

PROSPECTUS SUPPLEMENT NO. 2  
(to Prospectus dated March 28, 2022)



**Sema4 Holdings Corp.**  
**229,657,978 Shares of Common Stock**  
**7,236,667 Warrants to Purchase Shares of Common Stock**  
**21,994,972 Shares of Common Stock Underlying Warrants**

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This prospectus supplement supplements the prospectus dated March 28, 2022 (the “Prospectus”), which forms a part of our registration statement on Form S-1 (No. 333-258467). This prospectus supplement is being filed to update and supplement the information in the Prospectus with the information contained in Items 1.01, 2.01, 3.02, 5.02, 5.03, 8.01 and 9.01, and the related exhibits from our current report on Form 8-K, filed with the Securities and Exchange Commission (the “SEC”) on May 2, 2022. Accordingly, we have attached the information contained in Items 1.01, 2.01, 3.02, 5.02, 5.03, 8.01 and 9.01, and the related exhibits to this prospectus supplement.

The Prospectus and this prospectus supplement relate to the offer and sale from time to time by the selling securityholders named in this prospectus (the “Selling Securityholders”) of (A) up to 229,657,978 shares of our Class A common stock, par value \$0.0001 per share (“Class A common stock” or “common stock”), consisting of (i) up to 29,125,620 shares of our Class A common stock (the “Prior PIPE Shares”) issued in a private placement pursuant to subscription agreements each entered into on February 9, 2021 (the “Prior PIPE Investment”); (ii) up to 11,068,750 shares of our Class A common stock (the “Founder Shares”) issued in connection with the consummation of the Business Combination (as defined below), in exchange for shares of our Class B common stock originally issued in a private placement to CMLS Holdings LLC (the “Former Sponsor”); (iii) up to 182,917,984 shares of our Class A common stock issued or issuable to certain former stockholders and equity award holders of Sema4 (the “Sema4 equity holders”) in connection with or as a result of the consummation of the Business Combination, consisting of (a) up to 149,856,840 shares of our Class A common stock; (b) up to 14,039,568 shares of our Class A common stock issuable upon the exercise or vesting of certain equity awards; and (c) up to 19,021,576 shares of Class A common stock (the “Earn-Out Shares”) that certain Sema4 equity holders have the contingent right to receive upon the achievement of certain vesting conditions; and (iv) up to 7,236,667 shares of our Class A common stock issuable upon the exercise of the private placement warrants (as defined below); and (B) up to 7,236,667 warrants (the “private placement warrants”) originally issued in a private placement to the Former Sponsor and certain of the other Initial Stockholders (as defined in the Prospectus).

In addition, the Prospectus and this prospectus supplement relate to the offer and sale of: (i) up to 14,758,305 shares of our Class A common stock that are issuable by us upon the exercise of 14,758,305 warrants (the “public warrants”) originally issued in our initial public offering (the “IPO”); and (ii) up to 7,236,667 shares of our Class A common stock that are issuable by us upon the exercise of the private placement warrants following the public resale of the private placement warrants by the Selling Securityholders pursuant to the Prospectus and this prospectus supplement.

Our common stock and public warrants are listed on the Nasdaq Global Select Market (the “Nasdaq”) under the symbol “SMFR” and “SMFRW”, respectively. On April 29, 2022, the last reported sales price of our common stock was \$2.15 per share and the last reported sales price of our public warrants was \$0.40 per warrant.

This prospectus supplement updates and supplements the information in the Prospectus and is not complete without, and may not be delivered or utilized except in combination with, the Prospectus, including any amendments

or supplements thereto. This prospectus supplement should be read in conjunction with the Prospectus and if there is any inconsistency between the information in the Prospectus and this prospectus supplement, you should rely on the information in this prospectus supplement.

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

***Investing in our securities involves risks. See the section entitled “Risk Factors” beginning on page 9 of the Prospectus to read about factors you should consider before buying our securities.***

**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 supplement is May 2, 2022**

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

**FORM 8-K**

**CURRENT REPORT**

**Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934**

Date of Report (date of earliest event reported): **May 2, 2022 (April 29, 2022)**

**sema4**

**Sema4 Holdings Corp.**

(Exact name of registrant as specified in its charter)

<b>Delaware</b> (State or other jurisdiction of incorporation or organization)	<b>001-39482</b> (Commission File Number)	<b>85-1966622</b> (I.R.S. Employer Identification No.)
<b>333 Ludlow Street, North Tower, 8th Floor</b> <b>Stamford, Connecticut</b> (Address of Principal Executive Offices)		<b>06902</b> (Zip Code)

