

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM S-8

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

**SEMA4 HOLDINGS CORP.**

(Exact Name of Registrant as Specified in Its Charter)

**Delaware**  
(State or Other Jurisdiction  
of Incorporation or Organization)

**85-1966622**  
(I.R.S. Employer  
Identification No.)

**333 Ludlow Street, North Tower, 8th Floor**  
**Stamford, Connecticut 06902**  
(Address of Principal Executive Offices) (Zip Code)

**SEMA4 HOLDINGS CORP. 2021 EQUITY INCENTIVE PLAN**  
**SEMA4 HOLDINGS CORP. 2021 EMPLOYEE STOCK PURCHASE PLAN**  
**SEMA4 HOLDINGS CORP. EARN-OUT RSU AWARDS**  
(Full Title of the Plans)

**Eric Schadt**  
**Chief Executive Officer**  
**333 Ludlow Street, North Tower, 8th Floor**  
**Stamford, Connecticut 06902**  
(Name and Address of Agent For Service)  
**(800) 298-6470**  
(Telephone Number, including area code, of agent for service)

**Copies to:**

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**New York, New York 10010**  
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**General Counsel**  
**Sema4 Holdings Corp.**  
**333 Ludlow Street, North Tower, 8th Floor**  
**Stamford, Connecticut 06902**  
**(800) 298-6470**

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer   
Non-accelerated filer

Accelerated filer   
Smaller reporting company   
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 7(a)(2)(B) of the Securities Act.

**CALCULATION OF REGISTRATION FEE**

<b>Title of Securities To Be Registered</b>	<b>Amount To Be Registered<sup>(1)</sup></b>	<b>Proposed Maximum Offering Price Per Share</b>	<b>Proposed Maximum Aggregate Offering Price</b>	<b>Amount of Registration Fee</b>
Class A Common Stock, par value \$0.0001 per share:				
- Reserved for future issuance under the Sema4 Holdings Corp. 2021 Equity Incentive Plan	12,128,941 <sup>(2)</sup>	\$3.16 <sup>(3)</sup>	\$38,327,454 <sup>(3)</sup>	\$3,553
- Reserved for future issuance under the Sema4 Holdings Corp. 2021 Employee Stock Purchase Plan	2,425,788 <sup>(4)</sup>	\$2.68 <sup>(5)</sup>	\$6,501,112 <sup>(5)</sup>	\$603
<b>TOTAL</b>	14,554,729	—	\$44,828,566	\$4,156

(1) Pursuant to Rule 416(a) of the Securities Act of 1933, as amended (the "Securities Act"), this Registration Statement also covers such additional and indeterminate number of securities as may become issuable pursuant to the provisions of the Sema4 Holdings Corp. 2021 Equity Incentive Plan (the "2021 EIP") and the Sema4 Holdings Corp. 2021 Employee Stock Purchase Plan (the "2021 ESPP") by reason of any stock dividend, stock split, recapitalization or any other similar transaction effected without the Registrant's receipt of consideration which results in an increase in the number of outstanding shares of Class A common stock, par value \$0.0001 per share (the "Class A Common Stock"), of Sema4 Holdings Corp., a Delaware corporation (the "Registrant").

(2) Represents additional shares of Class A Common Stock that may be issued under the 2021 EIP resulting from the automatic annual increase in the number of authorized shares reserved and available for issuance under the 2021 EIP. The increase was effective as of January 1, 2022.

(3) Estimated pursuant to Rules 457(c) and (h) under the Securities Act solely for the purpose of calculating the registration fee. The price of \$3.16 per share represents the average high and low sales prices of the Class A Common Stock as quoted on the Nasdaq Global Select Market on January 21, 2022.

(4) Represents additional shares of Class A Common Stock reserved for issuance under the 2021 ESPP resulting from the automatic annual increase in the number of authorized shares reserved and available for issuance under the 2021 ESPP. The increase was effective as of January 1, 2022.

(5) Estimated solely for the purpose of calculating the registration fee in accordance with Rules 457(c) and (h) under the Securities Act and based upon the average of the high and low sales prices of the Class A Common Stock as quoted on the Nasdaq Global Select Market on January 21, 2022, multiplied by 85%.

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The Registration Statement shall become effective upon filing in accordance with Rule 462 under the Securities Act.

## EXPLANATORY NOTE

### REGISTRATION OF ADDITIONAL SHARES PURSUANT TO GENERAL INSTRUCTION E OF FORM S-8

Sema4 Holdings Corp., a Delaware corporation (the “Registrant”), has previously registered (A) pursuant to a Registration Statement on Form S-8 filed with the Securities and Exchange Commission (the “SEC”) on September 27, 2021 (Registration No. 333-259815) (including the reoffer prospectus (the “Prior Reoffer Prospectus”) contained therein, the “First Prior Registration Statement”) (i) 32,734,983 shares of Class A common stock, par value \$0.0001 per share (the “Class A Common Stock”), of the Registrant reserved for issuance under the Sema4 Holdings Corp. 2021 Equity Incentive Plan (the “2021 EIP”); (ii) 4,804,011 shares of Class A Common Stock reserved for issuance under the Sema4 Holdings Corp. 2021 Employee Stock Purchase Plan (the “2021 ESPP”); (iii) 28,880,501 shares of Class A Common Stock issuable upon the exercise of stock options granted under the Mount Sinai Genomics, Inc. 2017 Equity Incentive Plan (the “2017 EIP”); and (iv) 1,847,920 shares of Class A Common Stock (the “Earn-Out RSU Shares”) issuable upon the vesting of certain RSU awards (the “Earn-Out RSUs”) that were expected to be granted to certain former equity award holders of Sema4 and certain employees of the Registrant pursuant to the terms of that certain Agreement and Plan of Merger, dated as of February 9, 2021 (as amended, the “Merger Agreement”), by and among CM Life Sciences, Inc., S-IV Sub, Inc. and Mount Sinai Genomics, Inc. d/b/a Sema4 (“Sema4”), and outside of the 2021 EIP; and (B) pursuant to a Registration Statement on Form S-8 filed with the SEC on October 25, 2021 (Registration No. 333-260481) (the “Second Prior Registration Statement,” and together with the First Prior Registration Statement, the “Prior Registration Statements”) an additional 841,844 shares of Class A Common Stock issuable upon the vesting of certain additional Earn-Out RSUs that were expected to be granted to certain former equity award holders of Sema4 and certain employees of the Registrant pursuant to the terms of that certain Merger Agreement.

Pursuant to General Instruction E of Form S-8, the Registrant is filing this Registration Statement on Form S-8 (this “Registration Statement”) with the SEC to register additional 14,554,729 shares of Class A Common Stock which may be offered and sold pursuant to the 2021 EIP and the 2021 ESPP, in connection with increases in the number of shares available under each of the 2021 EIP and the 2021 ESPP, pursuant to the evergreen provisions included therein. This Registration Statement hereby incorporates by reference the contents of the Prior Registration Statements, except to the extent supplemented, amended or superseded by the information set forth herein.

Pursuant to General Instruction E of Form S-8, this Registration Statement also includes a revised prospectus (the “Reoffer Prospectus”) prepared in accordance with General Instruction C of Form S-8 and in accordance with the requirements of Part I of Form S-3, which supersedes and replaces the Prior Reoffer Prospectus in its entirety. This Reoffer Prospectus may be used for the reoffer and resale of shares of Class A Common Stock on a continuous or delayed basis that may be deemed to be “control securities” within the meaning of the Securities Act of 1933, as amended (the “Securities Act”), and the rules and regulations promulgated thereunder, that are issuable to certain of the Registrant’s directors and executive and other officers identified in the Reoffer Prospectus. The number of shares of Class A Common Stock included in the Reoffer Prospectus represents shares of Class A Common Stock (i) issuable to the selling stockholders pursuant to Earn-Out RSUs that have been or may be granted pursuant to the Merger Agreement and outside of the 2021 EIP and (ii) issued or issuable to the selling stockholders pursuant to awards granted under the 2021 EIP subsequent to the filing of the Prior Reoffer Prospectus, and does not necessarily represent a present intention to sell any or all such shares of Class A Common Stock. The number of shares of Class A Common Stock to be offered or resold by means of the Reoffer Prospectus by the selling stockholders, and any other person with whom any of them is acting in concert for the purpose of selling Class A Common Stock, may not exceed, during any three-month period, the amount specified in Rule 144(e) under the Securities Act.



