UNITED STATES SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 5, 2022 (May 5, 2022)

Ensysce Biosciences, Inc.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization) 001-38306 (Commission File Number) 82-2755287 (I.R.S. Employer Identification Number)

7946 Ivanhoe Avenue, Suite 201 La Jolla, California (Address of principal executive offices)

92037 (Zip Code)

(858) 263-4196

Registrant's telephone number, including area code

N/A

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation to the registrant under any of the following provisions:

□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

□ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

□ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

□ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered		
Common Stock, par value \$0.0001 per	ENSC	The Nasdaq Stock Market LLC		
share				
Warrants to purchase one share of	ENSCW	OTC Pink Open Market		
Common Stock				

Emerging growth company \boxtimes

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01 Regulation FD Disclosure.

On May 5, 2022, Ensysce Biosciences, Inc. issued a press release announcing new clinical trial results, a copy of which is furnished as Exhibit 99.1 hereto.

The information in Exhibit 99.1 attached hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, or incorporated by reference into any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in any such filing.

Item 8.01 Other Events.

On May 5, 2022, Ensysce Biosciences, Inc. delivered a presentation entitled "The Next Generation of Opioids?" at the 22nd Annual Pain Therapeutics Conference of SMi Group being held in London, England. A copy of the presentation is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

Exhibit No. Description

99.1	Press Release Announcing New Clinical Results, dated May 5, 2022
99.2	Presentation about Opioids delivered on May 5, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

2

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: May 5, 2022

Ensysce Biosciences, Inc.

By:	/s/ Lynn Kirkpatrick
Name:	Dr. Lynn Kirkpatrick
Title:	President and Chief Executive Officer

Ensysce Biosciences Announces New Clinical Results from Trials PF614-102 and PF614-MPAR-101

~ Results confirmed the safety and longer-lasting profile of PF614 versus OxyContin and provides first human data showing the potential for overdose protection with MPAR~

~ Announces corporate update call timing ~

San Diego, Ca., May 5, 2022, Ensysce Biosciences, Inc. ("Ensysce" or the "Company") (NASDAQ: ENSC, OTC: ENSCW), a clinical-stage biotech company applying transformative chemistry to improve prescription drug safety and performance with a current focus on reducing abuse and overdose, today presented results from the clinical trials PF614-102 and PF614-MPAR-101 at the SMi Pain Therapeutics meeting in London, UK.

PF614-102

The multi-ascending dose study (MAD) study examined 3 dose levels of PF614, a novel TAAP prodrug of oxycodone and the Company's lead candidate in Phase 2 development for the treatment moderate to severe pain. The MAD study evaluated PF614 delivered as an oral solution or as 100 mg capsules. The healthy volunteer study was designed to evaluate the safety and pharmacokinetics of five days of treatment with twice daily doses of PF614 to equivalent doses of OxyContin, the extended-release abuse deterrent formulation of oxycodone. The results of the study show the longer-lasting half-life of PF614 versus OxyContin as seen in the prior Phase 1 single-ascending dose study of PF614 oral solution versus OxyContin. The pharmacokinetic data demonstrated that PF614 has a delayed onset and extended activity after delivery, with a time to maximal drug concentration of 5.8 hour similar to Oxycontin's 4.5 hour. A distinguishing feature of PF614 is its terminal half-life which on Day 5 ranged from 13.75 to 28.4 hour as compared to 4.5 to 7.8 hour for OxyContin. We believe this data confirms the findings from our Phase 1 study that demonstrate PF614 should provide true twice daily dosing.

The safety data for the study also showed that PF614 performed similarly to OxyContin with no test article serious adverse events recorded. Treatment emergent adverse events (TEAE) were limited and opioid related.

The second part of the PF614-102 study, the bioequivalence (BE) arm, continues to be analyzed and as reported previously it is anticipated that this BE data will be available at the end of the second quarter of 2022.

PF614-MPAR-101

PF614-MPAR-101 overdose protection study examined PF614 administered orally alone or in combination with the trypsin inhibitor nafamostat (MPAR) to healthy volunteers. This data demonstrated how the combination product PF614-MPAR could reduce the trypsin activation and reduce the release of oxycodone in a simulated overdose situation. It also demonstrated the PF614 in the systemic circulation (simulated injection) did not convert to oxycodone. We believe this is the first step to identifying the first MPAR drug product that will be marketed in the coming years.

