

Prospectus Supplement No. 5
(To Prospectus dated June 24, 2022)

Comera Life Sciences Holdings, Inc.

1,946,846 Warrants to Purchase Common Stock

**15,093,712 Shares of Common Stock Including
1,946,846 Shares of Common Stock issuable upon the
exercise of Warrants and 342,755 Shares of Common Stock
issuable upon conversion of the
Series A Convertible Perpetual
Preferred Stock
offered by Selling Securityholders**

This prospectus supplement no. 5 (this “Prospectus Supplement”) updates, amends and supplements the prospectus dated June 24, 2022 (as amended or supplemented from time to time, the “Prospectus”) which forms a part of the Registration Statement on Form S-1 (Registration Statement No. 333-264686) filed by Comera Life Sciences Holdings, Inc. (“Holdco”). Capitalized terms used in this Prospectus Supplement and not otherwise defined herein have the meanings specified in the Prospectus.

This Prospectus Supplement is being filed to update, amend and supplement the information included or incorporated by reference in the Prospectus with the information contained in our Current Report on Form 8-K, filed with the Securities and Exchange Commission (the “SEC”) on November 18, 2022 (the “Current Report”). Accordingly, we have attached the Current Report to this Prospectus Supplement.

This Prospectus Supplement 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 any amendments or supplements thereto. 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.

The Holdco Common Stock is listed on The Nasdaq Capital Market (“Nasdaq”) under the symbol “CMRA” and the Holdco Warrants are listed on Nasdaq under the symbol “CMRAW”. On November 22, 2022, the closing sale price of the Holdco Common Stock as reported on Nasdaq was \$1.33 per share, and the closing sale price of the Holdco Warrants as reported on Nasdaq was \$0.0576 per warrant.

Investing in our securities involves a high degree of risk. Before buying any securities, you should carefully read the discussion of the risks of investing in our securities in “Risk Factors” beginning on page 14 of the Prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of the securities to be issued under the Prospectus or passed upon the accuracy or adequacy of the Prospectus. Any representation to the contrary is a criminal offense.

The date of this Prospectus Supplement is November 23, 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): November 18, 2022

Comera Life Sciences Holdings, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

1-41403
(Commission
File Number)

87-4706968
(IRS Employer
Identification No.)

**12 Gill Street
Suite 4650
Woburn, Massachusetts**
(Address of principal executive offices)

01801
(Zip Code)

Registrant's telephone number, including area code: (617) 871-2101

Not Applicable
(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 of 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	CMRA	The Nasdaq Stock Market LLC
Warrants	CMRAW	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

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 3.01. Notice of Delisting or Failure to Satisfy Continued Listing Rule or Standard; Transfer of Listing.

On November 18, 2022, Comera Life Sciences Holdings, Inc. (the “Company”) received a letter from the listing qualifications department staff of The Nasdaq Stock Market (“Nasdaq”) notifying the Company that for the last 30 consecutive business days, the Company’s minimum Market Value of Listed Securities (“MVLS”) was below the minimum of \$35 million required for continued listing on the Nasdaq Capital Market pursuant to Nasdaq listing rule 5550(b)(2).

The notice has no immediate effect on the listing of the Company’s common stock, and the Company’s common stock continues to trade on the Nasdaq Capital Market under the symbol “CMRA.”

In accordance with Nasdaq listing rule 5810(c)(3)(C), the Company has 180 calendar days, or until May 17, 2023, to regain compliance. The notice states that to regain compliance, the Company’s MVLS must close at \$35 million or more for a minimum of ten consecutive business days (or such longer period of time as the Nasdaq staff may require in some circumstances, but generally not more than 20 consecutive business days) during the compliance period ending May 17, 2023. The Company may also regain compliance by meeting the continued listing standard of a minimum stockholders’ equity of at least \$2.5 million.

If the Company does not regain compliance by May 17, 2023, Nasdaq staff will provide written notice to the Company that its securities are subject to delisting. At that time, the Company may appeal any such delisting determination to a Nasdaq hearings panel.

The Company intends to actively monitor the Company’s MVLS between now and May 17, 2023, and may, if appropriate, evaluate available options to resolve the deficiency and regain compliance with the MVLS rule. While the Company is exercising diligent efforts to maintain the listing of its common stock on Nasdaq, there can be no assurance that the Company will be able to regain or maintain compliance with Nasdaq listing standards.

SIGNATURE

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: November 23, 2022

COMERA LIFE SCIENCES HOLDINGS, INC.

By: /s/ Jeffrey S. Hackman

Name: Jeffrey S. Hackman

Title: Chairman, President and Chief Executive Officer