**Sema4 Holdings Corp.**  
**8,505,596 Shares of Class A Common Stock**

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This reoffer prospectus (this “Reoffer Prospectus”) relates to the offer and sale from time to time by the selling stockholders named in this Reoffer Prospectus (the “Selling Stockholders”), or their permitted transferees, of up to 8,505,596 shares of Class A common stock, par value \$0.0001 per share (“Class A Common Stock”), of Sema4 Holdings Corp., a Delaware corporation. This Reoffer Prospectus covers (i) 1,921,064 shares of Class A Common Stock issuable to each Selling Stockholder upon the vesting of the Earn-Out RSUs (as defined below) that have been or may be granted by us to the Selling Stockholders pursuant to the earn-out provisions of the Merger Agreement (as defined below) and outside the Sema4 Holdings Corp. 2021 Equity Incentive Plan (the “2021 EIP”) and (ii) 6,584,532 shares of Class A Common Stock issued or issuable to each Selling Stockholder upon the exercise or vesting of certain option, restricted stock unit (“RSU”) and stock bonus awards granted by us to the Selling Stockholders under the 2021 EIP (the “2021 EIP Awards”). We are not offering any shares of Class A Common Stock and will not receive any proceeds from the sale of the shares of Class A Common Stock by the Selling Stockholders pursuant to this Reoffer Prospectus. The Selling Stockholders are certain of our directors and executive and other officers, each of whom is an “affiliate” of our company (as defined in Rule 405 under the Securities Act of 1933, as amended (the “Securities Act”)).

Subject to the satisfaction of any conditions to vesting of the shares of Class A Common Stock offered hereby pursuant to the terms of the relevant Earn-Out RSU or 2021 EIP Award agreements, and subject to the expiration of any lock-up agreements described herein, the Selling Stockholders may from time to time sell, transfer or otherwise dispose of any or all of the shares of Class A Common Stock covered by this Reoffer Prospectus through underwriters or dealers, directly to purchasers (or a single purchaser) or through broker-dealers or agents. If underwriters or dealers are used to sell the shares of Class A Common Stock, we will name them and describe their compensation in a prospectus supplement. The shares of Class A Common Stock may be sold in one or more transactions at fixed prices, prevailing market prices at the time of sale, prices related to the prevailing market prices, varying prices determined at the time of sale or negotiated prices. We do not know when or in what amount the Selling Stockholders may offer the shares of Class A Common Stock for sale. The Selling Stockholders may sell any, all or none of the shares of Class A Common Stock offered by this Reoffer Prospectus. See “Plan of Distribution” beginning on page 14 for more information about how the Selling Stockholders may sell or dispose of the shares of Class A Common Stock covered by this Reoffer Prospectus. The Selling Stockholders will bear all sales commissions and similar expenses. We will bear all expenses of registration incurred in connection with this offering, including any other expenses incurred by us in connection with the registration and offering that are not borne by the Selling Stockholders.

Shares of Class A Common Stock that have or will be issued pursuant to the Earn-Out RSUs and 2021 EIP Awards that have been or may be granted to Selling Stockholders will be “control securities” under the Securities Act before their sale under this Reoffer Prospectus. This Reoffer Prospectus has been prepared for the purposes of registering the shares of Class A Common Stock under the Securities Act to allow for future sales by Selling Stockholders on a continuous or delayed basis to the public without restriction, provided that the amount of shares of Class A Common Stock to be offered or resold under this Reoffer Prospectus by each Selling Stockholder or other person with whom he or she is acting in concert for the purpose of selling shares of Class A Common Stock, may not exceed, during any three-month period, the amount specified in Rule 144(e) under the Securities Act.

On July 22, 2021, we consummated the transactions contemplated by that certain Agreement and Plan of Merger, dated as of February 9, 2021 (as amended, the “Merger Agreement”), by and among CM Life Sciences, Inc. (“CMLS” and, after the consummation of the Business Combination (as defined below), “Sema4 Holdings”), S-IV Sub, Inc. (“Merger Sub”) and Mount Sinai Genomics, Inc. d/b/a Sema4 (“Sema4”). In particular, on July 22, 2021, we consummated the merger contemplated by the Merger Agreement, whereby Merger Sub merged with and into Sema4, with Sema4 surviving the merger as a wholly-owned subsidiary of CMLS (the “Merger” and, together with the other transactions contemplated by the Merger Agreement, the “Business Combination”). In connection with the consummation of the Business Combination, CMLS changed its name to “Sema4 Holdings Corp.” and Sema4 changed its name to “Sema4 OpCo, Inc.”

Our Class A Common Stock and public warrants are listed on the Nasdaq Global Select Market (the “Nasdaq”) under the symbols “SMFR” and “SMFRW”, respectively.

**We are an “emerging growth company” under federal securities laws and are subject to reduced public company reporting requirements. Investing in our Class A Common Stock involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading “Risk Factors” on page 11 of this Reoffer Prospectus and under similar headings in the documents that are incorporated by reference into this Reoffer Prospectus, as well as “Cautionary Note Regarding Forward-Looking Statements” on page 7 of this Reoffer Prospectus.**

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

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The date of this Reoffer Prospectus is January 25, 2022.

TABLE OF CONTENTS

	<u>Page</u>
<a href="#">About This Prospectus</a>	<u>5</u>
<a href="#">Where You Can Find More Information</a>	<u>5</u>
<a href="#">Incorporation of Certain Information by Reference</a>	<u>5</u>
<a href="#">Cautionary Note Regarding Forward-Looking Statements</a>	<u>6</u>
Prospectus Summary	<u>7</u>
Risk Factors	<u>10</u>
<a href="#">Determination of Offering Price</a>	<u>10</u>
<a href="#">Use of Proceeds</a>	<u>10</u>
<a href="#">Description of Securities Being Offered</a>	<u>10</u>
<a href="#">Selling Stockholders</a>	<u>10</u>
<a href="#">Plan of Distribution</a>	<u>13</u>
<a href="#">Legal Matters</a>	<u>14</u>
<a href="#">Experts</a>	<u>14</u>

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You should rely only on the information contained or incorporated by reference in this Reoffer Prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. Neither we nor the Selling Stockholders are making 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 Reoffer Prospectus is accurate only as of the date hereof. Additionally, any information we have incorporated by reference in this Reoffer Prospectus is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this Reoffer Prospectus or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since that date.

When used in this Reoffer Prospectus, references to the “Company,” “we,” “us” or “our” refers to (i) Sema4 prior to the consummation of the Business Combination (the “Closing,” and such date of the consummation of the Business Combination, the “Closing Date”) and (ii) Sema4 Holdings and its subsidiary following the Closing.

