February 23, 2023

Ensysce Biosciences Provides Corporate Update

Answers Recently Asked Questions

SAN DIEGO, CA / ACCESSWIRE / February 23, 2023 /Ensysce Biosciences, Inc. ("Ensysce" or the "Company") (NASDAQ:ENSC), a clinical-stage biotech company applying transformative chemistry to improve prescription drug safety to reduce abuse and overdose, today issued a letter to shareholders from Chief Executive Officer, Dr. Lynn Kirkpatrick, to address the Company's most recent frequently asked questions.

Dear Fellow Shareholders,

As a clinical stage biotech company working through clinical development, our opportunities to touch base with our investor community are largely tied to Company milestones and the announcement of associated clinical data. Given our progress throughout the past year, I wanted to update shareholders and supporters of our work, addressing some questions we have recently received regarding our development progress and timelines.

What is our mission?

Our mission, simply put, is to improve drug safety. We have specific expertise in reducing abuse and overdose. We believe our technology has broad applications, and our first goal is to improve opioid analgesics by delivering safer options, thereby impacting the opioid crisis.

Are opioid products necessary?

Yes, we and many experts believe they are very necessary. Opioids have been used for over 3,000 years and are highly effective drugs to treat severe pain. Today opioids are still the most effective therapies available for many pain conditions. There have been extensive efforts to replace them without success. Due to the way conventional opioids work in the body, however, their use can lead to abuse and, unfortunately, overdose.

Why is Ensysce focusing on opioids?

Several companies have tried to improve the way opioids are delivered by formulating to release the drug slowly, referred to as abuse-deterrent formulations or ADFs. ADFs have been prescribed over the last two decades, but this approach has not solved the problem. Ensysce's technology is completely different from these formulated products and we believe it is perfectly suited to reduce the ability to abuse prescription drugs.

How does your technology work?

Our technology chemically modifies the opioid to make it inactive until swallowed. This

chemistry is difficult to overcome by manipulation in order to abuse our products. That doesn't mean it's impossible, but our clinical trials have demonstrated that it's very difficult to achieve the instant gratification, or "high", that can be achieved by manipulating ADF products.

What is unique about the Ensysce chemistry?

Our two core technology platforms are TAAP™ (Trypsin-Activated Abuse Protection) and MPAR™ (Multi-Pill Abuse Resistance). TAAP™ is designed to prevent opioid release from our products by making them inactive until swallowed and exposed to trypsin, the digestive enzyme found in the small intestine. This reduces chances for abuse by chewing, snorting or injecting since there is no trypsin exposure by these routes. The chemistry in TAAP™ also controls how fast the opioid is released, something that can't be changed by manipulation. Our first TAAP™ opioid is PF614 for severe pain. MPAR™ adds overdose protection to our TAAP™ products by adding a trypsin inhibitor to each capsule. When excess PF614-MPAR™ is consumed, the trypsin inhibitor blocks the release of opioid to avoid overdose. Together, we believe they will create a new class of "Next Generation" analgesics.

What does it mean that PF614 cannot be manipulated?

With manipulation, for example, by crushing and inhaling the current ADF opioids, they release more quickly and become more desirable to a drug abuser. With TAAP™, as I mentioned, the opioid is inactive unless it is swallowed. Even if you crush PF614, it still has to be swallowed in order for the opioid to be ‘released' from the chemical modification of TAAP™, and it releases the opioid slowly. Trying to release the active opioid by chemical manipulation is difficult. Simply put, TAAP™ makes it very difficult to alter the release of oxycodone from PF614 to use it for recreational purposes.

Why develop the Next Generation of opioids for strong pain relief, when you are trying to combat the opioid crisis?

The reason we refer to creating the Next Generation of opioids is because opioids remain important and are needed for severe pain. There are many people in chronic pain who need relief and today struggle to get access to opioid prescriptions due to restrictions placed on them. The opioids currently on the market have not solved the problem of abuse leading to addiction, and therefore some people are hesitant to take opioid products due to adverse publicity. Physicians are also reluctant to prescribe and are looking for new approaches. We believe our approach, by delivering an effective, yet potentially safer opioid product, with reduced ability for abuse, may alleviate some of that hesitancy to take or prescribe an opioid when needed.

What was accomplished in 2022?