Dr. William Schmidt, Senior VP of Clinical Development, commented, "The results of the 102 study are in-line with our expectations, and we are eager to continue making progress towards bringing our lead 'next generation' opioid to market. The results from this clinical trial represent a critical milestone for Ensysce confirming our previous findings that were highly encouraging, and a significant step towards our mission of providing safer, effective options for doctors and patients. We were also highly enthused by the first MPAR data as it is confirmation that our approach for overdose protection is a possibility – not just a hope."

Dr. Lynn Kirkpatrick, Chief Executive Officer, added, "We believe with these study results we have added to an already strong foundation of data supporting our novel approach to delivering pain relief, and begin to realize our stated mission – providing abuse and overdose protection where needed. It is exciting to see the first human data for MPAR, and as the study progresses, we feel our solidification of a final drug product is possible. We entered 2022 with clear progress against our clinical stage pipeline and this data further positions the Company for continued successes. We look forward to reviewing the data in further detail and sharing with all Ensysce' constituents in the coming weeks, ultimately this is a step towards value creation for our shareholders."

Corporate Update Call

Management will host a corporate update conference call on Tuesday, May 17, 2022, at 11:00am ET to provide a corporate update and review the recently discussed results from Clinical Trail PF614-102. The call will conclude with Q&A from participants. An accompanying presentation will be posted prior to the call to the Company's investor relations website.

Date: Tuesday, May 17, 2022 Time: 11:00am ET U.S. Dial-in: 1-877-407-0792 International Dial-in: 1-201-689-8263 Conference ID: 13729812 Webcast: <u>ENSC Corporate Update Call</u>

Please dial in at least 10 minutes before the start of the call to ensure timely participation. A playback of the call will be available through Tuesday, June 14, 2022. To listen, call 1-844-512-2921 within the United States and Canada or 1-412-317-6671 when calling internationally. Please use the replay pin number 13729812.

About Ensysce Biosciences

Ensysce Biosciences, based in San Diego, CA is a clinical-stage biotech company using its two novel proprietary technology platforms to develop safer prescription drugs. Leveraging its Trypsin-Activated Abuse Protection (TAAP) and Multi-Pill Abuse Resistance (MPAR^M) platforms, the Company is developing next-generation, tamper-proof opioids that prevent both drug abuse and overdoses. Ensysce's products are anticipated to provide safer options to treat severe pain and assist in preventing deaths caused by opioid abuse, reducing the human and economic costs. The platforms are covered by an extensive worldwide intellectual property portfolio encompassing a wide array of prescription drugs. For more information, please visit <u>www.ensysce.com</u>.

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," 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.

Ensysce Biosciences Company Contact:

Lynn Kirkpatrick, Ph.D. Chief Executive Officer (858) 263-4196

Ensysce Biosciences Investor Relations Contact: Shannon Devine

MZ North America Main: 203-741-8811 <u>ENSC@mzgroup.us</u>

Source: Ensysce Biosciences Inc.

Exhibit 99.2

The next generation of opioids?

NASDAQ: ENSC

Lynn Kirkpatrick, PhD $Ensysce^{\rm TM}$

SMi Presentation May 2022

Disclaimer

Ensysce's PF614 and nafamostat are currently in clinical and pre-clinical trials, involving both the TAAP platform and MPAR platform. Accordingly, PF614 and nafamostat have the risks and uncertainties inherent in any drug in trial-phase, which include, but are not limited to, a failure to show sufficient efficacy to obtain FDA approval, the risk that clinical trials may not confirm any safety, potency or other product characteristics described or assumed herein and the possibility that presently unknown safety risks may occur. The statements made concerning PF614, nafamostat, TAAP and MPAR are subject to the complete set of risks set forth in the Risk Factors disclosure found in the Company's most recent Quarterly Report on Form 10-K filed with the Securities and Exchange Commission on March 31, 2022.

Forward Looking Statements

Statements contained in this presentation 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," 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 based on estimates and assumptions 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 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. 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, futu

Analgesic care in 2022 – The next generation of opioids?





Analgesic care in 2022 – the next generation.

- Chronic and severe pain
- The opioid crisis
- 2 potential new classes of agents: TAAP™ and MPAR™
- PF614 data: the first TAAP opioid

Analgesic care in 2022 – the next generation.

Chronic and severe pain

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Analgesic care in 2022 – how are we doing?!









Analgesia 2022 – More pain More abuse More deaths





IN THE USA:

Chronic Pain – 50 million Opioid Rx – 191 million Cost – \$560 billion Deaths per day - 222



THE SCALE OF THE ISSUE - IN PERSPECTIVE



Pain is Up Painkillers are Down



Ref: IQVIA 2021

10

OPIOID USE/ABUSE A Global ISSUE

NOT JUST A USA PROBLEM



THE PATHOLOGY OF NOCICEPTION IS COMPLEX. OPIOIDS ARE STILL CRITICAL.