## ABOUT THIS PROSPECTUS

This Reoffer Prospectus contains important information you should know before investing, including important information about the Company and the securities being offered. You should carefully read this Reoffer Prospectus, as well as the additional information contained in the documents described under “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this Reoffer Prospectus, and in particular the periodic and current reporting documents we file with the Securities and Exchange Commission (the “Commission”). We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This Reoffer Prospectus is not an offer to sell these securities, and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

You should not assume that the information in this Reoffer Prospectus or any documents we incorporate by reference herein or therein is accurate as of any date other than the date on the front of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

## WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other documents with the Commission under the U.S. Securities Exchange Act of 1934, as amended (the “Exchange Act”). The Commission maintains a website that contains reports, proxy and information statements and other information regarding issuers, including the Company, that file electronically with the Commission. You may obtain copies of the registration statement and its exhibits and the other documents that we file with the Commission at [www.sec.gov](http://www.sec.gov).

We also make these documents available on the investor relations portion of our website at [www.sema4.com](http://www.sema4.com). Our website and the information contained or connected to our website is not incorporated by reference in this Reoffer Prospectus, and you should not consider it part of this Reoffer Prospectus. Our principal executive office is located at 333 Ludlow Street, North Tower, 8th Floor, Stamford, Connecticut 06902, and can be reached by telephone at (800) 298-6470.

## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The Commission rules permit us to incorporate by reference information in this Reoffer Prospectus. This means that we can disclose important information to you by referring you to another document filed separately with the Commission. The information incorporated by reference is considered to be part of this Reoffer Prospectus, except for information superseded by information contained in this Reoffer Prospectus itself or in any subsequently filed incorporated document. This Reoffer Prospectus incorporates by reference the documents set forth below that we have previously filed with the Commission, other than information in such documents that is deemed to be furnished and not filed. These documents contain important information about the Company and its business and financial condition.

- (a) the Company’s Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2021, June 30, 2021, and September 30, 2021, filed with the Commission on [May 24, 2021](#), [July 21, 2021](#), and [November 15, 2021](#), respectively (excluding the unaudited financial statements of CMLS included therein, which are comprised of the condensed balance sheets of CMLS as of June 30, 2021, March 31, 2021, and December 31, 2020 (audited); the related condensed statements of operations, condensed statements of changes in stockholders’ equity, and condensed statements of cash flows for the three and six months ended June 30, 2021 and the three months ended March 31, 2021; and the related notes to such financial statements (the “CMLS Unaudited Financial Statements” and, together with the CMLS Audited Financial Statements (as defined below), the “CMLS Financial Statements”));
- (b) the Company’s Current Reports on Form 8-K filed with the Commission on [February 11, 2021](#), [May 5, 2021](#), [July 19, 2021](#), [July 22, 2021](#), [July 28, 2021](#), as amended on [August 16, 2021](#) (excluding the CMLS Financial Statements incorporated by reference therein), [August 16, 2021](#) (but only with respect to Item 4.01 thereto), [October 14, 2021](#), [December 16, 2021](#) and January 18, 2022 (but only with respect to Items 1.01, 3.02, 5.02 and 9.01 thereto);
- (c) the Company’s Final Prospectus filed with the Commission on August 12, 2021 pursuant to Rule 424(b) promulgated under the Securities Act, as a part of the Registration Statement on [Form S-1](#) (File No. 333-258467) (the “Resale S-1”) under the Securities Act, initially filed with the Commission on August 4, 2021 (excluding (i) the audited financial statements of CMLS included therein, which are comprised of the balance sheet of CMLS as of December 31, 2020; the related statement of operations, statement of changes in stockholders’ equity, and statement of cash flows for the period from July 10, 2020 (inception) through December 31,

2020; the related notes to such financial statements; and the accompanying report of independent registered public accounting firm issued with respect thereto (the “CMLS Audited Financial Statements”), and (ii) the CMLS Unaudited Financial Statements included therein); and

- (d) the description of the Company’s Class A Common Stock contained in the Resale S-1, including any amendments or reports filed for the purpose of updating such description.

All documents subsequently filed by the Company with the Commission pursuant to Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act, prior to the filing of a post-effective amendment to the Registration Statement of which this Reoffer Prospectus forms a part which indicates that all securities offered have been sold or which deregisters all securities then remaining unsold, shall be deemed incorporated by reference into this Reoffer Prospectus and to be a part hereof from the date of the filing of such documents, except that information furnished to the Commission under Item 2.02 or Item 7.01 in Current Reports on Form 8-K and any exhibit relating to such information, shall not be deemed to be incorporated by reference in this Reoffer Prospectus.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference in this Reoffer Prospectus shall be deemed to be modified or superseded for purposes of this Reoffer Prospectus to the extent that a statement contained in this Reoffer Prospectus, or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this Reoffer Prospectus, modifies or supersedes such earlier statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Reoffer Prospectus.

The Company undertakes to provide without charge to each person, including any beneficial owner, to whom a copy of this Reoffer Prospectus is delivered, upon written or oral request of any such person, a copy of any and all of the information that has been incorporated by reference in this Reoffer Prospectus but not delivered with this Reoffer Prospectus other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into the information that this Reoffer Prospectus incorporates. Documents incorporated by reference in this Reoffer Prospectus may be obtained by requesting them in writing or by telephone from us at:

Sema4 Holdings Corp.  
333 Ludlow Street, North Tower, 8th Floor,  
Stamford, Connecticut 06902  
Tel.: (800) 298-6470

#### **CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This Reoffer Prospectus contains forward-looking statements within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. These statements are based on the current expectations and beliefs of our management, and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. These forward-looking statements include statements about our future financial and operating results; the benefits of the Business Combination; statements of the plans, strategies and objectives of our management for our future operations; and statements regarding future economic conditions or performance. Forward-looking statements may contain words such as “will be,” “will,” “expect,” “anticipate,” “continue,” “project,” “believe,” “plan,” “could,” “estimate,” “forecast,” “guidance,” “intend,” “may,” “plan,” “possible,” “potential,” “predict,” “pursue,” “should,” “target” or similar expressions, and include the assumptions that underlie such statements. These statements include, but are not limited to, statements about:

- our estimates of the sufficiency of our existing capital resources combined with future anticipated cash flows to finance our operating requirements;
- our expected losses;
- our expectations for incurring capital expenditures to expand our research and development and manufacturing capabilities;
- unforeseen circumstances or other disruptions to normal business operations, including supply chain interruptions and manufacturing constraints, arising from or related to COVID-19;
- our expectations for generating revenue or becoming profitable on a sustained basis;
- our expectations or ability to enter into service, collaboration and other partnership agreements;
- our expectations or ability to build our own commercial infrastructure to scale market and sell our products;

- actions or authorizations by the U.S. Food and Drug Administration or other regulatory authorities;
- risks related to governmental regulation and other legal obligations, including privacy, data protection, information security, consumer protection, and anti-corruption and anti-bribery;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- our ability to compete against existing and emerging technologies;
- our stock price and its volatility
- our ability to attract and retain key personnel;
- third-party payor reimbursement and coverage decisions;
- our reliance on third-party laboratories and service providers for our test volume in connection with our diagnostic solutions and data programs;
- our expectations for future capital requirements; and
- our ability to successfully implement our business strategy.

Factors that could cause the actual results to differ materially from those described in the forward-looking statements include those set forth in the risk factors included in this Reoffer Prospectus. Any forward-looking statements made in this Reoffer Prospectus are qualified in their entirety by the forward-looking statements contained or referred to in this section, and there is no assurance that the actual results or developments anticipated by us will be realized. All subsequent written and oral forward-looking statements concerning us, the Business Combination or other matters attributable to us or any person acting on our behalf are expressly qualified in their entirety by the forward-looking statements above. Except to the extent required by applicable law, we are under no obligation (and expressly disclaim any such obligation) to update or revise these forward-looking statements whether as a result of new information, future events, or otherwise.

You should read this Reoffer Prospectus, the documents that incorporated by reference herein, and the documents we have filed with the Commission as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.



