

PROSPECTUS

**27,863,058 SHARES OF COMMON STOCK**

This prospectus relates to the offer and resale from time to time by the Selling Stockholders named in this prospectus (the "Selling Stockholders") or their permitted transferees of up to 27,863,058 shares of common stock, \$0.0001 par value per share (the "Common Stock") of Comera Life Sciences Holdings, Inc. ("we," "us," "our," or the "Company"). The 27,863,058 shares of Common Stock being offered for resale by the Selling Stockholders consist of (i) 4,399,016 shares of Common Stock (the "First Closing Shares") and 10,997,550 shares of Common Stock (the "First Closing Warrant Shares") issuable upon the exercise of warrants (the "First Closing Warrants"), in each case issued to the Selling Stockholders in connection with an initial closing on July 31, 2023 (the "First Closing") of the sale and issuance of our securities as contemplated by a Securities Purchase Agreement, dated July 31, 2023 (the "Purchase Agreement" and the transactions contemplated thereby, the "July 2023 PIPE Financing") between the Company and the Selling Stockholders identified therein (the "Purchasers"), and (ii) 3,561,851 shares of Common Stock (the "Subsequent Closing Shares" and, together with the First Closing Shares, the "Shares") and 8,904,641 shares of Common Stock (the "Subsequent Closing Warrant Shares" and, together with the First Closing Warrant Shares, the "Warrant Shares") issuable upon the exercise of warrants (the "Subsequent Closing Warrants" and, together with the First Closing Warrants, the "Warrants"), in each case that may be issued to the Purchasers subject to the terms and the satisfaction of the conditions set forth in the Purchase Agreement in a second closing (the "Subsequent Closing"), including receipt of stockholder approval of the Subsequent Closing.

We are not selling any shares of Common Stock being offered by this prospectus and will not receive any of the proceeds from the sale of such shares by the Selling Stockholders. However, we may receive up to approximately \$12.2 million in aggregate gross proceeds upon the exercise of the Warrants, if any, as the Warrants have an exercise price of \$0.6135 per Warrant Share.

The Selling Stockholders may sell or otherwise dispose of the shares of Common Stock included in this prospectus in a number of different ways and at varying prices. See the section titled "*Plan of Distribution*" for more information about how the Selling Stockholders may sell or otherwise dispose of the Common Stock being offered in this prospectus.

Our shares of Common Stock and warrants to purchase Common Stock (the "Public Warrants") are listed on the Nasdaq Capital Market ("Nasdaq") under the symbols "CMRA" and "CMRAW," respectively. On September 12, 2023, the last reported sales price of Common Stock, as reported by Nasdaq, was \$0.375 per share, and the last reported sales price of the Public Warrants on Nasdaq was \$0.025 per warrant.

We are an "emerging growth company" and a "smaller reporting company" as defined under the federal securities laws and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and may elect to do so in future filings.

Investing in our Common Stock involves significant risks. See "Risk Factors" beginning on page 4 of this prospectus and in the documents incorporated by reference in this prospectus, and under similar

headings in the other documents that we have filed or that are filed after the date hereof and incorporated by reference into this prospectus for a discussion of the factors you should carefully consider before deciding to purchase our Common Stock.

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

The date of this prospectus is September 13, 2023.

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ABOUT THIS PROSPECTUS

Neither we nor the Selling Stockholders have authorized anyone to provide you with information other than that contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by us or on our behalf and filed with the U.S. Securities and Exchange Commission (the “SEC”). We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. Neither we nor the Selling Stockholders will make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, any post-effective amendment and any applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, regardless of the time of delivery of this prospectus or any sale of our securities. Our business, financial condition, results of operations and prospects may have changed since that date. Our business, financial condition, results of operations and prospects may have changed since those dates. You should rely only on the information contained in this prospectus, any supplement to this prospectus or in any free writing prospectus, filed with the SEC.

We may also file a prospectus supplement or post-effective amendment to the registration statement of which this prospectus forms a part that may contain material information relating to these offerings. The prospectus supplement or post-effective amendment, as the case may be, may add, update or change information contained in this prospectus with respect to such offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or post-effective amendment, you should rely on the prospectus supplement or post-effective amendment, as applicable. Before purchasing any Common Stock, you should carefully read this prospectus and any prospectus supplement and/or post-effective amendment, as applicable, together with the additional information described under “*Where You Can Find More Information.*”

For investors outside of the United States: Neither we nor the Selling Stockholders have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus, any prospectus supplement, any post-effective amendment or any free writing prospectus must inform themselves about, and observe any restrictions relating to, the offering of our securities and the distribution of such prospectus outside the United States.