THE "CHRONIFICATION" OF PAIN



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13

PAIN IMPACTS MANY AREAS



Ref: M Cheatle.

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A COMPLEX INTERPLAY



Ref: L Webster

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15

PAIN IMPACT - how bad is it!



How Treatment for Chronic Pain Can Help Reduce Suicide Risk

Reports show that 50 percent of chronic pain patients consider suicide to escape their physical pain. Treatments can help people choose life.

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Mental Health

Chronic Pain and Suicide: Signs You or a Loved One Needs Help, and How to Get It

PUBLISHED 12/10/20 BY SUSAN JARA

People with chronic pain from arthritis and other conditions may be at an increased risk of having suicidal thoughts and behavior. Learn more about this link and when and how to get help.

Outlawing is not the answer.



Ref: Ballotpedia

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PAIN IMPACT - ~ half of Americans worried about Rx drug addiction!

Which of the following would you describe as a major health problem in the U.S.? (multiple responses allowed)

Cancer	59%
Heart disease	52%
Diabetes	52%
Drug addiction	(47%)
Depression	42%
Alcoholism	37%
Alzheimer's disease	34%
Chronic pain	(18%)
Parkinson's disease	15%
Not sure	15%

urce: A Research!America poll of U.S. adults conducts In partnership with Zogby Analytics in March 2013.



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Abuse and addiction – multi-factorial



Ref: NIDA/ N Volkow.

Abuse and stress



Ref: L Webster

When liking becomes dangerous



Opioid response by individual



Opioid response by individual



Spot the abuser!?



Methods of opioid abuse

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Over-consuming

Crushing and drinking/ chewing

Crushing and snorting

Crushing and injecting

Combining with other drugs





ABUSE QUOTIENT - AQ

The attractiveness of a drug for abuse, the "abuse potential" of a drug increases as the value of the AQ increases



Extended release formulations (Abuse Deterrent Formulations; ADF) were developed to reduce AQ.



https://www.americanpharmaceuticalreview.com/Featured-Articles/182873-Innovative-Abuse-Deterrent-Opioid-Medications/ 2016

27

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ADFs: can all be broken

OxyContin: Intact vs manipulated



Words are important

Deterrent vs protectant

Deterrent: a thing that discourages or is intended to discourage someone from doing something.

"cameras are a major **deterrent to** crime".

Protectant: a substance that provides protection, e.g. against disease or ultraviolet radiation.



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The WHO Stepladder



Figure 1. A modern rendition of the original 1986 WHO pain ladder with 3 steps. Patients begin at the first rung and then based on pain intensity progress, rung by rung, up the ladder as pain worsens.

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31

HIGH RISK VS IDEAL OPIOID - 1977!





THE IDEAL OPIOID







IMAGINE AN OPIOID....

- > Impossible to alter PK profile
- > Disliked by, unattractive to, abusers
- > Yet highly effective in relieving severe pain

TAAPTM

TRYPSIN-ACTIVATED ABUSE PROTECTION

TAAP - 2-step verification mechanism to improve oral delivery, with release of active ingredient only in the small intestine with exposure to trypsin

35

IMPROVED TAMPER-PROOF DELIVERY PLATFORM

TAAP chemical modification

TAAP is only activated by trypsin,

TAAP not altered by manipulation.,

TAAP Two-Step Release Process

Step 1: Swallow drug

 Following ingestion, the drug is activated only after exposure to trypsin, a digestive enzyme that is active only in the small intestine.

Step 2: Timing chemically controlled

 A second step is required for full release of the active drug. The chemistry controls the rate of release, thereby making the Ensysce 2-step approach superior to other prodrug products.

Protects from:

Chewing Crushing and snorting Crushing and injecting





ANTI-OVERDOSE

PLATFORM

SMART

MULTI-PILL ABUSE RESISTANT

MPAR[™] is a smart anti-overdose platform that is designed to protect patients from overdosing when it is combined with TAAP opioids.

MPAR[™] is only triggered by an overdose.

MPAR[™] inhibits trypsin activation step

Using a prescribed dose gives pain relief



PF614-MPAR[™]

Blocks activation of PF614 and Oxycodone Release if Overdosed



TAAP + MPAR[™]: PRECLINICAL DATA

- Combination product of PF614 with an ultrapotent trypsin inhibitor, nafamostat
- Taken at prescribed doses there is no change in oxycodone release from PF614
- With increasing dose unit administration, increasing amounts of nafamostat blocks trypsin activation of PF614 and prevents opioid overdose
- PF614-MPAR™ entered Phase 1 clinical trial in December 2021
- Data expected H2 2022

39

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PF614: TAAP delayed release oxycodone prodrug AQ cannot be altered

Pre-clinical Blood Concentration of Opioid Vs. Time (dog)

- Unlike OxyContin, Ensysce's opioid PF614, even when crushed, has no altered release kinetics: AQ
- In Phase I studies have been able to **dose match** PF614 to marketed OxyContin dose units.