In 2022 we initiated four clinical studies to advance our products through development and are on track to deliver against our project timelines.

- In July 2022, we announced **positive data from the PF614-102 bioequivalence (BE) study** that provided data which we believe will support the substitution of PF614 for OxyContin in the marketplace. Additionally, the BE data from this study could support

the 505(b)(2) regulatory path for clinical development of PF614, which may allow PF614 to be approved more quickly.

- In October 2022, we reported **positive topline results for the inhalation study PF614-103, a Human Abuse Potential (HAP) study** to evaluate how much recreational drug users 'like' PF614 versus oxycodone when crushed and inhaled. The primary and secondary endpoints of reduced "drug liking," and 'Take Drug Again' were met compared to inhaled crushed immediate-release oxycodone. Recreational drug users did not 'like' PF614 as a means to get high. HAP studies are intended to support abuse-deterrent labeling upon final approval of PF614, which will be very important to our ability to differentiate PF614 from other opioids.
- In October 2022, **the first subjects were dosed in an oral HAP study**, PF614-104, comparing oral administration of PF614 versus oxycodone or placebo. We completed enrollment of this study in December 2022 and expect to report the results in March 2023.
- In December 2022, we reported the outcome of the first part of the PF614-MPAR-101 study, to evaluate overdose protection with our opioid products. The data demonstrated MPAR™ has the **potential to provide overdose protection to our TAAP opioids**. We are continuing the second half of this trial in 2023, which was initiated in January 2023.

What is the next Company milestone?

As noted above in 2022 Ensysce initiated four clinical studies:

- PF614-102 for bioequivalence.
- PF614-103 evaluating nasal abuse potential.
- PF614-104 evaluating oral abuse potential.
- PF614-MPAR-101 evaluating our overdose protection platform, MPAR™.

We have reported positive results on three of these studies, and we are currently awaiting data from our oral abuse potential study, PF614-104, at the end of March.

What does the Ensysce pipeline look like?

- Our lead product, PF614 is an oxycodone product for severe pain to go head-to-head with the current ADF products on the market.
- Our MPAR™ combination products provide overdose protection to our TAAP™ portfolio. PF614-MPAR will follow the launch of PF614. These two products offer improved oral delivery of oxycodone, reduced abuse potential and, ultimately, overdose protection.
- We believe we can use our TAAP platform to improve other prescription drugs and have a number of other clinical candidates identified to be rolled out as we progress. We are exploring these opportunities.

Why Partner with Quotient? What exactly are they providing?

Quotient Sciences has a unique manufacturing accelerator associated with its clinical pharmacy and phase 1 clinical testing unit, an integrated Translational Pharmaceutics© program. Ensysce was able to take advantage of their manufacturing accelerator to perfect our MPAR™ drug product and clinically test the results, reducing significant time from our

PF614-MPAR-101 study. This is a working partnership between the two companies and the outcome has been positive for Ensysce's clinical program.

How much cash is available to support continued clinical development?

As of September 30, 2022, we reported $4.5 million in cash on hand and $5.8 million of remaining federal government grant support. Recent financing transactions include a $4.1 million public offering in December 2022 and a $3.0 million registered direct offering in February 2023. We will be reporting our updated cash position as of December 31, 2022, with our Form 10-K filing in March 2023.

Why has the share price not responded as planned?

While we do not believe it is appropriate to speculate as to why the share price performance is not stronger, despite our continued execution against our developmental plans, we want to express our disappointment. We cannot control the stock market and therefore are focused on the variables of our business that we can control. As a result, we hope that our continued diligence and execution translates to value that is ultimately reflected in our share price.

We remain committed to our mission, to helping people in pain, and to our shareholders.

Should we be worried about further dilution or the Company's cash position?

Ensysce is a pre-revenue, clinical stage biotech company. As we advance our clinical development toward commercialization, our cash burn is expected to increase. We believe we have made exceptional strides to advance our programs with limited financial resources. We are mindful of market conditions and have been thoughtful with our sources for funding, including the use of non-dilutive financing through grants from the federal government. Committed long-term shareholders are our most important constituent right now. Hence, we are constantly looking for the best opportunity for capital, while being mindful of potential shareholder dilution.

If you have additional questions that were not answered today, please submit them to ENSC@mzgroup.us.

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 (TAAP) 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 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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