## PROSPECTUS SUMMARY

This Reoffer Prospectus is part of a registration statement that we filed with the Commission. We have provided to you in this Reoffer Prospectus a general description of the Selling Stockholders and the distribution of the shares. To the extent there is a conflict between the information contained in this Reoffer Prospectus and any of our subsequent filings with the Commission, the information in the document having the later date shall modify or supersede the earlier statement.

As permitted by the rules and regulations of the Commission, the registration statement of which this Reoffer Prospectus forms part includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the Commission at the Commission's website or at the Commission's offices described above under the heading "Incorporation of Certain Information by Reference" if necessary.

### Company Overview

We are a patient-centered, health intelligence company with a mission to use artificial intelligence, or AI, and machine learning to enable personalized medicine for all. Our integrated information platform leverages longitudinal patient data, AI-driven predictive modeling, and genomics in combination with other molecular and high-dimensional data in our efforts both to deliver better outcomes for patients and to transform the practice of medicine, including how disease is diagnosed, treated, and prevented.

We have established one of the largest, most comprehensive, and fastest growing integrated health information platforms, collecting and leveraging genomic and clinical data in partnership with patients, healthcare providers and an extensive ecosystem of life science industry contributors. We are now generating and processing over 39 petabytes of data per month, growing by almost 1.4 petabytes per month, and maintain a database that includes 12 million de-identified clinical records, many with genomic profiles, integrated in a way that enables physicians to proactively diagnose and manage disease. This expanding database is a virtuous cycle of data: new data enables us to further develop, train, and refine predictive models and drive differentiated insights. We deploy these models and insights through our next generation diagnostic and research solutions and portals to support clinicians and researchers and engage patients, all of which interactions generate more data to continue the cycle.

Today, by providing differentiated insights through genomics testing solutions to physicians and patients across the United States in areas such as reproductive health, or Women's Health, population health, and oncology, or Oncology, we are reimbursed by payors, providers, and patients for providing these services. In collaboration with pharmaceutical and biotech, or Biopharma, companies, we receive payments for a broad range of services relating to the aggregated data on our information platform, such as consenting and recontacting patients, the development and implementation of a wide range of predictive models, including drug discovery programs, conducting real-world evidence studies, and aiding in the identification and recruitment of patients into clinical trials. Over the next several years, we expect to focus on expanding the revenue from our health system and Biopharma partners, while also working to continue to grow the volumes and revenues from our genomics testing solutions.

While there are many companies seeking to harness the potential of "big data" to address the challenges within the healthcare ecosystem, we believe that few have the scale of our company combined with our revenue-generating genomics testing business and origins as a company conceived and nurtured within a world-class health system. These characteristics have enabled us to build a significant and highly differentiated technological and informational asset positioned to drive precision medicine into the standard of care in an unparalleled way. The mailing address of our principal executive office is located at 333 Ludlow Street, North Tower, 8th Floor Stamford, Connecticut 06902, and can be reached by telephone at (800) 298-6470.

### Recent Developments

On July 22, 2021, we consummated the Merger, whereby Merger Sub merged with and into Sema4, with Sema4 surviving the Merger as a wholly-owned subsidiary of CMLS. In connection with the consummation of the Business Combination, CMLS changed its name to "Sema4 Holdings Corp." and Sema4 changed its name to "Sema4 OpCo, Inc."

### The Offering

This Reoffer Prospectus relates to the public offering by the Selling Stockholders listed in this Reoffer Prospectus of up to (i) 1,921,064 shares of Class A Common Stock issuable to each Selling Stockholder upon the vesting of the Earn-Out RSUs that have been granted by the Company to the Selling Stockholders, as well as Earn-Out RSUs that may be granted by the Company to the Selling Stockholders in connection with a reallocation of Earn-Out RSU Shares (as defined below), in each case, pursuant to the earn-out provisions of the Merger Agreement and outside of the 2021 EIP and (ii) 6,584,532 shares of Class A Common Stock issued or issuable to each Selling Stockholder upon the exercise or vesting of the 2021 EIP Awards granted by the Company to the Selling Stockholders under the 2021 EIP. Subject to the satisfaction of any conditions to vesting of the shares of Class A Common Stock offered hereby pursuant to the terms of the relevant Earn-Out RSU or 2021 EIP Award agreements, and subject to the expiration of any lock-up agreements described herein, the Selling Stockholders may from time to time sell, transfer or otherwise dispose of any or all of the shares of Class A Common Stock covered by this Reoffer Prospectus through underwriters or dealers, directly to purchasers (or a single purchaser) or through broker-dealers or agents. We will receive none of the proceeds from the sale of the shares of Class A Common Stock by the Selling Stockholders. The Selling Stockholders will bear all sales commissions and similar expenses in connection with this offering. We will bear all expenses of registration incurred in connection with this offering, as well as any other expenses incurred by us in connection with the registration and offering that are not borne by the Selling Stockholders.

## **RISK FACTORS**

Investing in shares of our Class A Common Stock involves a high degree of risk. Investors should carefully consider the risks we have described as set forth under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2021, filed with the Commission on [November 15, 2021](#), which is incorporated by reference herein, and subsequent reports filed with the Commission, together with the financial and other information contained or incorporated by reference in this Reoffer Prospectus. If any of the events or developments we have described occur, our business, financial condition, or results of operations could be materially or adversely affected. As a result, the market price of our Class A Common Stock could decline, and investors could lose all or part of their investment. The risks and uncertainties we have described are not the only risks and uncertainties that we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. The risks we have described also include forward-looking statements, and our actual results may differ substantially from those discussed in these forward-looking statements. See “Cautionary Note Regarding Forward-Looking Statements.”

## **DETERMINATION OF OFFERING PRICE**

The Selling Stockholders will determine at what price they may sell the offered shares of Class A Common Stock, and such sales may be made at prevailing market prices or at privately negotiated prices. See “Plan of Distribution” below for more information.

## **USE OF PROCEEDS**

We will not receive any proceeds from the sale of shares of our Class A Common Stock by the Selling Stockholders.

## **DESCRIPTION OF SECURITIES BEING OFFERED**

The information set forth under the caption “Description of Securities” in the Resale S-1 is incorporated herein by reference.

## **SELLING STOCKHOLDERS**

The table below sets forth information concerning the resale of the shares by the Selling Stockholders. We will not receive any proceeds from the resale of the shares by the Selling Stockholders.

The table below sets forth, as of December 31, 2021 (the “Determination Date”), (i) the name of each person who is offering the resale of shares by this Reoffer Prospectus; (ii) the number of shares (and the percentage, if 1% or more) of Class A Common Stock beneficially owned (determined in the manner described in footnote (1) to the table below) by each person; (iii) the number of shares that each Selling Stockholder may offer for sale from time to time pursuant to this Reoffer Prospectus, whether or not such Selling Stockholder has a present intention to do so; and (iv) the number of shares (and the percentage, if 1% or more) of Class A Common Stock each person will own after the offering, assuming they sell all of the shares offered. Unless otherwise indicated, beneficial ownership is direct and the person indicated has sole voting and investment power. The address for each Selling Stockholder listed in the table below is c/o Sema4 Holdings Corp., 333 Ludlow Street, North Tower, 8th Floor Stamford, Connecticut 06902.

The shares offered by the Selling Stockholders hereunder consist of (i) up to 1,921,064 shares of Class A Common Stock issuable to each Selling Stockholder upon the vesting of the Earn-Out RSUs that have been granted by us to the Selling Stockholders, as well as Earn-Out RSUs that may be granted by us to the Selling Stockholders in connection with a reallocation of Earn-Out RSU Shares as described below, in each case, pursuant to the earn-out provisions of the Merger Agreement and outside of the 2021 EIP and (ii) up to 6,584,532 shares of Class A Common Stock (the “2021 EIP Award Shares”) issued or issuable to each Selling Stockholder upon the exercise or vesting of the 2021 EIP Awards granted by us to the Selling Stockholders under the 2021 EIP.