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PF614 FEATURES

TAAP chemical modification protects from manipulation and abuse

Cannot snort for joy – no trypsin in the nasal passage

Cannot inject for joy – no trypsin in the blood stream

Cannot crush to make work faster

Added protection for OD (MPAR)

PF614-101 Designed for Safer, More Efficient & Longer-Lasting Pain Relief



PF614-101 Phase 1

 PF614 provides slow onset with maximum blood concentration reached at 4 to 6 hr after swallowing;

Good Safety Profile

 PF614 has shown no unexpected adverse events in Phase I

Efficient conversion to oxycodone

• PF614 is effectively converted to Oxycodone after it is swallowed providing **dose equivalency in a** ratio of 2.5:1 PR614:OxyContin.

PF614 LONGER LASTING COMPARED TO OXYCONTIN



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43

PF614-101Phase 1

- Ensysce's opioid PF614's half-life is 12.7 hours, versus OxyContin's 7.6 hours
- As a result, Ensysce's PF614 is more convenient for the patient, since PF614 needs to be taken only twice-a-day, in contrast to OxyContin (which some patients end up taking three times per day)

NEW DATA: PF614-102 MAD/BE

Multi-Ascending Dose Study

A Phase 1b, Randomized, 2-Part Single-Center Study to Evaluate the Pharmacokinetics and Safety of Multiple-Ascending Oral Doses of PF614 and the Food Effect and Bioavailability/Bioequivalence

of Single Oral Doses of PF614 Relative to OxyContin in Healthy Adult Subjects

The primary objectives of the study are:

To assess the safety, tolerability and pharmacokinetics of intact prodrug, PF614, as well as oxycodone,

Administration

Oral twice daily (BID) doses for 5 days to groups of healthy adult subjects, naltrexone blocked

3 Ascending Dose Cohorts

PF614	50 mg	n = 6	OxyContin	20 mg	n = 2
PF614	100 mg	n = 6	OxyContin	40 mg	n = 2
PF614	200 mg	n = 6	OxyContin	80 mg	n = 2

NEW DATA: PF614-102 MAD

PF614 and OxyContin produce identical Adverse Events

Table of Adverse Events

	PF614	OxyContin	PF614	OxyContin	PF614	OxyContin
	50 mg	20 mg	100 mg	40 mg	200 mg	80 mg
	ⁿ⁼⁶	n=2	ⁿ⁼⁶	n=2	ⁿ⁼⁶	n=2
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total subjects with at least 1 TFAF*	2 (33.3)	1 (50.0)	1 (16.7)	1 (50.0)	6 (100.0)	2 (100.0)

* Treatment Emergent Adverse Events: Vertigo, Photophobia, Nausea, Constipation, Diarrhea, Vomiting Urinary Tract infection, Tooth fracture, Decreased appetite, Dizziness, Headache, Depressed mood, Rhinorrhoea, Dermatitis

46

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45

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NEW DATA: PF614-102 MAD PK of oxycodone release from PF614 or OxyContin





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NEW DATA: PF614-102 MAD

Oxycodone from OxyContin or PF614





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NEW DATA: PF614-102 MAD Oxycodone from OxyContin or PF614 AUC_{0-t}



49

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NEW DATA: PF614-102 MAD Oxycodone from OxyContin or PF614 AUC_{0-t}



NEW DATA: PF614-MPAR-101 PF614 (25 mg) with and without nafamostat (10 mg)





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Analgesic care in 2022 – The next generation of opioids?



- BASIS TO BELIEVE WE COULD BE THE NEXT GENERATION OF OPIOIDS.
- TAAP and MPAR EMPLOY SOPHISTICATED CHEMISTRY.
- DATA STRONG FOR TAAP AND MPAR AS PF614 ENTERS PHASE 3.
- MPAR OVERDOSE PROTECTION DEMONSTRATED IN HUMANS.
- WIDESPREAD SUPPORT WITH FAST TRACK AND NIH/NIDA.
- TAAP AND MPAR: POTENTIAL TO SAVE MANY LIVES.

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Thank you

Lynn Kirkpatrick, PhD www.ensysce.com