Unless the context indicates otherwise, references in this prospectus to the “Company,” “we,” “us,” “our” and similar terms refer to Comera Life Sciences Holdings, Inc., and its consolidated subsidiaries.

Trademarks

This document includes trademarks, tradenames and service marks, certain of which belong to us and others that are the property of other organizations. Solely for convenience, trademarks, tradenames and service marks referred to in this document appear without the ®, TM and SM symbols, but the absence of those symbols is not intended to indicate, in any way, that we will not assert our rights or that the applicable owner will not assert its rights to these trademarks, tradenames and service marks to the fullest extent under applicable law. We do not intend our use or display of other parties’ trademarks, trade names or service marks to imply, and such use or display should not be construed to imply a relationship with, or the endorsement or sponsorship of the Company by, these other parties.

Market and Industry Data

This prospectus and the documents incorporated by reference herein contain estimates, projections, and other information concerning our industry and business, as well as data regarding market research, estimates, and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled “*Risk Factors*.” Unless otherwise expressly stated, we obtained this industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry and general publications, government data, and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from sources which we paid for, sponsored, or conducted, unless otherwise expressly stated or the context otherwise requires. While we have compiled, extracted, and reproduced industry data from these sources, we have not independently verified the data. Forecasts and other forward-looking information with respect to industry, business, market, and other data are subject to the same qualifications and additional uncertainties regarding the other forward-looking statements in this document. See “*Cautionary Note Regarding Forward-Looking Statements*.”

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This registration statement, of which this prospectus forms a part, contains forward-looking statements. All statements other than statements of historical fact contained herein, including statements regarding our business plans or strategies, projected or anticipated benefits or other consequences of our plans or strategies are forward-looking statements. Words such as “anticipates,” “assumes,” “believes,” “can,” “could,” “estimates,” “expects,” “forecasts,” “guides,” “intends,” “is confident that,” “may,” “plans,” “seeks,” “projects,” “targets,” and “would,” and their opposites and similar expressions, as well as statements in future tense, are intended to identify forward-looking statements. Forward-looking statements should not be read as a guarantee of future performance or results and may not be accurate indications of when such performance or results will actually be achieved. Forward-looking statements are based on information we have when those statements are made or our management’s good faith belief as of that time with respect to future events and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in or suggested by the forward-looking statements. Important factors that could cause such differences include, but are not limited to:

- the risk that we will need to raise additional capital to execute our business plan, which may not be available on acceptable terms or at all;
 - our ability to maintain the listing of our securities on the Nasdaq Capital Market (“Nasdaq”);
 - the price of our securities may be volatile due to a variety of factors, including volatility in the capital markets generally, the low trading volume for our Common Stock, changes in the competitive and highly regulated industries in which we plan to operate, variations in performance across competitors, changes in laws and regulations affecting our business and changes in our capital structure;
 - the ability to implement business plans, forecasts, and identify and realize additional opportunities;
 - the risk of downturns and the possibility of rapid change in the highly competitive industry in which we operate;
 - the risk that we and our current and future collaborators are unable to successfully develop and commercialize our products or services, or experience significant delays in doing so;
 - the risk that we may never achieve or sustain profitability;
 - the risk that we experience difficulties in managing our growth and expanding operations;
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- the risk that third-party suppliers and manufacturers are not able to fully and timely meet their obligations;
- the risk that we are unable to secure or protect our intellectual property;
- the effect of COVID-19 or other pandemics or epidemics on our business;
- general economic conditions; and
- other risks and uncertainties described in this registration statement and prospectus, and included in our other public filings, including those under the section entitled “Risk Factors.”

Should one or more of these risks or uncertainties materialize or should any of the assumptions made by the management of the Company prove incorrect, actual results may vary in material respects from those projected in these forward-looking statements.

You should read this prospectus, any prospectus supplement, the documents that we incorporate by reference herein and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PROSPECTUS SUMMARY

This summary highlights certain information appearing elsewhere in this prospectus. Because it is only a summary, it does not contain all of the information that you should consider before investing in our securities and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus. Before you decide to invest in our securities, you should read the entire prospectus carefully, including the section titled “Risk Factors” and our financial statements and related notes thereto incorporated by reference in this prospectus.

