral opioid analgesic designed with built-in overdose protection if taken in amounts greater than a prescribed dose.

This program continues to receive strong support from the National Institute on Drug Abuse (NIDA). In June 2025, Ensysce received the second $5 million installment of its second multi-year NIDA grant, bringing total non-dilutive funding for this program to over $25 million to date. The current grant extends through 2027, with a third $5 million installment expected in June 2026.

Key MPAR® program developments during 2025 included:

- Continued advancement of PF614-MPAR under Breakthrough Therapy designation from the FDA
- Encouraging feedback from the FDA regarding overdose protection labeling and support for a streamlined 505(b)(2) registration pathway
- Progress in our PF614-MPAR-102 clinical study supported by multi-year NIDA funding, which continues to generate important data to support regulatory discussions
- Collaborative work with the FDA on a scientific whitepaper that articulates the rationale behind overdose protection labeling

In September 2025, we presented updates on both PF614 and PF614-MPAR at PainWeek 2025, the world's largest pain management conference. Our standing-room-only symposium,

"Pain Management, Re-Invented: A New Era for Analgesia," featured leading experts in pain medicine and highlighted Ensysce's vision for opioids that treat severe pain while actively protecting patients with increased safety features built into the medications.

Opioid Use Disorder Program Update

In parallel, we continued advancing our opioid use disorder (OUD) program as a natural extension of our mission. In 2025, we identified PF9001 as our lead OUD candidate. PF9001 leverages both TAAP™ and MPAR® technologies and is designed to limit abuse, reduce cardiovascular risk, and incorporate built-in overdose protection.

This program is supported by another multi-year grant through the HEAL (Helping to End Addiction Long-term) program and with encouragement from NIDA. As opioid addiction continues to impact millions of individuals, we believe Ensysce can contribute a differentiated and safer therapeutic approach in this critical area of unmet medical need.

Expanding Intellectual Property Portfolio

In November 2025, the U.S. Patent and Trademark Office issued a Notice of Allowance for a new MPAR® patent, extending intellectual property protection through 2042. This patent includes both composition-of-matter and method-of-use claims, representing the strongest form of patent protection available. This milestone significantly enhances the long-term value of the MPAR® platform and reinforces the differentiated nature of our technology.

Strengthened Financial Position to Advance Late-Stage Clinical Programs

Throughout 2025, Ensysce was able to attract a number of investments that have allowed the Company to continue progressing its major program toward its pivotal studies. Most recently, in November 2025, we completed an additional $4 million convertible preferred financing, opening up access to up to $20 million in total capital over the course of the following 24 months. This capital supports the execution of our PF614 Phase 3 program and extends our operating runway.

The financing structure includes a fixed conversion price of $2.50 per share, subject to adjustment, and 50% warrant coverage, reflecting continued investor confidence and alignment with upcoming clinical and regulatory milestones. This financing, added to our continued grant support by NIDA, provides ENSC the ability to continue to progress its critical programs in 2026.

Looking Ahead

As we enter 2026, Ensysce is positioned for continued momentum. Key anticipated milestones include:

- Continued enrollment and execution of the PF614-301 Phase 3 trial
- Advancement of PF614-MPAR under Breakthrough Therapy designation
- Additional FDA interactions supporting commercial manufacturing readiness
- Further data generation to support overdose-protection labeling for MPAR products

- Advancement of PF9001 toward IND-enabling activities

We remain committed to advancing the next generation of powerful analgesics that address the severest of pain while incorporating safeguards aligned with modern public health priorities.

Subsequent to Year End: January 7, 2025 Shareholder Meeting

Finally, I would like to advise that our 2025 Annual Shareholders meeting will be held January 7, 2026. We thank our shareholders for their engagement and encourage you to vote through to the 7th in support of the Company's strategic priorities.

On behalf of the entire Ensysce team, thank you for your continued confidence in our science, our strategy, and our mission. The progress achieved in 2025 has laid a strong foundation for the year ahead, and we look forward to sharing additional milestones as we continue to build long-term value.

Sincerely,
Dr. Lynn Kirkpatrick
Chief Executive Officer
Ensysce Biosciences, Inc.

About Ensysce Biosciences

Ensysce Biosciences is a clinical-stage company with a goal of disrupting the analgesic landscape by introducing a new class of highly novel opioids for the treatment of severe pain. Leveraging its Trypsin-Activated Abuse Protection (TAAP™) and Multi-Pill Abuse Resistance (MPAR®) platforms, the Company is developing unique, tamper-proof treatment options for pain that minimize the risk of both drug abuse and overdose. Ensysce's products are anticipated to provide safer options to treat patients suffering from severe pain and assist in preventing deaths caused by medication abuse. For more information, please visit www.ensysce.com.

Forward-Looking Statements

Statements contained in this press release 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," "possible," "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, possible NASDAQ delisting, 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; continuation of government funding; 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 quarterly report on Form 10-Q and current reports on Form 8-K, 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.

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