Pursuant to the earn-out provisions of the Merger Agreement, we may issue an aggregate of up to 19,021,576 shares of Class A Common Stock upon the occurrence of certain triggering events provided for in the Merger Agreement, which shares are comprised of an initial allocation of up to 16,331,812 shares of Class A Common Stock (the “Earn-Out Shares”) issuable to certain former stockholders of Sema4 and up to 2,689,764 shares of Class A Common Stock (the “Earn-Out RSU Shares”) issuable upon the vesting of certain RSU awards (“Earn-Out RSUs”) that have been granted to certain former equity award holders of Sema4 and certain employees of our company. As of the date of this Reoffer Prospectus, an aggregate of 2,669,679 Earn-Out RSUs are outstanding, including 1,921,064 Earn-Out RSUs owned by the Selling Stockholders. In the event any Earn-Out RSUs are forfeited following the Closing (for example, as a result of an Earn-Out RSU recipient no longer being an employee of our company), the Merger Agreement provides for a forfeiture pool in respect of the Earn-Out RSU Shares that were originally allocated to such forfeited Earn-Out RSUs, with such Earn-Out RSU Shares becoming available for issuance to the other recipients of Earn-Out Shares and Earn-Out RSUs. In the case of each Selling Stockholder, the table below includes

the Earn-Out RSU Shares underlying the Earn-Out RSU such Selling Stockholder that have been granted in respect of the initial allocation of Earn-Out RSU Shares (such Selling Stockholder's "Allocated Earn-Out RSU Shares" and such Selling Stockholder's "Allocated Earn-Out RSU", respectively), as well as such Selling Stockholder's pro rata portion of the reallocated Earn-Out RSU Shares underlying an Earn-Out RSU granted to such Selling Stockholder (such Selling Stockholder's "Reallocated Earn-Out RSU Shares"), assuming that 100% of the Allocated Earn-Out RSUs (other than such Selling Stockholder's Allocated Earn-Out RSU) are forfeited after the Closing.

The Selling Stockholders identified below may have sold, transferred or otherwise disposed of some or all of their shares since the date on which the information in the following table is presented in transactions exempt from or not subject to the registration requirements of the Securities Act. Information concerning the Selling Stockholders may change from time to time and, if necessary, we will amend or supplement this Reoffer Prospectus accordingly. We cannot give an estimate as to the number of shares of Class A Common Stock that will actually be held by the Selling Stockholders upon termination of this offering because the Selling Stockholders may offer some or all of their Class A Common Stock under the offering contemplated by this Reoffer Prospectus or acquire additional shares of Class A Common Stock. The total number of shares that may be sold hereunder will not exceed the number of shares offered hereby. Please read the section entitled "Plan of Distribution" in this Reoffer Prospectus.

Name	Shares of Class A Common Stock			
	Number Beneficially Owned Prior to Offering <sup>(1)</sup>	Number Registered for Sale Hereby	Number Beneficially Owned After Offering	Percent Owned After Offering <sup>(2)</sup>
<b>Executive Officers</b>				
Anthony Prentice <sup>(3)</sup>	2,490,435	352,681	2,137,754	*
Daniel Clark <sup>(4)</sup>	1,640,276	266,068	1,374,208	*
Eric Schadt <sup>(5)</sup>	10,184,779	2,974,096	7,210,683	3.0%
James M. Coffin <sup>(6)</sup>	3,586,613	911,010	2,675,603	1.1%
Isaac Ro <sup>(7)</sup>	1,809,048	1,809,048	—	—
Kareem Saad <sup>(8)</sup>	559,149	559,149	—	—
Karen White <sup>(9)</sup>	206,465	142,056	64,409	*
Shawn Assad <sup>(10)</sup>	299,177	299,177	—	—
<b>Directors</b>				
Dennis Charney <sup>(11)</sup>	—	—	—	—
Eli Casdin <sup>(12)</sup>	22,765,541	35,122	22,730,419	9.4%
Emily Leproust <sup>(13)</sup>	226,788	35,122	191,666	*
Jason Ryan <sup>(14)</sup>	874,479	874,479	—	—
Joshua Ruch <sup>(15)</sup>	70,244	70,244	—	—
Keith Meister <sup>(16)</sup>	17,730,419	—	17,730,419	7.3%
Michael Pellini <sup>(17)</sup>	70,244	70,244	—	—
Nat Turner <sup>(18)</sup>	226,788	35,122	191,666	*
Rachel Sherman <sup>(19)</sup>	253,587	71,978	181,609	*
<b>TOTALS</b>	<b>62,994,032</b>	<b>8,505,596</b>	<b>54,488,436</b>	<b>22.5%</b>

