Prospectus Supplement No. 2 (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. 2 (this "<u>Prospectus Supplement</u>") updates, amends and supplements the prospectus dated June 24, 2022 (as amended or supplemented from time to time, the "<u>Prospectus</u>") which forms a part of the Registration Statement on Form S-1 (Registration Statement No. 333-264686) filed by Comera Life Sciences Holdings, Inc. ("<u>Holdco</u>"). 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 a Current Report on Form 8-K, filed with the Securities and Exchange Commission (the "SEC") on August 31, 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 August 30, 2022, the closing sale price of the Holdco Common Stock as reported on Nasdaq was \$1.80 per share, and the closing sale price of the Holdco Warrants as reported on Nasdaq was \$0.0712 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 August 31, 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): August 31, 2022

	Comera Lif	e Sciences Hold	lings, Inc.
		ne of registrant as specified in its cha	O 1
	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		01801
	(Address of principal executive offices)		(Zip Code)
		one number, including area code: (6 Not applicable ne or former address, if changed since last re	,
	eck the appropriate box below if the Form 8-K filing is in owing provisions:	tended to simultaneously satisfy the fi	ling obligation of the registrant under any of the
	Written communications pursuant to Rule 425 under the	ne 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))		
Sec	urities 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 Warrants	CMRA CMRAW	The Nasdaq Stock Market LLC The Nasdaq Stock Market LLC
	icate by check mark whether the registrant is an emerging pter) or Rule 12b-2 of the Securities Exchange Act of 19		405 of the Securities Act of 1933 (§230.405 of this
Em	erging growth company $oxtimes$		
	n emerging growth company, indicate by check mark if the or revised financial accounting standards provided purs		

Item 1.01 Entry into a Material Definitive Agreement.

On August 31, 2022, Comera Life Sciences Holdings, Inc. ("we," "us," "our" or the "Company") entered into a purchase agreement (the "Purchase Agreement") with Arena Business Solutions Global SPC II, Ltd. ("Arena"), pursuant to which Arena has committed to purchase up to \$15 million (the "Commitment Amount") of our common stock, par value \$0.0001 per share (the "Common Stock"), at our direction from time to time, subject to the satisfaction of the conditions in the Purchase Agreement. The Commitment Amount is subject to increase, at the Company's option (the "Option"), by an additional \$15,000,000 of Common Stock (the "Additional Commitment Amount").

Such sales of Common Stock, if any, will be subject to certain limitations, and may occur from time to time at our sole discretion over the approximately 36-month period commencing on the date of the Purchase Agreement, provided that a registration statement (the "Registration Statement") covering the resale by Arena of the shares of Common Stock purchased from us (which we have agreed to file) is declared effective by the U.S. Securities and Exchange Commission (the "SEC") and remains effective, and the other conditions set forth in the Purchase Agreement are satisfied.

Arena has no right to require us to sell any shares of Common Stock to Arena, but Arena is obligated to make purchases at our direction subject to certain conditions. There is no upper limit on the price per share that Arena could be obligated to pay for the Common Stock under the Purchase Agreement.

Actual sales of shares of Common Stock to Arena from time to time will depend on a variety of factors, including, among others, market conditions, the trading price of our Common Stock and determinations by us as to the appropriate sources of funding for us and our operations. The net proceeds that we may receive under the Purchase Agreement cannot be determined at this time, since it will depend on the frequency and prices at which we sell shares of our Common Stock to Arena, our ability to meet the conditions of the Purchase Agreement and the other limitations, terms and conditions of the Purchase Agreement. The Company expects that any proceeds received by the Company from such sales to Arena will be used for working capital and general corporate purposes.

Under the applicable rules of the Nasdaq Stock Market LLC ("Nasdaq") and the Purchase Agreement, we will not sell or issue to Arena shares of our Common Stock in excess of 3,884,044 shares, inclusive of the Commitment Fee Shares (the "Exchange Cap"), which is 19.99% of the shares of Common Stock outstanding as of the date of the Purchase Agreement, unless (i) we obtain stockholder approval to issue shares of Common Stock in excess of the Exchange Cap or (ii) the average price of all applicable sales of shares of Common Stock under the Purchase Agreement (including the Commitment Fee Shares and the Additional Commitment Fee Shares described below in the number of shares sold for these purposes) equals or exceeds \$1.80 per share (which represents the lower of (i) the closing price of our Common Stock on Nasdaq (as reflected on Nasdaq.com) immediately preceding the signing of the Purchase Agreement or (ii) the average closing price of the Common Stock (as reflected on Nasdaq.com) for the five trading days immediately preceding the signing of the Purchase Agreement). In any event, we may not issue or sell any shares of our Common Stock under the Purchase Agreement if such issuance or sale would breach any applicable Nasdaq rules.

The Purchase Agreement also prohibits us from directing Arena to purchase any shares of Common Stock if those shares, when aggregated with all other shares of our Common Stock then beneficially owned by Arena and its affiliates as a result of purchases under the Purchase Agreement, would result in Arena and its affiliates having beneficial ownership of more than the 4.99% of our then outstanding Common Stock.

