EnsysceTM

This prospectus supplement amends and supplements the prospectus dated September 27, 2021, as supplemented or amended from time to time (the '*Prospectus*''), which forms a part of our Registration Statement on Form S-1 (No. 333-258609). This prospectus supplement is being filed to update and supplement the information in the Prospectus with the information contained in our Current Report on Form 8-K, filed with the U.S. Securities and Exchange Commission on October 27, 2022 (the "*Current Report*"). Accordingly, we have attached the Current Report to this prospectus supplement.

The Prospectus and this prospectus supplement relate to the issuance by us and the resale by the selling security holders named in the Prospectus (the Selling Securityholders") of up to an aggregate of 27,132,398 shares of our common stock, par value \$0.0001 per share ("common stock"), which consists of (i) up to 500,000 shares of common stock that are issuable upon the exercise of 500,000 warrants issued to DelMorgan Group LLC ("DelMorgan") under the terms of the Email Agreement, dated January 31, 2021, among Ensysce Biosciences, Inc. (the "Company") and DelMorgan, as amended by the First Amendment to the Email Agreement, dated June 7, 2021 (the "Email Agreement"), (ii) up to an aggregate of approximately 10,000,000 shares of common stock that are issuable upon the exercise of 10,000,000 warrants (the Public Warrants") issued in connection with the initial public offering of our predecessor company, Leisure Acquisition Corp., a Delaware corporation ("LACQ"), (the "LACQ IPO"), (iii) up to an aggregate of 6,325,000 shares of common stock that are issuable upon the exercise of 6,325,000 warrants issued in connection with a private placement that closed simultaneously with the consummation of the LACQ IPO (the "Private Placement Warrants"), (iv) up to an aggregate of 1,000,001 shares of common stock that are issuable upon the exercise of 1,000,001 warrants issued in exchange for outstanding loans under the Expense Advancement Agreement dated December 1, 2017 among LACQ, Hydra Management, LLC ("Hydra"), Matthews Lane Capital Partners LLC ("MLCP" and together with Hydra, the "Sponsors"), and HG Vora Capital Management LLC on behalf of one or more funds or accounts managed by it (the "Strategic Investor") (the "Expense Advancement Agreement"), (v) up to an aggregate of 566,288 shares of common stock that are issuable upon exercise of 566,288 warrants issued in exchange for previously outstanding loans under the Expense Advancement Agreement dated December 5, 2019 between LACQ and Gateway Holdings Limited, as amended (the "GTWY Expense Advancement Agreement") (collectively with the warrants described in (iv) herein, the "other private warrants"), (vi) up to an aggregate of 510,001 shares of common stock that are issuable upon exercise of 510,001 warrants issued at the closing of the business combination (as defined below) in exchange for outstanding loans under the Expense Advancement Agreement, (vii) up to 1,106,108 shares of common stock that are issuable upon exercise of 1,106,108 warrants issued at the closing of the business combination (as defined below) in connection with the GEM Agreement (as defined below) (the "GEM Warrants"), (viii) 125,000 shares of common stock issuable in satisfaction of \$2,000,000 of deferred underwriting fees payable to the underwriters, (ix) 500,000 shares of common stock issuable to DelMorgan under the terms of the Email Agreement, (x) 5,000,000 shares of common stock purchased by the Sponsors and Strategic Investor in a private placement prior to the LACQ IPO (the "founder shares"), (xi) up to an aggregate of 500,000 shares of common stock issuable to David J. Kovacs and Mercury FundingCo, LLC (David Tanzer, Managing Member) (together, the "Consultants"), and (xii) up to 1,000,000 shares of common stock that are issuable upon the exercise of 1,000,000 warrants issued to the Consultants.

On June 30, 2021, we consummated the transactions contemplated by that certain Agreement and Plan of Merger, dated as of January 31, 2021 (the *Merger Agreement*"), by and among the Company, LACQ and EB Merger Sub, Inc., a Delaware corporation and wholly-owned subsidiary of LACQ ("*Merger Sub*"), with the Company surviving such merger as a wholly-owned subsidiary of LACQ (the "*Merger*"). The Merger, together with the other transactions contemplated by the Merger Agreement and the related agreements, are referred to herein as the "*Transactions*." In connection with the consummation of the Transactions, LACQ changed its name to "Ensysce Biosciences, Inc."

