January 8, 2024

Ensysce Biosciences Issues 2024 Shareholder Letter

SAN DIEGO, CA / ACCESSWIRE / January 8, 2024/ Ensysce Biosciences, Inc. ("Ensysce" or the "Company") (NASDAQ:ENSC), a clinical-stage company applying transformative chemistry to improve prescription drug safety, today issued a letter to shareholders from Chief Executive Officer, Dr. Lynn Kirkpatrick.

Dear Fellow Shareholders,

I am very pleased to provide you with an update on the outstanding progress we made over the last year and to extend sincere thanks from the Ensysce team for your ongoing support. During 2023, our focus was to demonstrate that our innovative approaches to severe pain could be delivered safely and effectively, and with the unique benefit of overdose protection. I believe we achieved that, and we are continuing to move our lead analgesic through to commercialization, as we also add to our pipeline of products to treat pain.

I will recap the milestones achieved over the last 12 months and discuss next steps as we gear up for what we hope to be a transformational year in 2024. The significant corporate progress we made and the clinical progress of our two lead programs in 2023 is outlined below.

One objective for 2023 was to increase the awareness of health care professionals and the public about what we describe as our 'Next Generation' analgesics. We highlighted the data we generated from our technology platforms, TAAP™ and MPAR®, by presenting along with key experts at industry events and scientific venues. Our leadership team hosted seminars, presented clinical data, and served as featured speakers at major therapeutic and business events. As we made strong progress with the development of our programs, we presented the results throughout the year at the following events:

- The annual PAINWeek scientific meeting
- The 4th Annual NIH 'Helping End Addiction Long-Term' (HEAL) Meeting
- Drug, Chemical & Associated Technologies Association (DCAT) Week
- The College on Problems of Drug Dependence (CPDD) 85th Annual Scientific Meeting
- The European Pharmaceutical Market Research Association (EPHMRA) Annual Conference
- The Controlled Release Society (CRS) 2023 Annual Meeting & Expo
- The American Association of Pharmaceutical Scientists (AAPS) 2023 PharmSci 360 event
- The Fierce New Product Planning Summit 2023
- The 17th Annual Pain Therapeutics Summit

The highlight event of the year was the Ensysce hosted Symposium for a global community of leading pain professionals during PAINWeek 2023 in September. Along with industry

experts, we provided a review of the current landscape for severe pain treatment, reviewed drug use and abuse in America and then examined the safety and effectiveness of PF614 and PF614-MPAR, our two leading ‘next generation' analgesics. A video highlighting the PAINWeek Symposium can be viewed here.

It was gratifying that after all of our presentations, we received very positive feedback from world renowned experts in pain to our clinical trial data and the underlying science of our products.

Our development progress with PF614, a TAAP™ extended-release oxycodone to treat severe pain, involved completion of a number of clinical trials and non-clinical studies required for approval, as well as the completion of key manufacturing activities. This work has culminated in a body of data that has been compiled into the regulatory submission for our End of Phase 2 discussions with the FDA, scheduled for January 30, 2024. We achieved our primary goal of advancing our PF614 program to define the Phase 3 strategy and generated critical safety and abuse potential data. We were pleased to be able to report that clinically PF614 was found to be bioequivalent to OxyContin for delivering oxycodone, yet it has a much longer half-life that we believe could improve the pain-relieving qualities of PF614 and provide twice daily dosing for strong analgesia.

Additional clinical data was announced in April, when we reported positive results from PF614-104, a study that evaluated the oral abuse potential of PF614. The study met key endpoints and showed that oral administration of PF614 had significantly lower scores for "Overall Drug Liking" and willingness to "Take Drug Again" than the oxycodone comparator.

Mid-year we also quickly began planning our first study to measure the onset of pain-relief for PF614, a key study suggested by FDA, to ensure it was completed in time for our meeting with the FDA. The timeline was short, but we received Investigational Review Board ("IRB") approval of the PF614-201 clinical protocol entitled ‘A Randomized, Double-Blind, Placebo-Controlled Crossover Study of PF614 on Analgesic Response in the Cold Pressor Test in Healthy Male Subjects' in August; we initiated the study in September and completed a timely participant enrollment in November. Finally in December 2023, we reported the study's final data that showed the time-of-efficacy-onset of PF614 and importantly its ability to reduce pain intensity. The rapid execution of this study was important to support the design of our Phase 3 protocols, adding to the favorable results from the other three clinical studies completed during 2023.

To ensure the market readiness of our lead drug candidate PF614, we also secured partnerships and worked with Commercial Manufacturing Organizations to prepare drug substance and drug product, a key step in ensuring commercial supply capabilities.

