January 11, 2023

Ensysce Biosciences Issues 2023 Shareholder Letter

SAN DIEGO, CA / ACCESSWIRE / January 11, 2023 /Ensysce Biosciences, Inc. ("Ensysce" or the "Company") (NASDAQ:ENSC)(OTC PINK:ENSCW), 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.

Dear Fellow Shareholders,

I want to take this opportunity to thank our shareholders for their continued support in 2022. As you all know, it has been a challenging year in the market and our management team and board, as fellow equity holders, too have been impacted by the turbulence. However, our science is strong as evidenced by the positive clinical data we reported throughout 2022, and we are continuing to develop a new approach to deliver opioid pain relief that we believe will save lives. I am pleased to summarize last year's events and recap the milestones achieved.

During 2022 we made important progress across all of our clinical development programs, accomplishing key milestones that further advance our two lead programs which address opioid abuse and overdose. We hosted a major symposium at a meeting of pain experts, receiving very encouraging feedback on our performance and underlying science. We are highly focused on positioning our technology platforms, TAAP™ (Opioid Abuse Deterrent Program) and MPAR™ (Opioid Abuse Deterrent and Overdose Protection Program) as "next generation" opioid products, providing strong efficacy with a unique goal of curbing prescription drug abuse and overdose.

Our efforts to improve prescription drug safety by reducing abuse and overdose could not come at a better time. 2022 has shown that the opioid crisis is not going away. We believe our TAAP™ opioids can provide relief to the millions of people in the U.S. suffering from chronic pain every day who are now struggling to gain access to drugs that allow them to lead a productive and somewhat pain-free life. At our foundation is our mission - a commitment to provide powerful pain relief while stemming the prescription drug abuse epidemic and the tragic loss of 100,000+ lives each year. This occurs not only from overdose of illicit opioid products, but also from suicide when patient access to opioid pain medication is removed.

We believe our mission can also have a profound impact on the economy. Today over 1 in 5 Americans suffer from pain and 35 million are experiencing severe pain, making pain the leading cause of doctor visits. The cost of treating pain in the U.S. is a staggering $560 billion each year, creating an enormous opportunity for a new class of opioid that is designed to be highly effective yet have safety built in. To provide further context, the global pain management drug market is $82.1 billion annually,* with the global opioids market at $22.4

billion annually.**

At Ensysce, our two highly novel technology platforms have been applied to a number of prescription drugs, with the goal of driving internal growth and providing external partnering opportunities. The approach is supported by over 100 patents issued in 25 countries, ensuring an opportunity to address the need for safer pain medication globally. While we are currently focused on applying our chemistry to opioids, we believe our platforms have the unique ability to be applied to many classes of prescription drugs, driving tremendous opportunity for our platforms and potential partnerships.

Turning to the year's program achievements, PF614 is our lead product in a new class of analgesia, a "Trypsin-Activated Abuse Protection" (TAAP^{TM}) oxycodone prodrug. TAAP^{TM} technology is a unique chemical modification that improves drug performance and is designed to be highly resistant to tampering and abuse. Our approach has created a "new generation" of opioid pain medication following over a decade of disappointing performance from abuse-deterrent formulation products.

This year we initiated three clinical studies to advance PF614 through development. In July we announced positive data from a bioequivalence (BE) study PF614-102 that compared PF614 to OxyContin. We believe the data will support the substitution of PF614 for OxyContin in the marketplace. We also expect that the BE data from this study will support the 505(b)(2) regulatory path for clinical development of PF614, an abbreviated pathway to FDA approval that allows reference to available safety and clinical data from an approved product.

We initiated two Human Abuse Potential (HAP) studies to evaluate how much recreational drug users ‘like' PF614 versus oxycodone when crushed and inhaled or just taken orally. These HAP studies are intended to support abuse-deterrent labeling upon final approval of PF614. The first inhalation study, PF614-103, produced positive topline results which we reported in October. PF614 demonstrated significantly reduced "drug liking," the primary endpoint, when compared to inhaled crushed immediate-release oxycodone, meaning that drug users did not like the effects from the drug to get high.

Additionally, in October, the first subjects were dosed in a second HAP study, PF614-104, comparing oral administration of PF614 versus oxycodone or placebo. We completed enrollment of this study in December 2022 and data is expected in early 2023.

Our second program, PF614-MPAR™ is a combination product designed to add overdose protection to the abuse protection of TAAP™. MPAR™ (Multi-Pill Abuse Resistance) ‘turns off' the release of the opioid in an overdose situation, providing an additional layer of protection to all of our TAAP™ pain medications. This program has been supported and funded by the National Institute on Drug Abuse (NIDA) and the federal government HEAL initiative (Helping End Addiction Long-term).

In June we received notice of award for the 4th year providing $2.8 million in funding from NIDA for our MPAR™ platform to support the final part of the ongoing clinical trial PF614-MPAR-101. This brought the total funding from NIDA to Ensysce under this grant to $10.8 million. In August we announced the partnership we formed with Quotient Sciences to undertake the product development and clinical testing of PF614-MPAR^{TM}. Quotient

Sciences is using its integrated Translational Pharmaceutics® platform to aid Ensysce in optimizing PF614-MPAR™. The goal of the work is to identify the optimal combination for PF614-MPAR™ which will allow pain relief at the prescribed dose but reduce conversion to opioid if more than the prescribed dose is consumed in an overdose situation.

In the second half of the year, in November we completed Part A of the clinical portion of overdose protection trial PF614-MPAR-101. This trial provided us with data that showed we had successfully demonstrated opioid overdose protection with PF614-MPAR™. We are expanding the study into a Part B in 2023 to provide additional support to confirm that PF614-MPAR™ provides overdose protection.

Operationally and financially, we took several important steps in 2022. A $8.0 million convertible note financing mid-year strengthened our balance sheet and provided us with necessary proceeds to continue the advancement of our lead clinical trial programs. More recently, in November, we closed on a $4.1 million public offering. However, we are aware that additional funds will be necessary to advance our two programs.

Finally, we rounded out our Board of Directors with the appointment of Lee Rauch, an experienced biotech Chief Executive Officer and Strategic Advisor. During her near 40-year career, Ms. Rauch successfully built companies ranging in focus from pre-clinical research to advanced clinical development, undertook mergers and acquisitions and secured financing for both public and private biotech companies.

Looking ahead, we are highly focused on the continued execution of our clinical development timeline. We expect additional clinical data from our oral HAP study, PF614-104, to be reported in the first quarter of 2023. We will continue our development of PF614-MPAR™, with data expected in the second half of the year. We are also planning regulatory discussions with the FDA to aid our future clinical development plans, and we are aiming to bring PF614 into additional clinical studies by the year end.

Taken together, we are incredibly proud of our accomplishments in the past year, achieving all our expected milestones and progressing our unique goal to address the prescription drug abuse epidemic in the U.S., as well as globally. 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 biotech company using its proprietary technology platforms to develop safer prescription drugs. Leveraging TAAP™ and MPAR™, 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.

Definitions

'TAAP': trypsin activated abuse protection - designed to protect against prescription drug abuse.

‘MPAR': multi-pill abuse resistance - designed to protect against abuse and accidental overdose.

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.

* https://www.grandviewresearch.com/industry-analysis/opioids-market

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