\* Less than 1%

- (1) The numbers of shares of Class A Common Stock reflect all Earn-Out RSU Shares and all 2021 EIP Award Shares of each Selling Stockholder (including both shares beneficially owned on the Determination Date and shares which the Selling Stockholder has a contingent right to receive).
- (2) Assumes all of the shares of Class A Common Stock being offered are sold in the offering, that shares of Class A Common Stock beneficially owned by such Selling Stockholder on the Determination Date but not being offered pursuant to this prospectus (if any) are not sold, and that no additional shares are purchased or otherwise acquired other than pursuant to the Earn-Out RSUs and 2021 EIP Awards relating to the shares being offered.
- (3) Includes 2,157,145 shares underlying options to purchase common stock that are exercisable and RSUs that vest within 60 days of December 31, 2021. Shares hereby offered consist of (A) Earn-Out RSU Shares consisting of (i) 207,462 Allocated Earn-Out RSU Shares and (ii) 33,880 Reallocated Earn-Out RSU Shares and (B) 111,339 2021 EIP Award Shares.
- (4) Includes 298,000 shares of common stock and 1,095,142 shares underlying options to purchase common stock that are exercisable and RSUs that vest within 60 days of December 31, 2021. Shares hereby offered consist of (A) Earn-Out RSU Shares consisting of (i) 133,359 Allocated Earn-Out RSU Shares and (ii) 21,827 Reallocated Earn-Out RSU Shares and (B) 110,882 2021 EIP Award Shares.
- (5) Includes 7,484,116 shares underlying options to purchase common stock that are exercisable and RSUs that vest within 60 days of December 31, 2021. Shares hereby offered consist of (A) Earn-Out RSU Shares consisting of (i) 741,153 Allocated Earn-Out RSU Shares and (ii) 120,551 Reallocated Earn-Out RSU Shares and (B) 2,112,392 2021 EIP Award Shares. Mr. Schadt is member of Sema4 Holdings Corp.'s board of directors.
- (6) Includes 2,759,035 shares underlying options to purchase common stock that are exercisable and RSUs that vest within 60 days of December 31, 2021. Shares hereby offered consist of (A) Earn-Out RSU Shares consisting of (i) 259,804 Allocated Earn-Out RSU Shares and (ii) 42,355 Reallocated Earn-Out RSU Shares and (B) 608,851 2021 EIP Award Shares.
- (7) Includes 395,294 shares underlying options to purchase common stock that are exercisable and RSUs that vest within 60 days of December 31, 2021. Shares hereby offered consist of (A) Earn-Out RSU Shares consisting of (i) 197,607 Allocated Earn-Out RSU Shares and (ii) 32,119 Reallocated Earn-Out RSU Shares and (B) 1,579,322 2021 EIP Award Shares.
- (8) Includes 125,684 shares underlying options to purchase common stock that are exercisable and RSUs that vest within 60 days of December 31, 2021. Shares hereby offered consist of (A) Earn-Out RSU Shares consisting of (i) 62,875 Allocated Earn-Out RSU Shares and (ii) 10,302 Reallocated Earn-Out RSU Shares and (B) 485,972 2021 EIP Award Shares.
- (9) Includes 80,466 shares underlying options to purchase common stock that are exercisable and RSUs that vest within 60 days of December 31, 2021. Shares hereby offered consist of (A) Earn-Out RSU Shares consisting of (i) 17,964 Allocated Earn-Out RSU Shares and (ii) 2,950 Reallocated Earn-Out RSU Shares and (B) 121,142 2021 EIP Award Shares.
- (10) Includes 49,773 shares underlying options to purchase common stock that are exercisable and RSUs that vest within 60 days of December 31, 2021. Shares hereby offered consist of 299,177 2021 EIP Award Shares.
- (11) Mr. Charney is a member of Sema4 Holdings Corp.'s board of directors.
- (12) Includes 5,000,000 shares of common stock held indirectly by Casdin Partners Master Fund L.P., and 10,993,750 shares of common stock and 6,736,669 shares of common stock underlying warrants held indirectly by CMLS Holdings LLC. Shares hereby offered consist of 35,122 2021 EIP Award Shares. The Board of Managers of CMLS Holdings LLC, is comprised of Mr. Eli Casdin and Mr. Keith Meister who share voting and investment discretion with respect to the common stock held of record by CMLS Holdings LLC. C-LSH LLC and M-LSH LLC are the members of CMLS Holdings LLC, and Mr. Casdin and Mr. Meister are the managing members of C-LSH LLC and M-LSH LLC, respectively. As such, each of the foregoing may be deemed to have or share beneficial ownership of the common stock held directly by CMLS Holdings LLC. The business address of the Sponsor is c/o Corvex Management LP, 667 Madison Avenue, New York, NY 10065. Mr. Casdin is member of Sema4 Holdings Corp.'s board of directors.
- (13) Consists of 25,000 shares of common stock and 166,666 shares of common stock underlying warrants. Shares hereby offered consist of 35,122 2021 EIP Award Shares. Ms. Leproust is member of Sema4 Holdings Corp.'s board of directors.
- (14) Includes 2,476 shares underlying options to purchase common stock that are exercisable within 60 days of December 31, 2021. Shares hereby offered consist of 874,479 2021 EIP Award Shares. Mr. Ryan is member of Sema4 Holdings Corp.'s board of directors.
- (15) Includes 2,476 shares underlying options to purchase common stock that are exercisable within 60 days of December 31, 2021. Shares hereby offered consist of 70,244 2021 EIP Award Shares. Mr. Ruch is member of Sema4 Holdings Corp.'s board of directors.
- (16) Includes 10,993,750 shares of common stock and 6,736,669 shares of common stock underlying warrants held indirectly by CMLS Holdings LLC. The Board of Managers of CMLS Holdings LLC, is comprised of Mr. Eli Casdin and Mr. Keith Meister who share voting and investment discretion with respect to the common stock held of record by CMLS Holdings LLC. C-LSH LLC and M-LSH LLC are the members of CMLS Holdings LLC, and Mr. Casdin and Mr. Meister are the managing members of C-LSH LLC and M-LSH LLC, respectively. As such, each of the foregoing may be deemed to have or share beneficial ownership of the common stock held directly by CMLS Holdings LLC. The business address of CMLS Holdings LLC is c/o Corvex Management LP, 667 Madison Avenue, New York, NY 10065. Mr. Meister is member of Sema4 Holdings Corp.'s board of directors.
- (17) Includes 2,476 shares underlying options to purchase common stock that are exercisable within 60 days of December 31, 2021. Shares hereby offered consist of 70,244 2021 EIP Award Shares. Mr. Pellini is member of Sema4 Holdings Corp.'s board of directors.
- (18) Consists of 25,000 shares of common stock held by Nat Turner and 166,666 shares of common stock underlying warrants held by NTWJ Holdings, LLC ("NTWJ"). Shares hereby offered consist of 35,122 2021 EIP Award Shares. Mr. Turner is a managing member of NTWJ. The address for NTWJ is 139 Reade Street, New York, New York 10013. Mr. Turner is member of Sema4 Holdings Corp.'s board of directors.

(19) Includes 181,609 shares underlying options to purchase common stock that are exercisable within 60 days of December 31, 2021. Shares hereby offered consist of (A) Earn-Out RSU Shares consisting of (i) 31,659 Allocated Earn-Out RSU Shares and (ii) 5,197 Reallocated Earn-Out RSU Shares and (B) 35,122 2021 EIP Award Shares. Ms. Sherman is member of Sema4 Holdings Corp.'s board of directors.

## **Other Material Relationships with the Selling Stockholders**

### ***Employment Relationships***

We entered into employment agreements with each of Eric Schadt, James Coffin, Daniel Clark, Anthony Prentice, Isaac Ro, Kareem Saad and Karen White prior to and in connection with the Business Combination. Each of Eric Schadt, James Coffin, Anthony Prentice, Isaac Ro, Kareem Saad and Karen White have provided and continue to provide services to the Company commensurate with his or her role, as applicable.

Each of Dr. Schadt, Dr. Coffin, Mr. Clark, Mr. Prentice and Ms. White have agreed that, during the nine-month period following the Closing, he or she will not: (i) sell, offer to sell, contract or agree to sell, hypothecate, pledge, grant any option to purchase or otherwise dispose of or agree to dispose of, directly or indirectly, or establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of Section 16 of the Exchange Act, with respect to any shares of Class A Common Stock, (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of any of such shares, in cash or otherwise, or (iii) publicly announce any intention to effect any transaction specified in clause (i) or (ii).

### ***Indemnification Agreement***

Our amended and restated certificate of incorporation (the "Certificate of Incorporation") contains provisions limiting the liability of directors, and our restated bylaws (the "Bylaws") provide that we will indemnify each of our directors to the fullest extent permitted under Delaware law. The Certificate of Incorporation and Bylaws also provide the board of directors with discretion to indemnify officers and employees when determined appropriate by our board of directors.

We have entered into indemnification agreements with each of our directors and executive officers and certain other key employees. The indemnification agreements provide that we will indemnify each of our directors, executive officers, and such other key employees against any and all expenses incurred by that director, executive officer, or other key employee because of his or her status as one of our directors, executive officers, or other key employees, to the fullest extent permitted by Delaware law, the Certificate of Incorporation and Bylaws. In addition, the indemnification agreements provide that, to the fullest extent permitted by Delaware law, we will advance all expenses incurred by its directors, executive officers, and other key employees in connection with a legal proceeding involving his or her status as a director, executive officer, or key employee.

## **PLAN OF DISTRIBUTION**

The shares of Class A Common Stock covered by this Reoffer Prospectus are being registered by the Company for the account of the Selling Stockholders. The shares of Class A Common Stock offered may be sold from time to time directly by or on behalf of each Selling Stockholder in one or more transactions on the Nasdaq or any other stock exchange on which the Class A Common Stock may be listed at the time of sale, in privately negotiated transactions, or through a combination of such methods, at market prices prevailing at the time of sale, at prices related to such prevailing market prices, at fixed prices (which may be changed) or at negotiated prices. The Selling Stockholders may sell shares through one or more agents, brokers or dealers or directly to purchasers. Such brokers or dealers may receive compensation in the form of commissions, discounts or concessions from the Selling Stockholders and/or purchasers of the shares or both. Such compensation as to a particular broker or dealer may be in excess of customary commissions. The amount of shares of Class A Common Stock to be reoffered or resold under the Reoffer Prospectus by each Selling Stockholder and any other person with whom he or she is acting in concert for the purpose of selling shares of Class A Common Stock, may not exceed, during any three-month period, the amount specified in Rule 144(e) under the Securities Act.