Overview and Corporate Information

We are a preclinical stage biotechnology company dedicated to promoting a compassionate new era in medicine. We apply a deep knowledge of formulation science and proprietary technology to optimize biologic medicines. Our internal portfolio of proprietary techniques known as our SQore™ platform, is designed to potentially:

- transform essential biologic medicines from intravenous (“IV”) to subcutaneous (“SQ”) forms;
- optimize current versions of subcutaneous biologics; and
- produce biosimilar versions of existing subcutaneous products.

We aim to develop these potentialities in order to transform administration from IV to SQ and thereby provide patients using biological products through intravenous infusion, and their families, with the freedom of self-injectable care which, we believe, would allow them to enjoy both the potential benefits of biologic treatments and the potential of their own lives while simultaneously lowering healthcare costs and increasing patient compliance.

The SQore™ platform, which is the foundation of our work, is supported by an extensive patent portfolio and encompasses years of knowledge and development from our team of scientists, including industry-leading experts in polymer engineering and interfacial dynamics (the way that different molecules interact) who are inventors on dozens of patents and have published widely-cited research in their fields. We believe that our combined polymer and small molecule capability will allow us to leverage a mechanistic understanding of protein-protein and protein-solvent interactions to identify suitable excipients for specific formulations, that allows the active, therapeutic ingredient to enter the body and arrive with sufficient potency.

We aim to achieve our mission by developing our own portfolio of therapeutic product candidates and by collaborating with pharmaceutical and biotechnology companies to transform their biologic medicines into enhanced SQ formulations.

Since our founding in 2014, we have primarily engaged in early-stage, preclinical studies, commissioned on a fee-for-services basis by larger pharmaceutical companies and have not yet developed any products approved for marketing. Our studies for larger companies were generally early-stage investigations, often amounting to proof-of-concept work, aimed at moving existing formulations from IV infusion to SQ delivery via injection.

In 2021, we brought on a new leadership team and carried out a transition of our business model. We shifted away from simple “fee for services” formulation work and focused our efforts on engaging with higher-value-add partners in integrated, collaborative projects to develop formulations for their key products. We are currently working with multiple companies under research and development service agreements. These agreements typically have a term of less than 12 months and provide for an initial payment by the company of a fee to us for the evaluation by us of our proprietary technology for viscosity reduction with the other company’s proprietary biotherapeutic agent. The agreements set forth the detailed research plans and the related timeline for completion of the research. The agreements provide that each party retains ownership of its technology throughout the process. Upon completion of the project, the parties may negotiate in good faith the terms of a license agreement. If the parties do not successfully negotiate a license, each party retains ownership of its technology and neither party may use the joint invention. Because these research and development service agreements may result in the future negotiation and execution of licensing agreements, we believe these projects provide far greater opportunities for generating revenue. When we meet our partners’ defined project criteria for the formulations, we will seek a license agreement to receive license fees, milestone payments, and longer-term and more stable royalty revenue on commercial assets that are vital to our partners.

On January 7, 2022, we changed the name of our operating subsidiary from ReForm Biologics, Inc. to Comera Life Sciences, Inc. This change marks our development into a revenue-generating, commercially-focused business with the potential to derive future revenue from multiple existing and future partnering opportunities.

On May 19, 2022, we consummated a business combination, contemplated by the Business Combination Agreement, dated January 31, 2022 (as amended, the “Business Combination Agreement”), by and among the Company, OTR Acquisition Corp. (“OTR”), CLS Sub Merger 1 Corp., CLS Sub Merger 2 Corp. and Comera Life Sciences, Inc. (“Legacy Comera”). Pursuant to the Business Combination Agreement, CLS Sub Merger 1 Corp. merged with and into Legacy Comera and CLS Merger 2 Corp. merged with and into OTR resulting in Legacy Comera and OTR becoming wholly owned subsidiaries of the Company. Collectively, we refer herein to these transactions as the “Transaction.”