We may direct Arena to purchase amounts of our Common Stock under the Purchase Agreement that we specify from time to time in a written notice (an "Advance Notice") delivered to Arena on any trading day up to the Commitment Amount, as increased by the Additional Commitment Amount, if applicable. The maximum amount that we may specify in any one Advance Notice is equal to the following: (A) if the Advance Notice is received by 8:30 A.M. Eastern time, then the maximum amount that we may specify is equal to the lesser of (i) an amount equal to thirty percent (30%) of the Daily Value Traded of the Common Stock of the ten trading days immediately preceding such Advance Notice, or (ii) \$10.0 million; and (B) if the Advance Notice is received after 8:30 A.M. Eastern Time but prior to 10:30 A.M. Eastern Time, then the maximum amount that we may specify in an Advance Notice is equal to the lower of: (i) an amount equal to twenty percent (20%) of the Daily Value Traded of the Common Stock on the ten trading days immediately preceding such Advance Notice and (ii) \$10.0 million. For

these purposes, "Daily Value Traded" is the product obtained by multiplying the daily trading volume of our Common Stock on Nasdaq during regular trading hours, as reported by Bloomberg L.P., by the VWAP (as defined in the Purchase Agreement) for that trading day. Subject to the satisfaction of the conditions under the Purchase Agreement, we may deliver Advance Notices from time to time, provided that the Pricing Period for all prior advances has been completed. For these purposes, "Pricing Period" means one trading day, as notified by the Company to Arena in the applicable Advance Notice, commencing on the date of the Advance Notice.

The purchase price of the shares of Common Stock will be equal to 96% of the simple average of the daily VWAP of the Common Stock during the Pricing Period.

Arena has agreed that, during the term of the Purchase Agreement, neither Arena nor any of its affiliates will engage in any short sales or hedging transactions with respect to our Common Stock, provided that upon receipt of an Advance Notice, Arena may sell shares that it is obligated to purchase under such Advance Notice prior to taking possession of such shares.

Unless earlier terminated as provided in the Purchase Agreement, the Purchase Agreement will terminate automatically on the earliest to occur of:

- the first day of the month next following the 36-month anniversary of the date of the Purchase Agreement; and
- the date on which Arena shall have purchased shares of Common Stock under the Purchase Agreement for an aggregate gross purchase price equal to Commitment Amount and the Additional Commitment Amount, if applicable, under the Purchase Agreement.

We have the right to terminate the Purchase Agreement at any time, at no cost or penalty, upon five trading days' prior written notice to Arena, provided that there are no outstanding Advance Notices the shares of Common Stock under which have not yet been issued. We and Arena may also terminate the Purchase Agreement at any time by mutual written consent.

As consideration for Arena's irrevocable commitment to purchase shares of the Company's Common Stock upon the terms of and subject to satisfaction of the conditions set forth in the Purchase Agreement, upon execution of the Purchase Agreement, the Company has agreed to issue a total of \$650,000 worth of shares of Common Stock (the "Commitment Fee Shares") based on a price per share equal to the simple average daily VWAP of the Common Stock during the ten trading days immediately preceding the date on which the SEC declares the Registration Statement effective, provided that we issue Arena a minimum of 65,000 shares as Commitment Fee Shares. Additionally, upon the execution of the Purchase Agreement, we agreed to issue 185,714 shares of Common Stock to Arena (the "Estimated Commitment Fee Shares"), provided that (i) in the event the number of the Commitment Fee Shares exceeds the number of Estimated Commitment Fee Shares and (ii) in the event the number of the issued Estimated Commitment Fee Shares exceeds the Commitment Fee Shares, Arena shall return such excess shares. Additionally, if the Company exercises its Option under the Purchase Agreement, the Company has agreed to issue \$300,000 worth of shares of Common Stock (the "Additional Commitment Fee Shares"), based on a price per share equal to the simple average of the daily VWAP of the Common Stock during the ten trading days immediately preceding the date on which we notify Arena of our exercise of the Option.

The Purchase Agreement contains customary representations, warranties, conditions and indemnification obligations of the parties.

The foregoing description of the Purchase Agreement is qualified in its entirety by reference to the full text of such agreement, a copy of which is attached hereto as Exhibit 10.1, and which is incorporated herein in its entirety by reference.

This Current Report on Form 8-K (this "report") shall not constitute an offer to sell or a solicitation of an offer to buy any shares of Common Stock in any state or jurisdiction in which such an offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or other jurisdiction.

Item 3.02 Unregistered Sales of Equity Securities.

The information contained in Item 1.01 of this report is hereby incorporated by reference into this Item 3.02.

In the Purchase Agreement, Arena represented to the Company, among other things, that it is an "accredited investor" (as such term is defined in Rule 501(a) of Regulation D under the Securities Act of 1933, as amended (the "Securities Act")). The securities referred to in this report are being issued and sold by the Company to Arena in reliance upon the exemption from the registration requirements of the Securities Act afforded by Section 4(a)(2) of the Securities Act.

Item 7.01 Regulation FD Disclosure.

On August 31, 2022, the Company issued a press release announcing the Company's entry into the Purchase Agreement with Arena. A copy of the press release is set forth as Exhibit 99.1 and is incorporated by reference herein.

The information contained in this Item 7.01 of this report and 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, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	<u>Description</u>
10.1	<u>Purchase Agreement, dated August 31, 2022, between Comera Life Sciences Holdings, Inc. and Arena Business Solutions Global SPC II, Ltd.</u>
99.1	Press release dated August 31, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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: August 31, 2022 COMERA LIFE SCIENCES HOLDINGS, INC.

By: /s/ Jeffrey S. Hackman

Name: Jeffrey S. Hackman

Title: Chairman, President and Chief Executive Officer