In connection with their sales, a Selling Stockholder and any participating broker or dealer may be deemed to be "underwriters" within the meaning of the Securities Act, and any commissions they receive and the proceeds of any sale of shares may be deemed to be underwriting discounts and commissions under the Securities Act. We are bearing all costs relating to the registration of the shares of Class A Common Stock. Any commissions or other fees payable to brokers or dealers in connection with any sale of the shares will be borne by the Selling Stockholders or other party selling such shares. Sales of the shares must be made by the Selling Stockholders in compliance with all applicable state and federal securities laws and regulations, including the Securities Act. In addition to any shares

sold hereunder. Selling Stockholders may sell shares of Class A Common Stock in compliance with Rule 144. There is no assurance that the Selling Stockholders will sell all or a portion of the shares of Class A Common Stock offered hereby. The Selling Stockholders may agree to indemnify any broker, dealer or agent that participates in transactions involving sales of the shares against certain liabilities in connection with the offering of the shares arising under the Securities Act. We have notified the Selling Stockholders of the need to deliver a copy of this Reoffer Prospectus in connection with any sale of the shares of Class A Common Stock.

The anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares of Class A Common Stock and activities of the Selling Stockholders, which may limit the timing of purchases and sales of any of the shares of Common Stock by the Selling Stockholders and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of Class A Common Stock to engage in passive market-making activities with respect to the shares of Class A Common Stock. Passive market making involves transactions in which a market maker acts as both our underwriter and as a purchaser of shares of Class A Common Stock in the secondary market. All of the foregoing may affect the marketability of the shares of Class A Common Stock and the ability of any person or entity to engage in market-making activities with respect to the shares of Class A Common Stock.

Once sold under the registration statement of which this Reoffer Prospectus forms a part, the shares of Class A Common Stock will be freely tradable in the hands of persons other than our affiliates.

#### **LEGAL MATTERS**

Fenwick & West LLP will issue an opinion regarding the legality of certain of the offered securities.

#### **EXPERTS**

The financial statements of Mount Sinai Genomics, Inc. have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 2 to the financial statements) included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

**PART II**  
**INFORMATION REQUIRED IN THE REGISTRATION STATEMENT**

**Item 3. Incorporation of Documents by Reference.**

The following documents filed by Sema4 Holdings Corp. (the “Registrant”) with the Commission pursuant to the Securities Act and the Securities Exchange Act of 1934, as amended (the “Exchange Act”), are incorporated herein by reference:

- (a) the Registrant’s Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2021, June 30, 2021, and September 30, 2021, filed with the Commission on [May 24, 2021](#), [July 21, 2021](#), and [November 15, 2021](#), respectively (excluding the unaudited financial statements of CMLS included therein, which are comprised of the condensed balance sheets of CMLS as of June 30, 2021, March 31, 2021, and December 31, 2020 (audited); the related condensed statements of operations, condensed statements of changes in stockholders’ equity, and condensed statements of cash flows for the three and six months ended June 30, 2021 and the three months ended March 31, 2021; and the related notes to such financial statements (the “CMLS Unaudited Financial Statements” and, together with the CMLS Audited Financial Statements (as defined below), the “CMLS Financial Statements”));
- (b) the Registrant’s Current Reports on Form 8-K filed with the Commission on [February 11, 2021](#), [May 5, 2021](#), [July 19, 2021](#), [July 22, 2021](#), [July 28, 2021](#), as amended on [August 16, 2021](#) (excluding the CMLS Financial Statements incorporated by reference therein), [August 16, 2021](#) (but only with respect to Item 4.01 thereto), [October 14, 2021](#), and [December 16, 2021](#) and January 18, 2022 (but only with respect to Items 1.01, 3.02, 5.02 and 9.01 thereto);
- (c) the Registrant’s Final Prospectus filed with the Commission on August 12, 2021 pursuant to Rule 424(b) promulgated under the Securities Act, as a part of the Registration Statement on [Form S-1](#) (File No. 333-258467) (the “Resale S-1”) under the Securities Act, initially filed with the Commission on August 4, 2021 (excluding (i) the audited financial statements of CMLS included therein, which are comprised of the balance sheet of CMLS as of December 31, 2020; the related statement of operations, statement of changes in stockholders’ equity, and statement of cash flows for the period from July 10, 2020 (inception) through December 31, 2020; the related notes to such financial statements; and the accompanying report of independent registered public accounting firm issued with respect thereto (the “CMLS Audited Financial Statements”), and (ii) the CMLS Unaudited Financial Statements included therein); and; and
- (d) the description of the Registrant’s Class A Common Stock contained in the Resale S-1, including any amendments or reports filed for the purpose of updating such description.

For the avoidance of doubt, the CMLS Financial Statements, to the extent incorporated by reference in the Prior Registration Statements, are not incorporated herein by reference.

All documents subsequently filed by the Registrant with the Commission pursuant to Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act, prior to the filing of a post-effective amendment to the Registration Statement which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference into this Registration Statement and to be a part hereof from the date of the filing of such documents, except that information furnished to the Commission under Item 2.02 or Item 7.01 in Current Reports on Form 8-K and any exhibit relating to such information, shall not be deemed to be incorporated by reference in this Registration Statement.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference in this Registration Statement shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained in this Registration Statement, or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this Registration Statement, modifies or supersedes such earlier statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Registration Statement.



**Item 8. Exhibits.**

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
4.1	<a href="#">Third Amended and Restated Certificate of Incorporation of Sema4 Holdings Corp.</a>	8-K	001-39482	3.1	July 28, 2021	
4.2	<a href="#">Bylaws of Sema4 Holdings Corp., as currently in effect.</a>	8-K	001-39482	3.2	July 28, 2021	
5.1	<a href="#">Opinion of Fenwick &amp; West LLP.</a>					X
23.1	<a href="#">Consent of Ernst &amp; Young LLP, Independent Registered Public Accounting Firm for Sema4 Holdings Corp.</a>					X
23.2	Consent of Fenwick & West LLP (contained in Exhibit 5.1).					X
24.1	Power of Attorney (included on the signature page of this Registration Statement).					X
99.1	<a href="#">Sema4 Holdings Corp. 2021 Equity Incentive Plan.</a>	8-K	001-39482	10.5	July 28, 2021	
99.2	<a href="#">Form of Stock Option Agreement under the Sema4 Holdings Corp. 2021 Equity Incentive Plan.</a>	8-K	001-39482	10.6	July 28, 2021	
99.3	<a href="#">Form of RSU Agreement under the Sema4 Holdings Corp. 2021 Equity Incentive Plan.</a>	8-K	001-39482	10.7	July 28, 2021	
99.4	<a href="#">Form of Earn-Out RSU Agreement.</a>	8-K	001-39482	10.8	July 28, 2021	
99.5	<a href="#">Sema4 Holdings Corp. 2021 Employee Stock Purchase Plan.</a>	8-K	001-39482	10.9	July 28, 2021	

**SIGNATURES**

Pursuant to the requirements of the Securities Act, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Stamford, State of Connecticut, on the 25th day of January, 2022.