Our registration of the securities covered by the Prospectus and this prospectus supplement does not mean that either we or the Selling Securityholders will issue, offer or sell, as applicable, any of the securities hereby registered. The Selling Securityholders may offer, sell, or distribute all or a portion of the securities hereby registered publicly or through private transactions at prevailing market prices or at negotiated prices. We will not receive any of the proceeds from such sales of our common stock or warrants by the Selling Securityholders pursuant to the Prospectus and this prospectus supplement, except with respect to amounts received by us upon exercise of the Warrants to the extent such Warrants are exercised for cash. We will bear all costs, expenses and fees in connection with the registration of these securities, including with regard to compliance with state securityholders are subject to lock-up arrangements. See "*Plan of Distribution*" beginning on page 128 of the Prospectus.

You should read the Prospectus, this prospectus supplement and any additional prospectus supplement or amendment carefully before you invest in our securities.

Our common stock is listed on the Nasdaq under the symbol "ENSC" and our Public Warrants are listed on the OTC Pink Open Market under the symbol "ENSCW." On October 26, 2022, the closing sale price of our common stock as reported on Nasdaq was \$0.1983 and the last sale price on that date for our Public Warrants as reported on the OTC Pink Open Market was \$0.025.

This prospectus supplement updates and supplements the information in the Prospectus and is not complete without, and may not be delivered or utilized except in combination with, the Prospectus, including any amendments or supplements thereto. This prospectus supplement should be read in conjunction with the Prospectus and if there is any inconsistency between the information in the Prospectus and this prospectus supplement, you should rely on the information in this prospectus supplement.

We are an "emerging growth company" as defined in Section 2(a) of the Securities Act of 1933, as amended, and, as such, have elected to comply with certain reduced disclosure and regulatory requirements.

Our business and investing in our securities involves a high degree of risk. See "Risk Factors" beginning on page 9 of the Prospectus and in the other documents that are incorporated by reference in the Prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if the Prospectus or this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is October 27, 2022.

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): October 27, 2022 (October 27, 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 share	ENSC	The Nasdaq Stock Market LLC
Warrants to purchase one share of Common Stock	ENSCW	OTC Pink Open Market

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 5.03 Amendments to Articles of Incorporation or Bylaws; Change in Fiscal Year.

On October 27, 2022, Ensysce Biosciences, Inc. (the "Company" or "we" or "our") filed an amendment to the Company's Third Amended and Restated Certificate of Incorporation (as amended to date, the "Certificate of Incorporation"), with the Secretary of State of the State of Delaware to effect a one-for-twenty (1-for-20) reverse stock split (the "Reverse Stock Split") of our common stock, par value \$0.0001 (the "Common Stock"). The Reverse Stock Split will be effective as of 12:01 am on October 28, 2022 (the "Effective Time").

As previously described in detail in our definitive proxy statement filed with the Securities and Exchange Commission on July 29, 2022, the Company held a special meeting of stockholders on September 8, 2022, at which meeting the stockholders approved, among other things, amendment of our Certificate of Incorporation to effect a reverse stock split of our Common Stock at a ratio of not less than 1-for-5 and not more than 1-for-20 and authorized our board of directors to effect a reverse stock split with the exact ratio to be determined in the Board's discretion. Our Board thereafter selected the 1-for-20 reverse stock split ratio and authorized the implementation of the Reverse Stock Split.

As a result of the Reverse Stock Split, at the Effective Time, every twenty (20) shares of our pre-Reverse Stock Split Common Stock will be combined and reclassified into one (1) share of our Common Stock. Our post-Reverse Stock Split Common Stock will begin trading on October 28, 2022 with a new CUSIP number of 293602207. The Reverse Stock Split does not affect any stockholder's ownership percentage of the Common Stock and does not change our authorized number of shares, alter the par value of the Common Stock or modify any voting rights or other terms of the Common Stock

At the Effective Time, the exercise prices and the number of shares of Common Stock issuable upon exercise of the Company's warrants will automatically be adjusted, in accordance with their terms, in proportion to the Reverse Stock Split ratio.

As of the Effective Time, proportionate adjustments will be made to the per share exercise price and/or the number of shares issuable upon the exercise or vesting of all stock options and restricted stock unit awards issued by the Company and outstanding immediately prior to the effective time of the Reverse Stock Split, which will result in a

proportionate decrease in the number of shares of Common Stock reserved for issuance upon exercise or vesting of such stock options and restricted stock unit awards, and a proportionate increase in the exercise price of all such stock options and restricted stock unit awards. Concurrently, the number of shares reserved for issuance under the Company's Amended and Restated 2021 Omnibus Incentive Plan immediately prior to the effective time of the Reverse Stock Split will be reduced proportionately.

No fractional shares will be issued in connection with the Reverse Stock Split. In lieu of the issuance of fractional shares, the Company will round up any fractional shares resulting from the Reverse Stock Split to the nearest whole share.