We continued to grow our leadership team in 2022, with a focus on expanding the scope of work over research collaborations and developing our internal pipeline. In July 2022, we announced favorable topline results from our SEQURUS-1 study, which provides supportive evidence of the safety of our lead caffeine-based SQore excipient when administered as a SQ biologic drug product formulation with a monoclonal antibody (mAb). In October 2022, we announced favorable safety and pharmacokinetic results from our SEQURUS-2 study. Also in October 2022, we announced our lead pipeline candidate CLS-001 as an SQ formulation of vedolizumab, a currently marketed product for the treatment of IBD including Crohn’s disease and ulcerative colitis.

Our Common Stock and Public Warrants are listed on Nasdaq under the symbols “CMRA” and “CMRAW,” respectively.

The address of our principal executive office is 12 Gill Street, Suite 4650, Woburn, Massachusetts 01801. Our telephone number is (617) 871-2101. Our website address is www.comeralifesciences.com. Information contained on our website or connected thereto does not constitute part of, and is not incorporated by reference into, this prospectus.

THE OFFERING

Common stock offered by Selling Stockholders

27,863,058 shares of Common Stock

Use of proceeds

We will not receive any proceeds from the sale of shares of Common Stock included in this prospectus by the Selling Stockholders. However, we may receive up to approximately \$12.2 million in aggregate gross proceeds upon the exercise of the Warrants, if any. For more information see the section herein titled "*Use of Proceeds.*"

Nasdaq Capital Market trading symbol

"CMRA"

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks and uncertainties described under the section captioned “Risk Factors” contained in our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings we make with the SEC from time to time, which are incorporated by reference herein in their entirety, together with other information in this prospectus and in the documents incorporated by reference in this prospectus. We caution you that the risks and uncertainties we have described, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in filings with the SEC, press releases, communications with investors and oral statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares of Common Stock offered pursuant to this prospectus. The Selling Stockholders will receive all of the proceeds from the sale of the shares of Common Stock offered by this prospectus. However, assuming exercise of all of the Warrants for cash in full, the Selling Stockholders would pay us an aggregate of approximately \$12.2 million. The proceeds to us of such Warrant exercises, if any, will not be subject to any restrictions. For information about the Selling Stockholders, see “Selling Stockholders.”

The Selling Stockholders will pay any underwriting discounts and commissions and expenses incurred by the Selling Stockholders for brokerage or legal services or any other expenses incurred by the selling stockholders in disposing of the shares of Common Stock covered by this prospectus. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including all registration and filing fees and expenses of our counsel and accountants.

SELLING STOCKHOLDERS

This prospectus relates to the offer and sale by the Selling Stockholders of up to 27,863,058 shares of our common stock, consisting of (i) 4,399,016 First Closing Shares and 10,997,550 First Closing Warrant Shares issuable upon the exercise of the First Closing Warrants, in each case issued to the Selling Stockholders on July 31, 2023, in connection with the First Closing of the July 2023 PIPE Financing pursuant to the Purchase Agreement, and (ii) 3,561,851 Subsequent Closing Shares and 8,904,641 Subsequent Closing Warrant Shares issuable upon exercise of Subsequent Closing Warrants, in each case that may be issued to the Selling Stockholders, subject to the terms and the satisfaction of the conditions set forth in the Purchase Agreement in the Subsequent Closing, including receipt of stockholder approval of the Subsequent Closing. We are registering the shares of Common Stock included in this prospectus pursuant to the Purchase Agreement and the Registration Rights Agreement, dated July 31, 2023, entered into with the Purchasers (the “Registration Rights Agreement”), in order to permit the Selling Stockholders to offer such shares for resale from time to time. When we refer to the “Selling Stockholders” in this prospectus, we refer to the persons listed in the table below, and the pledgees, donees, transferees, assignees, successors and other permitted transferees that hold any of the Selling Stockholders’ interests in the securities after the date of this prospectus.

The table below presents information regarding the Selling Stockholders and the shares of our Common Stock that may be resold by the Selling Stockholders from time to time under this prospectus. This table is prepared based on information supplied to us by the Selling Stockholders, and reflects holdings as of August 18, 2023. The number of shares in the column “Number of Shares of Common Stock Being Offered” represents all of the shares of our Common Stock being offered for resale by the Selling Stockholders under this prospectus. The Selling Stockholders may sell some, all or none of the shares being offered for resale in this offering. We do not know how long the Selling Stockholders will hold the shares before selling them. Except as set forth in the section titled “Plan of Distribution” in this prospectus, we are not aware of any existing arrangements between the Selling Stockholders and any other stockholder, broker, dealer, underwriter or agent relating to the sale or distribution of the shares of our Common Stock being offered for resale by this prospectus.

Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the SEC under the Securities Exchange Act of 1934, as amended (the “Exchange Act”) and includes shares of our Common Stock with respect to which the Selling Stockholder has sole or shared voting and investment power. The percentage of shares of our Common Stock beneficially owned by the Selling Stockholders prior to the offering shown in the table below is based on an aggregate of 27,175,945 shares of our common stock outstanding on August 18, 2023. The fourth column, titled “Shares of Common Stock to be Beneficially Owned After this Offering”, assumes the exercise of all Warrants and the resale by the Selling Stockholder of all of the shares of Common Stock being offered for resale pursuant to this prospectus, including the Warrant Shares.

The Warrants contain beneficial ownership limitations that may be waived at the option of each holder upon 61 days’ notice to us, but in no event may such beneficial ownership limitation exceed 19.99% of the number of shares of outstanding Common Stock (the “Cap”). If we obtain stockholder approval for the July 2023 PIPE Financing, the Cap will no longer apply to the Warrants. The number of shares in the second column does not reflect this limitation or other similar limitations that may exist on other warrants held by the Selling Stockholders listed below. The Selling Stockholders may sell all, some or none of their shares in this offering. Please see the section entitled “*Plan of Distribution*” for further information regarding the Selling Stockholders’ methods of distributing these securities.

For information regarding transactions between us and the Selling Stockholders, see the section entitled “*Relationships with the Selling Stockholders*” below.

Name of Selling Stockholder	Shares of Common Stock Owned Prior to this Offering		Number of Shares of Common Stock Being Offered (1)	Shares of Common Stock to be Owned After this Offering	
	Number	Percentage		Number	Percentage
Charles Cherington (2)	13,148,612	34.25 %	10,268,946	2,879,666	9.27%
IAF, LLC (3)	7,407,341	20.91 %	5,237,161	2,170,180	6.85%
Freebird Partners LP (4)	3,709,509	11.20 %	2,396,086	1,313,423	4.18%
John D. Halpern Revocable Trust (5)	2,716,716	8.42 %	1,711,490	1,005,226	3.24%
Denny Family Partners II LLC (6)	2,579,797	8.02 %	1,574,571	1,005,226	3.24%
Regolith Capital Investments L.P. (7)	2,396,086	7.40 %	2,396,086	-	*
OTR Acquisition Sponsor LLC (8)	1,891,561	5.98 %	1,369,191	522,370	1.70%
Stephen Older (9)	356,046	1.15 %	342,296	13,750	*
The Alexander V. Soane 2019 Irrevocable Trust dated June 7, 2019 (10)	908,459	2.90 %	684,596	223,863	*
The Nicholas V. Soane 2019 Irrevocable Trust dated June 7, 2019 (11)	908,458	2.92 %	684,595	223,863	*
Tucker R. Halpern 2020 Trust (12)	513,445	1.66 %	513,445	-	*
Warren Street Legacy, LLC (13)	684,595	2.20 %	684,595	-	*

* Represents beneficial ownership of less than 1% of the outstanding shares of Common Stock.

- (1) Represents shares of Common Stock and shares of Common Stock issuable upon exercise of the Warrants acquired pursuant to the July 2023 PIPE Financing.
- (2) Includes (i) 880,195 Shares and 2,200,488 Warrant Shares issued in connection with the First Closing and (ii) 2,053,789 Shares and 5,134,474 Warrant Shares issuable in connection with the Second Closing, if any. Does not include (a) 1,268,761 shares of Common Stock held by Cherington Holdings LLC, (b) 95,328 shares of Holdco Common Stock held by each of The Ashley S. Pettus 2012 Irrevocable Trust FBO Benjamin P. Cherington and The Ashley S. Pettus 2012 Irrevocable Trust FBO Henry S. Cherington, or (c) 95,327 shares of Holdco Common Stock held by The Ashley S. Pettus 2012 Irrevocable Trust FBO Cyrus B. Cherington (together with the Ashley S. Pettus 2012 Irrevocable Trust FBO Benjamin P. Cherington and Ashley S. Pettus 2012 Irrevocable Trust FBO Henry S. Cherington, the “Cherington Trusts”). Charles Cherington is the trustee of each of the Cherington Trusts and a partner of Cherington Holdings LLC, and may be deemed to beneficially own the shares of Holdco Common Stock held thereby. The business address of Charles Cherington, Cherington Holdings LLC and each of the Cherington Trusts is c/o ARA Partners, 222 Berkeley Street, Suite 1270, Boston, MA 02116.

