December 9, 2025

Ensysce Biosciences Achieves Major Milestone with Initiation of Enrollment in Pivotal Phase 3 Trial of PF614, Its Next-Generation Opioid

~ Engineered to Deliver Potent Pain Relief with Unique, Built-In, Abuse Protection ~

SAN DIEGO, CA / ACCESS Newswire / December 9, 2025 /Ensysce Biosciences, Inc. (NASDAQ:ENSC) ("Ensysce" or the "Company"), a clinical-stage pharmaceutical company pioneering novel solutions for severe pain with built-in abuse and overdose protection, today announced that the first patient has been enrolled in the Company's pivotal Phase 3 clinical trial of PF614, its lead product candidate.

This landmark study, PF614-301, *'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 after Abdominoplasty',"* is designed to demonstrate PF614's ability to provide strong, consistent post-surgical pain relief while incorporating an innovative chemical mechanism intended to reduce the risk of abuse. The trial will also evaluate PF614's potential to provide a smoother, safer treatment of severe acute pain using twice daily dosing with reduced highs and lows in blood drug concentration, an approach which is seen as beneficial by leaders in the field.

Enrollment has commenced at CenExel JBR in Salt Lake City, Utah, under the leadership of Dr. Todd Bertoch, and CenExcel Atlanta under the leadership of Dr. Jessica McCoun, both recognized expert in anesthesiology and pain medicine and the study's Principal Investigators.

"This is a significant milestone for Ensysce and for the millions of patients who depend on opioid analgesia during recovery from serious surgery." said Dr. Lynn Kirkpatrick, CEO of Ensysce. "Initiation of our pivotal Phase 3 program moves us one step closer to redefining pain care. We aim to show that PF614 can reliably deliver the level of pain control patients need, while its built-in protective features help safeguard against the dangers of abuse. We believe PF614 represents a next generation of safety for opioid therapy and this Phase 3 trial marks a significant step on our pathway to commercialization."

About Ensysce Biosciences

Ensysce Biosciences is a clinical-stage pharmaceutical company disrupting the pain treatment landscape with its proprietary **Trypsin-Activated Abuse Protection (TAAP™)** and **Multi-Pill Abuse Resistance (MPAR®)** platforms. By engineering opioids with intrinsic safeguards against tampering, misuse, and overdose, Ensysce aims to offer safer, life-saving options for patients in need of powerful pain relief. Learn more at: 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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SOURCE: Ensysce Biosciences Inc.