April 15, 2025

Ensysce Biosciences Announces Positive Data from Opioid Overdose Protection Study

~ Additional Evidence of PF614-MPAR Overdose Protection after Completion of Part 1 of Clinical Study ~

SAN DIEGO, CA / ACCESS Newswire / April 15, 2025 /Ensysce Biosciences, Inc. (NASDAQ:ENSC) ("Ensysce" or the "Company"), a clinical-stage pharmaceutical company developing innovative solutions for severe pain relief while reducing the potential for opioid abuse and overdose, today announced completion of Part 1 of its second clinical trial to evaluate PF614-MPAR for overdose protection. PF614-MPAR-102 demonstrated that the combined Ensysce TAAP™ and MPAR® technologies can deliver strong relief for severe pain yet protect from the risk of excessive doses when consumed accidentally or deliberately.

Part 1 of this second study of PF614-MPAR overdose protection confirmed that a 100 mg dosage of PF614-MPAR delivers oxycodone to treat severe pain and provides overdose protection when a greater-than-prescribed dose is consumed. Subjects were studied as their own control and received up to five 100 mg doses of the overdose-protected PF614-MPAR versus the unprotected PF614. The data showed that the maximum amount of oxycodone released from PF614-MPAR, when three or more doses were taken at one time (C_{max}) was reduced compared to that released following the consumption of same amount of PF614 alone, evidence of overdose protection. When five doses of PF614-MPAR were administered, overdose protection was appropriately greater than that observed from three dose units. Additionally, safety data from the trial showed that there were no unexpected adverse events from either PF614 or PF614-MPAR.

We believe this data, combined with that from a previous study, PF614-MPAR-101, demonstrates overdose protection across the full dosage range of PF614-MPAR planned for commercialization. This complete analysis will be discussed with the FDA in an upcoming meeting focusing on the full development plans for PF614-MPAR.

The trial will now continue to enroll Part 2 to examine potential food effect and Part 3 to evaluate repeat dosing of PF614 vs. PF614-MPAR. The aggregate data will allow the Company to focus on perfecting a final drug product to move into commercialization.

Dr. Bill Schmidt, Chief Medical Officer of Ensysce, commented, "These clinical data demonstrate that MPAR® is a vital tool to limit overdoses from prescription medications. Our initial study demonstrated the unique overdose protection built into PF614-MPAR, which is the only opioid product to have been granted FDA's Breakthrough Therapy designation. Our goal of bringing PF614-MPAR and a new generation of safer analgesics to the market to

alleviate suffering from severe pain is now closer to the finish line."

Dr. Lynn Kirkpatrick, CEO of Ensysce, added, "Each phase of our MPAR related clinical studies thus far have provided highly encouraging data supporting the safety features of PF614 and PF614-MPAR that other opioids don't have. We are continuing to quickly execute the final stages of this study with Quotient Sciences and their Translational Pharmaceutics® platform, and we are working with a commercial manufacturing partner to prepare this unique product for the market. We look forward to productive discussions with the FDA to establish our path to registration for the first overdose-protected opioid."

PF614-MPAR 102 Clinical Study Description

Clinical study PF614-MPAR-102, 'A Single and Multiple Dose Study to Evaluate the Pharmacokinetics of Oxycodone and PF614 when PF614 Capsule is Co-Administered with Nafamostat as a Combination of Immediate Release Solution and Extended Release Capsule Formulations (PF614-MPAR) in Healthy Subjects,' was designed to evaluate the full dosage range of PF614-MPAR, study potential food effects, and to conduct a multiple ascending dose study with the final PF614-MPAR combination.

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, 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-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.

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