- (3) Includes (i) 1,047,432 Shares and 2,618,581 Warrant Shares issued in connection with the First Closing and (ii) 448,899 Shares and 1,122,249 Warrant Shares issuable in connection with the Second Closing, if any. David W. Laughlin is the Sole Manager of IAF, LLC and may be deemed to share beneficial ownership of the securities held thereby. Mr. Laughlin disclaims beneficial ownership in the securities held by IAF, LLC, except to the extent of any pecuniary interest therein. The principal business address of the Selling Stockholder is 115 Church Street, Charleston, South Carolina 29401.
- (4) Includes (i) 479,217 Shares and 1,198,044 Warrant Shares issued in connection with the First Closing and (ii) 205,378 Shares and 513,447 Warrant Shares issuable in connection with the Second Closing, if any. Freebird Investments LLC serves as the general partner of Freebird Partners LP. Mr. Curtis Huff is the sole member and 100% owner of Freebird Investments LLC, the President of Freebird Partners LP and the Managing Member of Freebird Investments LLC. By virtue of these relationships, each of Freebird Investments LLC and Mr. Huff may be deemed to share beneficial ownership of the securities held of record by Freebird Partners LP. The principal business address of the Selling Stockholder is 2800 Post Oak Blvd, Suite 2000, Houston, Texas 77056.
- (5) Includes (i) 342,298 Shares and 855,745 Warrant Shares issued in connection with the First Closing and (ii) 146,699 Shares and 366,748 Warrant Shares issuable in connection with the Second Closing, if any. Does not include 80,651 Earn-Out Shares held by John Halpern. John Halpern is the trustee of the John D. Halpern Revocable Trust and may be deemed to share beneficial ownership of the securities held thereby. The principal business address of the Selling Stockholder is 260 Palmetto Lane, West Palm Beach, Florida 33405.
- (6) Includes (i) 314,914 Shares and 787,286 Warrant Shares issued in connection with the First Closing and (ii) 134,963 Shares and 337,408 Warrant Shares issuable in connection with the Second Closing, if any. George Denny is the Manager of Denny Family Partners II LLC and may be deemed to share beneficial ownership of the securities held thereby. The principal business address of the Selling Stockholder is 14 Grayvik Dr., Key Largo, Florida 33037.
- (7) Includes (i) 479,217 Shares and 1,198,044 Warrant Shares issued in connection with the First Closing and (ii) 205,378 Shares and 513,447 Warrant Shares issuable in connection with the Second Closing, if any. Does not include 397,120 shares of Common Stock held by Shameek Konar. Shameek Konar is the General Partner or Regolith Capital Investments L.P. and may be deemed to share beneficial ownership of the securities held thereby. The principal business address of the Selling Stockholder is 1917 Oakleigh Way, Knoxville, Tennessee 37919.
- (8) Includes (i) 273,838 Shares and 684,596 Warrant Shares issued in connection with the First Closing and (ii) 117,359 Shares and 293,398 Warrant Shares issuable in connection with the Second Closing, if any. OTR Acquisition Sponsor LLC was the sponsor of OTR Acquisition Corp., the special purpose acquisition company with which the Company completed the Transaction with pursuant to the Business Combination Agreement, in May 2022. The principal business address of the Selling Stockholder is 1395 Brickell Avenue, Suite 800, Miami, Florida 33131.
- (9) Includes (i) 68,459 Shares and 171,149 Warrant Shares issued in connection with the First Closing and (ii) 29,339 Shares and 73,349 Warrant Shares issuable in connection with the Second Closing, if any. OTR Acquisition Sponsor LLC is managed by its board of managers, comprised of three individuals, which has voting and dispositive power over the securities held by OTR Acquisition Sponsor LLC. The Warrants are subject to a beneficial ownership limitation of 4.99%, which such limitation restricts OTR Acquisition Sponsor LLC from exercising that portion of the Warrants that would result in OTR Acquisition Sponsor LLC and its affiliates from owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The principal business address of the Selling Stockholder is 139 Edgemont Road, Scarsdale, NY 10583.
- (10) Includes (i) 136,919 Shares and 342,298 Warrant Shares issued in connection with the First Closing and (ii) 58,680 Shares and 146,699 Warrant Shares issuable in connection with the Second Closing, if any. Does not include (a) 589,786 shares of Common Stock held by David Soane, (b) 223,863 shares of Common Stock held by The Nicholas V. Soane 2019 Irrevocable Trust (and, together with The Alexander V. Soane 2019 Irrevocable Trust, the "Soane Trusts") or (c) 3,471,696 shares of Common Stock held by The Soane Family Trust. Zoya Soane and Nancy Wrieden are each a trustee of each of the Soane Trusts and may therefore be deemed to beneficially own the shares of Common Stock held thereby. In addition, David Soane, an immediate family member of Zoya Soane, the beneficiary of the Soane Trusts and the former Chief Technology Officer and member of the advisory board of Legacy Comera, may be deemed to