**SEMA4 HOLDINGS CORP.**

By:           /s/ Eric Schadt            
Eric Schadt  
Chief Executive  
Officer

## POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Eric Schadt, Daniel Clark and Jason Ryan, and each of them, as his or her true and lawful attorneys-in-fact, proxies and agents, each with full power of substitution and resubstitution and full power to act without the other, for him or her in any and all capacities, to sign any and all amendments to this registration statement (including post-effective amendments or any abbreviated registration statement and any amendments thereto filed pursuant to Rule 462(b) increasing the number of securities for which registration is sought), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact, proxies and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact, proxies and agents, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof. Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Eric Schadt</u> Eric Schadt	Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	January 25, 2022
<u>/s/ Isaac Ro</u> Isaac Ro	Chief Financial Officer <i>(Principal Financial Officer)</i>	January 25, 2022
<u>/s/ Shawn Assad</u> Shawn Assad	Chief Accounting Officer <i>(Principal Accounting Officer)</i>	January 25, 2022
<u>/s/ Jason Ryan</u> Jason Ryan	Chairman and Director	January 25, 2022
<u>/s/ Dennis Charney</u> Dennis Charney	Director	January 25, 2022
<u>/s/ Eli D. Casdin</u> Eli D. Casdin	Director	January 25, 2022
<u>/s/ Emily Leproust</u> Emily Leproust	Director	January 25, 2022
<u>/s/ Joshua Ruch</u> Joshua Ruch	Director	January 25, 2022
<u>/s/ Keith Meister</u> Keith Meister	Director	January 25, 2022
<u>/s/ Michael Pellini</u> Michael Pellini	Director	January 25, 2022
<u>/s/ Nat Turner</u> Nat Turner	Director	January 25, 2022
<u>/s/ Rachel Sherman</u> Rachel Sherman	Director	January 25, 2022

January 25, 2022

Sema4 Holdings Corp.  
333 Ludlow Street, North Tower, 8th Floor  
Stamford, Connecticut

Ladies and Gentlemen:

At your request, as your counsel, we have examined the Registration Statement on Form S-8 (the "**Registration Statement**") to be filed by Sema4 Holdings Corp., a Delaware corporation (the "**Company**"), with the Securities and Exchange Commission (the "**Commission**") on or about January 25, 2022 in connection with the registration under the Securities Act of 1933, as amended (the "**Securities Act**"), of an aggregate of 14,554,729 shares (the "**Company Shares**") of the Company's Class A Common Stock, \$0.0001 par value per share (the "**Common Stock**"), subject to issuance by the Company (a) upon the exercise or settlement of awards to be granted under the Company's 2021 Equity Incentive Plan (the "**2021 Plan**") pursuant to the provision of the 2021 Plan providing for an automatic annual increase in the number of shares reserved and available for issuance under the 2021 Plan and (b) pursuant to purchase rights to acquire shares of Common Stock to be granted under the Company's 2021 Employee Stock Purchase Plan (the "**Purchase Plan**") and, together with the 2021 Plan, the "**Plans**") pursuant to the provision of the Purchase Plan providing for an automatic annual increase in the number of shares reserved and available for issuance under the Purchase Plan. In addition, the Registration Statement registers the resale of up to 8,505,596 shares (the "**Selling Stockholder Shares**" and, together with the Company Shares, the "**Shares**") of Common Stock issuable to certain selling stockholders (the "**Selling Stockholders**") listed in the reoffer prospectus included in the Registration Statement (the "**Reoffer Prospectus**") upon (i) the vesting of certain restricted stock units ("**RSU**") awards (the "**Earn-Out RSUs**") that have been or may be granted outside the 2021 Plan to the Selling Stockholders pursuant to the earn-out provisions of that certain Agreement and Plan of Merger, dated as of February 9, 2021 (as amended, the "**Merger Agreement**"), by and among CM Life Sciences, Inc., S-IV Sub, Inc. and Mount Sinai Genomics, Inc. d/b/a Sema4 and (ii) the exercise or vesting of certain option, RSU and stock bonus awards granted to the Selling Stockholders under the 2021 Plan (the "**2021 Plan Awards**").

At your request we are providing this letter to express our opinion on the matters set forth below in this letter ("**our opinion**").

In connection with our opinion, we have examined such matters of fact as we have deemed necessary, which included examination of originals or copies of: (a) the Company's Amended and Restated Certificate of Incorporation and Restated Bylaws (collectively, the "**Charter Documents**"), the Plans, the forms of Earn-Out RSU and 2021 Plan Awards, the Registration Statement and the exhibits thereto and the Reoffer Prospectus, (b) certain corporate proceedings of the Company's board of directors (the "**Board**") and the Company's stockholders relating to adoption or approval of the Company Charter Documents, the Plans, the Earn-Out RSUs, the 2021 Plan Awards, and (c) such other documents as we have deemed advisable, and we have examined such questions of law as we have considered necessary.

In our examination of documents for purposes of this opinion, we have assumed, and express no opinion as to, the authenticity and completeness of all documents submitted to us as originals, the genuineness of signatures on documents reviewed by us, the conformity to originals and the completeness of all documents submitted to us as copies, the legal capacity of all parties executing any documents (other than the Company), the lack of any undisclosed termination or modification or waiver of any document, the absence of any extrinsic agreements or documents that might change or affect the interpretation or terms of documents, and the due authorization, execution and delivery of all documents by each party thereto other than the Company. We have also assumed that any certificates or instruments representing the Shares, when issued, will be executed by the Company and by officers of the Company duly authorized to do so. In rendering our opinion, we have also relied upon a certificate of good standing issued by the Delaware Secretary of State with respect to the Company and representations and certifications made to us by the Company, including without limitation representations in a Management Certificate addressed to us of even date herewith that the Company has available a sufficient number of

authorized shares of Common Stock that are not currently outstanding or reserved for issuance under other outstanding securities or plans of the Company, to enable the Company to issue and deliver all of the Shares as of the date of this letter.

We render this opinion only with respect to, and we express no opinion herein concerning the application or effect of the laws of any jurisdiction other than, the existing Delaware General Corporation Law now in effect. We express no opinion with respect to the securities or "blue sky" laws of any state.

Based upon, and subject to, the foregoing, it is our opinion that the Shares have been duly authorized and, when the Shares that may be issued and sold (a) upon the exercise or settlement of awards to be granted under the 2021 Plan, (b) pursuant to purchase rights to acquire shares of Common Stock to be granted under the Purchase Plan, (c) upon the vesting of Earn-Out RSUs to be granted pursuant to the Merger Agreement (including upon the vesting of Earn-Out RSUs to be granted to the Selling Stockholders pursuant to the Merger Agreement), and (d) upon the exercise or vesting of the outstanding 2021 Plan Awards, have been issued and sold by the Company against the Company's receipt of payment therefor (in an amount and type of consideration not less than the par value per Share) in accordance with the terms (including, without limitation, payment and authorization provisions) of the applicable Plan or Earn-Out RSU, and have been duly registered on the books of the transfer agent and registrar for the Shares in the name or on behalf of the holders thereof, such Shares will be validly issued, fully paid and non-assessable.

We consent to the use of this opinion as an exhibit to the Registration Statement and further consent to all references to us, if any, in the Registration Statement, the Reoffer Prospectus and any amendments or supplements thereto. We do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission thereunder. This opinion is intended solely for use in connection with the issuance, sale and resale of the Shares subject to the Registration Statement and the Reoffer Prospectus, and is not to be relied upon for any other purpose. In providing this letter, we are opining only as to the specific legal issues expressly set forth above, and no opinion shall be inferred as to any other matter or matters. This opinion is rendered on, and speaks only as of, the date of this letter first written above, and does not address any potential change in facts or law that may occur after the date of this opinion letter. We assume no obligation to advise you of any fact, circumstance, event or change in the law or the facts that may hereafter be brought to our attention, whether or not such occurrence would affect or modify any of the opinions expressed herein.

Very truly yours,

*/s/ Fenwick & West LLP*

**FENWICK & WEST LLP**

**Consent of Independent Registered Public Accounting Firm**

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (Form S-8) pertaining to the Sema4 Holdings Corp. 2021 Equity Incentive Plan, Sema4 Holdings Corp. 2021 Employee Stock Purchase Plan, and Sema4 Holdings Corp. Earn-out RSU Awards and to the incorporation by reference therein of our report dated May 6, 2021, with respect to the financial statements of Mount Sinai Genomics, Inc. included in the Registration Statement on Form S-1 of Sema4 Holding Corp., filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

New York, NY  
January 25, 2022