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Ensysce Biosciences Announces Positive Results from Oral Human Abuse Potential Trial for PF614

~ Reduced Drug Liking of PF614 versus Oxycodone ~

SAN DIEGO, CA / ACCESSWIRE / April 3, 2023 /Ensysce Biosciences, Inc. ("Ensysce" or the "Company") (NASDAQ:ENSC), today announced positive results from a key study on the oral human abuse potential of PF614, a potential next generation pain medicine.

The study met all key endpoints and showed PF614 had significantly lower scores of "Drug Liking" than the oxycodone comparator at both the low and mid doses studied. These results should allow Ensysce to start the next phase of development, by entering into end of phase 2 discussions with the FDA for commencement of phase 3 trials.

On the primary endpoint of "Drug Liking at this moment" PF614 produced statistically lower effects than oxycodone at the lowest dose ($p<0.0001$), and statistically significant "Overall Drug Liking" at both the low and mid doses ($p<0.0001$ and $p=0.0025$, respectively). PF614 also had a significantly longer median time to reach peak levels for "Drug Liking" than oxycodone at all three dose levels, which is important for reducing abuse potential of opioid agents.

The secondary endpoint "Take Drug Again" was met at both the low and mid dose of PF614 ($p<0.001$ and $p=0.0038$ respectively) and was numerically lower than comparator even at the high dose, demonstrating that recreational drug users are less motivated to abuse PF614 compared to immediate-release oxycodone.

Lynn Kirkpatrick, CEO of Ensysce said, "I am very pleased with these results and proud of the effort my team has put into the studies over the last year. PF614 could make a real difference to people in severe pain. HAP studies are critical for labeling, and we believe the study shows we have a product which is unattractive to people who may wish to abuse opioids. As we look at the data we have generated over the last year, we believe we now have a product with equivalent efficacy to OxyContin, which is well tolerated and less liked by those who may attempt to abuse it."

Dr Lynn Webster, Senior Fellow, Center for U.S. Policy and a leading expert on HAP studies, commented, "These results are very positive and, when examined with previous intranasal and efficacy studies, suggest that PF614 may be an important new type of product to treat severe pain. I am especially encouraged that the data on "take drug again", which is the ultimate measure of whether the product is likely to be abused, shows PF614 has a unique profile." Dr Webster continued, "I believe the data from this clinical trial demonstrates that PF614, even at doses double that of other oxycodone products, is less likely to be "taken again" for recreational purposes, an outcome that is very important and most likely due to its

pharmacokinetic profile that was designed specifically to take a longer time to reach maximal blood levels. PF614 may have an important place in therapy, for those in severe pain who may be concerned about the ease of manipulating conventional opioids that leads to the most serious forms of abuse."

The Study: PF614-104

Blinded test agents included PF614 (50, 100 and 200 mg, equivalent to 20, 40 and 80 mg oxycodone), oxycodone HCl (40 mg), or placebo, all administered orally among 32 recreational drug users. A total of 28 subjects who completed all 5 cross-over comparisons in the study constituted the modified completer population (MCP). The study examined "Drug Liking" at peak effect (Emax) (Primary endpoint), "Take Drug Again" Emax (Secondary endpoint).

About PF614

PF614 is a Trypsin Activated Abuse Protected (TAAP™) product designed as a delayed onset extended-release oxycodone prodrug. TAAP™ chemical modification inactivates the active ingredient in Ensysce's products including PF614 until they are swallowed. This provides abuse deterrence, resistance to manipulation and other forms of recreational drug abuse, while providing a high degree of pain relief for those who require opioid analgesics for 24/7 round-the-clock severe pain. This study builds on the safety and pharmacokinetic results already seen in the prior clinical studies and improves the understanding of how PF614 compares to currently available commercial products.

About Ensysce Biosciences

Ensysce Biosciences is a clinical-stage biotech company using its proprietary technology platforms to develop safer prescription drugs. Leveraging its Trypsin Activated Abuse Protection (TAAPä) and Multi-Pill Abuse Resistance (MPAR™) platforms, the Company is in the process of developing a unique, tamper-proof treatment option for pain that minimizes the risk of both drug abuse and overdoses. 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 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.

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