beneficially own the shares of Common Stock held by the Soane Trusts. The principal business address of the Selling Stockholder is c/o Soane Labs, LLC, 380 NE 72nd Terrace, Miami, Florida 33138.

- (11) Includes (i) 136,919 Shares and 342,298 Warrant Shares issued in connection with the First Closing and (ii) 58,679 Shares and 146,699 Warrant Shares issuable in connection with the Second Closing, if any. Does not include (a) 589,786 shares of Common Stock held by David Soane, (b) 223,863 shares of Common Stock held by The Alexander V. Soane 2019 Irrevocable Trust or (c) 3,471,696 shares of Common Stock held by The Soane Family Trust. Zoya Soane and Nancy Wrieden are each a trustee of each of the Soane Trusts and may therefore be deemed to beneficially own the securities held by the Soane Trusts. In addition, David Soane, an immediate family member of Zoya Soane, the beneficiary of the Soane Trusts and the former Chief Technology Officer and member of the advisory board of Legacy Comera, may be deemed to beneficially own the shares of Common Stock held thereby. The principal business address of the Selling Stockholder is c/o Soane Labs, LLC, 380 NE 72nd Terrace, Miami, Florida 33138.
- (12) Includes (i) 102,689 Shares and 256,723 Warrant Shares issued in connection with the First Closing and (ii) 44,009 Shares and 110,024 Warrant Shares issuable in connection with the Second Closing, if any. Tucker R. Halpern is the trustee of the Tucker R. Halpern 2020 Trust and may therefore be deemed to beneficially own the securities held thereby. The principal business address of the Selling Stockholder is 205 Monroe Avenue, West Palm Beach, Florida 33405.
- (13) Includes (i) 136,919 Shares and 342,298 Warrant Shares issued in connection with the First Closing and (ii) 58,679 Shares and 146,699 Warrant Shares issuable in connection with the Second Closing, if any. Ian H. Halpern is the manager of Warren Street Legacy, LLC and may therefore be deemed to beneficially own the securities held thereby. The principal business address of the Selling Stockholder is 410 Colon Avenue, San Francisco, California 94127.

Relationships with the Selling Stockholders

Except for the ownership of the Shares and the Warrants issued pursuant to the Purchase Agreement and the registration rights set forth in the Registration Rights Agreement, and except as disclosed above or as disclosed in our SEC filings incorporated by reference herein, the Selling Stockholders have not had any material relationship with us within the past three years.

PLAN OF DISTRIBUTION

Each Selling Stockholder and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their securities covered by this prospectus, on the Nasdaq Capital Market or any other stock exchange, market or trading facility on which the securities are traded or in private transactions. These sales may be at fixed or negotiated prices. A Selling Stockholder may use any one or more of the following methods when selling securities:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales entered into after the date of this prospectus;
- in transactions through broker-dealers that agree with the Selling Stockholders to sell a specified number of such securities at a stipulated price per security;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;

- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The Selling Stockholders may also sell securities under Rule 144 or any other exemption from registration under the Securities Act, if available, rather than under this prospectus. The Selling Stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on one or more exchanges or in the over-the-counter market or otherwise, at prices and under terms then prevailing or at prices related to the then current market price or in negotiated transactions.