In parallel to advancing PF614, we also continued to make clinical progress with the first opioid product with overall overdose protection, PF614-MPAR. MPAR® reduces or ‘turns off' the release of the opioid from our TAAP prodrugs to prevent overdose. We believe this is the only technology that may reduce prescription drug overdoses stemming from oral abuse, ultimately saving lives. Currently marketed abuse deterrent technologies do not effectively deter one of the most common and dangerous forms of opioid abuse - swallowing an increased number of tablets than are prescribed. The CDC has stated that from 1999 to 2021, nearly 280,000 people died in the United States from overdoses involving prescription opioids, a number that does not include those that died from fentanyl overdoses. The clinical

data we generated over the past year is the first evidence that oral overdose protection is a real possibility. Our MPAR® combination technology can reduce release of oxycodone from PF614, when consumed in overdose, yet still provide adequate pain relieve when taken in prescribed doses. A regulatory submission has been made to discuss our MPAR development program with the FDA and a meeting is scheduled for February 20, 2024.

The clinical overdose-protection data generated for PF614-MPAR was reported in May 2023, when we successfully completed the Phase 1 study, PF614-MPAR-101. The study examined increasing doses of PF614-MPAR consumed simultaneously, and successfully showed that PF614-MPAR delivered oxycodone appropriately when one or two doses were consumed yet reduced opioid delivery when three or more doses were taken orally, representing a simulated overdose situation.

We believe the clinical results described above are evidence that PF614 and PF614-MPAR analgesics will disrupt the opioid pain market. These ‘next generation' analgesics have proven they are equally safe and effective as current prescription opioids. This is important as opioids remain a vital element in the treatment of severe conditions such as post-operative and cancer pain.

In addition to our clinical progress, we continue to build our efforts in commercialization as we engaged a firm with extensive Business Development expertise, Alacrita Consulting, for the purpose of exploring partnering and licensing opportunities. This engagement enhances Ensysce's business development opportunities and boosts near-term revenue potential by looking at all geographies where our products or platforms could provide benefit. We believe TAAP and MPAR can be applied to a number of prescription drugs, and provide an ongoing opportunity to securing partnerships to drive additional future revenue.

Another option to strengthen our commercial offerings arose with our new relationship with the Swedish company, OncoZenge AB ("OncoZenge"). We announced in a Letter of Intent that Ensysce was exploring a role in the US for developing a bupivacaine lozenge, BupiZenge, to treat the pain associated with oral mucositis caused by cancer treatment. This relationship will allow us to diversify our portfolio of pain agents outside of opioids. OncoZenge has already demonstrated the efficacy of BupiZenge™ in four clinical trials in Europe, and Ensysce has a long-term goal of bringing BupiZenge through FDA approval and to commercialization in the United States where there is a large market potential and unmet need.

Operationally and financially, we took several important steps allowing us to advance the clinical development of our highly unique programs. During 2023, we completed three financing transactions for total gross proceeds of $12 million before fees and expenses, which provided us with necessary funds to continue the advancement of our lead clinical trial programs.

As we enter 2024, we are focused on our near-term discussions with the FDA on our Phase 3 protocol design for PF614. Our End of Phase 2 discussions are scheduled with the FDA on January 30, 2024, and will solidify our Phase 3 program that we intend to initiate in the second half of the year. Likewise, we are continuing regulatory discussions with the FDA in February 2024 to aid our future clinical development plans for PF614-MPAR. Ultimately our focus is seeking to move each program through regulatory approval in an expedient fashion through the shortened 505(B)(2) pathway and to expand the use cases of our TAAP^{TM} and

MPAR® technology platforms.

The accomplishments we've achieved in 2023, and our tangible forward goals, are a result of the hard work and commitment of our entire team. We are passionate about our mission to deliver new and improved forms of analgesia both in the U.S. and globally and are exploring ways to broaden our pipeline. From presenting our programs at key industry events, to successfully conducting clinical trials, each step has contributed to our long-term success.

We are entering 2024 with real excitement for what we believe will be a pivotal year for Ensysce. We thank you, our shareholders, for your support and we thank our employees for fueling the direction of our clinical, operational, and financial execution. We look forward to sharing our accomplishments in the coming year as we strive to create value for our shareholders, employees, and communities, and we thank all of you for your dedication to our mission.

Sincerely,
Dr. Lynn Kirkpatrick
Chief Executive Officer

About Ensysce Biosciences
Ensysce Biosciences is a clinical-stage company using its proprietary technology platforms to develop safer prescription drugs. 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. The platforms are covered by an extensive worldwide intellectual property portfolio for a wide array of prescription drug compositions. 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, 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 quarterly report on Form 10-Q 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.

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