Our transfer agent, Continental Stock Transfer & Trust Company, is acting as agent for the Reverse Stock Split. Stockholders who hold their shares in brokerage accounts or in "street name" will not be required to take any action to effect the exchange of their shares.

A copy of the Certificate of Amendment of our Certificate of Incorporation is filed as Exhibit 3.1 to this Current Report on Form 8-K and is incorporated herein by reference.

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Item 9.01. Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
3.1	Certificate of Second Amendment to the Third Amended and Restated Certificate of Incorporation.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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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: October 27, 2022

Ensysce Biosciences, Inc.

 By:
 /s/ Lynn Kirkpatrick

 Name:
 Dr. Lynn Kirkpatrick

 Title:
 President and Chief Executive Officer

Exhibit 3.1

CERTIFICATE OF SECOND AMENDMENT OF THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION OF ENSYSCE BIOSCIENCES, INC.

Ensysce Biosciences, Inc., a corporation organized and existing under the General Corporation Law (the "*DGCL*") of the State of Delaware (the "*Corporation*"), DOES HEREBY CERTIFY:

FIRST. The name of the corporation is Ensysce Biosciences, Inc. The Corporation was incorporated by the filing of its original Certificate of Incorporation, under the name GLL Acquisition Corp., with the Secretary of State of the State of Delaware on September 11, 2017 and was amended by the Certificate of Amendment, which was filed with the Secretary of State of Delaware on September 11, 2017.

SECOND. A first amended and restated certificate of incorporation was filed with the Secretary of State of the State of Delaware on November 30, 2017. A second amended and restated certificate of incorporation was filed with the Secretary of State of Delaware on December 1, 2017 (the "*Second Amended and Restated Certificate*"). A first amendment to the Second Amended and Restated Certificate was filed with the Secretary of State of Delaware on December 5, 2019. A second amendment to the Second Amended and Restated Certificate was filed with the Secretary of State of Delaware on March 26, 2020. A third amendment to the Second Amended and Restated Certificate was filed with the Secretary of State of Delaware on March 26, 2020. A third amendment to the Second Amended and Restated Certificate was filed with the Secretary of State of Delaware on November 30, 2020. A third amendment to the Second Amended and Restated Certificate was filed with the Secretary of State of Delaware on Second Amended and Restated Certificate was filed with the Secretary of State of Delaware on Second Amended and Restated Certificate was filed with the Secretary of State of Delaware on Second Amended and Restated Certificate was filed with the Secretary of State of Delaware on June 30, 2020. A third amendment to the Second Amended and Restated Certificate was filed with the Secretary of State of Delaware on June 30, 2021 (the "*Certificate*"). An amendment to the Certificate was filed with the Secretary of State of Delaware on September 9, 2022.

THIRD. The terms and provisions of this Certificate of Amendment have been duly adopted in accordance with Section 242 of the DGCL. The following two paragraphs are hereby added to precede the first paragraph of Article IV of the Certificate:

"Contingent and effective as of 12:01am on October 28, 2022 (the "*Effective Time*"), each twenty (20) shares of the Company's Common Stock, par value \$0.0001 per share (the "*Common Stock*"), issued and outstanding prior to the Effective Time shall, automatically and without any action on the part of the respective holders thereof, be combined and converted into one (1) share of Common Stock, par value \$0.0001 per share, of the Company (the "*Reverse Split*"). No fractional share shall be issued in connection with the foregoing combination of the shares pursuant to the Reverse Split. In lieu of the issuance of fractional shares, the Company will round up any fractional shares resulting from the Reverse Split to the nearest whole share.

The Reverse Split shall occur automatically without any further action by the holders of Common Stock, and whether or not the certificates representing such shares have been surrendered to the Company; provided, however, that the Company shall not be obligated to issue certificates evidencing the shares of Common Stock issuable as a result of the Reverse Split unless the existing certificates evidencing the applicable shares of stock prior to the Reverse Split are either delivered to the Company, or the holder notifies the Company that such certificates have been lost, stolen or destroyed, and executes an agreement satisfactory to the Company to indemnify the Company from any loss incurred by it in connection with such certificates."

FOURTH. This Certificate of Second Amendment of the Third Amended and Restated Certificate of Incorporation so adopted (i) shall be effective as of 12:01am on October 28, 2022, (ii) reads in full as set forth above and (iii) is hereby incorporated into the Third Amended and Restated Certificate of

Incorporation by this reference. All other provisions of the Third Amended and Restated Certificate of Incorporation, as amended, remain in full force and effect.

IN WITNESS WHEREOF, the undersigned has caused this Certificate of Second Amendment to be executed by the duly authorized officer below as of this 26th day of October 2022.