In addition, a Selling Stockholder that is an entity may elect to make an in-kind distribution of securities to its members, partners or stockholders pursuant to the registration statement of which this prospectus is a part by delivering a prospectus with a plan of distribution. Such members, partners or stockholders would thereby receive freely tradeable securities pursuant to the distribution through a registration statement. To the extent a distributee is an affiliate of ours (or to the extent otherwise required by law), we may file a prospectus supplement in order to permit the distributees to use the prospectus to resell the securities acquired in the distribution. The Selling Stockholders also may transfer the securities in other circumstances, in which case the transferees, pledgees or other successors-in-interest will be the selling beneficial owners for purposes of this prospectus. Upon being notified by the Selling Stockholders that a donee, pledgee, transferee, other successor-in-interest intends to sell our securities, we will, to the extent required, promptly file a supplement to this prospectus to name specifically such person as a Selling Stockholder.

Broker-dealers engaged by the Selling Stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the Selling Stockholders (or, if any broker-dealer acts as agent for the purchaser of securities, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2121; and in the case of a principal transaction a markup or markdown in compliance with FINRA Rule 2121.

In connection with the sale of the securities or interests therein, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the securities in the course of hedging the positions they assume. The Selling Stockholders may also sell securities short and deliver these securities to close out their short positions, or loan or pledge the securities to broker-dealers that in turn may sell these securities. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of securities offered by this prospectus, which securities such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The Selling Stockholders and any broker-dealers or agents that are involved in selling the securities may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the securities purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each Selling Stockholder has informed us that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the securities.

We are required to pay certain fees and expenses incurred by us incident to the registration of the securities. We have agreed to indemnify the Selling Stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We agreed to use our reasonable best efforts to keep this prospectus effective until the earlier of (i) the date on which the securities may be resold by the Selling Stockholders without registration and without regard to any volume or manner-of-sale limitations by reason of Rule 144 without the requirement for us to be in compliance with the current public information under Rule 144 under the Securities Act or (ii) all of the securities have been sold pursuant to this prospectus or Rule 144 under the Securities Act. The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale securities covered hereby may not be sold unless they have been registered or qualified for sale in

the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale securities may not, subject to certain exceptions, simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the Selling Stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of the common stock by the Selling Stockholders or any other person. We will make copies of this prospectus available to the Selling Stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

LEGAL MATTERS

The validity of the shares offered by this prospectus has been passed upon by Foley Hoag LLP.

EXPERTS

Our consolidated financial statements as of December 31, 2022 and 2021 and for each of the years then ended, incorporated by reference in this prospectus, have been audited by Baker Tilly US, LLP, an independent registered public accounting firm, as set forth in their report thereon, and is incorporated by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing. The report on the consolidated financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the shares of Common Stock offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, some of which is contained in exhibits to the registration statement as permitted by the rules and regulations of the SEC. For further information with respect to the Company, we refer you to the registration statement, including the exhibits filed as a part of the registration statement.

Statements contained in this prospectus concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The SEC maintains an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-36570):

- our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2022, filed with the SEC on March 17, 2023;

- our Definitive Proxy Statement on Schedule 14A (other than information furnished rather than filed), filed with the SEC on August 11, 2023;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, filed with the SEC on May 12, 2023;
- our Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, filed with the SEC on August 10, 2023;
- our Current Reports on Form 8-K filed with the SEC on January 4, 2023, February 21, 2023, May 5, 2023, May 19, 2023 and August 1, 2023; and
- the description of our securities filed as Exhibit 4.6 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2022.

In addition, we incorporate by reference all documents that we may file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after (1) the date of the initial registration statement and prior to the effectiveness of the registration statement of which this prospectus is a part and (2) the date of effectiveness of the registration statement until the date on which this registration statement has been withdrawn. These documents will become a part of this prospectus from the date that the documents are filed with the SEC. These documents include periodic reports, such as annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, excluding any information filed or furnished pursuant to Item 2.02 or Item 7.01, unless such Form 8-K expressly provides to the contrary.

Upon oral or written request and at no cost to the requester, we will provide to each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference in this prospectus but not delivered with this prospectus. You may obtain copies of these documents, at no cost to you, from our website (<https://ir.comeralifesciences.com/financial-information/sec-filings>), or by writing or telephoning us at the following address: Comera Life Sciences Holdings, Inc. 12 Gill Street, Suite 4650, Woburn, Massachusetts 01801. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