**(800) 298-6470**

Registrant's telephone number, including area code  
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Class A common stock, par value \$0.0001 per share	SMFR	The Nasdaq Global Select Market
Warrants to purchase one share of Class A common stock, each at an exercise price of \$11.50 per share	SMFRW	The Nasdaq Global Select Market

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

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

## Introductory Note

As previously announced, on January 18, 2022, Sema4 Holdings Corp. (the “Company” or “Sema4”) entered into an Agreement and Plan of Merger and Reorganization dated January 14, 2022 (as amended, the “Merger Agreement”), by and among the Company, GeneDx, Inc. (“GeneDx”), a wholly-owned subsidiary of OPKO Health, Inc. (“OPKO”), OPKO, Orion Merger Sub I, Inc. (“Merger Sub I”), a wholly-owned subsidiary of the Company, Orion Merger Sub II, LLC (“Merger Sub II” and together with Merger Sub I, “Merger Subs”), a wholly-owned subsidiary of the Company, and GeneDx Holding 2, Inc. (“Holdco”), which provided for, among other things, the Company’s acquisition of GeneDx. The transactions contemplated by the Merger Agreement, including the Mergers (as defined below), are referred to herein as the “Acquisition”. On April 29, 2022 (the “Closing Date”), following approvals by the stockholders of the Company at a special meeting held on April 27, 2022 (the “Special Meeting”), the Mergers were consummated (the “Closing”) and the Company took various other actions, as discussed further below.

### **Item 1.01. Entry into a Material Definitive Agreement.**

#### ***Transition Services Agreement***

In connection with the Closing, GeneDx and OPKO entered into a Transition Services Agreement dated as of April 29, 2022 (the “Transition Services Agreement”) pursuant to which OPKO has agreed to provide, at cost, certain services in support of the acquisition of the GeneDx business through December 31, 2022, subject to certain limited exceptions, in order to facilitate the transactions contemplated by the Merger Agreement, including human resources, information technology support, and finance and accounting.

The foregoing description of the Transition Services Agreement and the transactions contemplated thereby is not complete and is subject to, and qualified in its entirety by reference to the Transition Services Agreement, a copy of which is included as Exhibit 10.1 to this Report.

### **Item 2.01. Completion of Acquisition or Disposition of Assets.**

On April 29, 2022, pursuant to the Merger Agreement, Merger Sub I merged with and into HoldCo (the “First Merger”), with HoldCo being the surviving entity of the First Merger and following the First Merger, HoldCo merged with and into Merger Sub II, with Merger Sub II being the surviving entity of this second merger (the “Second Merger” and, together with the First Merger, the “Mergers”).

Pursuant to the terms of the Merger Agreement, each share of HoldCo common stock issued and outstanding immediately prior to the First Merger Effective Time (as defined in the Merger Agreement) was cancelled and automatically converted into the right to receive the following consideration (such aggregate consideration, the “Merger Consideration”), with OPKO receiving, subject to the Merger Agreement’s escrow fund provisions described above, (i) \$150 million in cash, subject to adjustment at Closing pursuant to the terms of the Merger Agreement (the “Cash Consideration”) and (ii) 80 million shares of the Company’s Class A common stock (the “Stock Consideration”). OPKO will also be entitled to receive, if and only to the extent payable, up to \$150 million if certain revenue-based milestones are achieved for each of the fiscal years ended December 31, 2022 and December 31, 2023 (the “Milestone Payments”). As previously disclosed, each Milestone Payment, if and to the extent earned under the terms of the Merger Agreement, will be satisfied through the payment and/or issuance of a combination of cash and shares of the Company’s Class A common stock (valued at \$4.86 per share based on the average of the daily volume average weighted price of the Class A common stock over the period of 30 trading days ended January 12, 2022), with such mix to be determined in the Company’s sole discretion.

The Milestone Payment in respect of the fiscal year ending December 31, 2023 is subject to acceleration on the terms described in the Merger Agreement.

The parties have also provided for an indemnification escrow consisting of a mix of cash and shares of the Company's Class A common stock for certain indemnifiable matters pursuant to the terms of, and subject to the applicable limitations set forth in, the Merger Agreement.

The description of the Merger Agreement and related transactions (including, without limitation, the Mergers) in this Report does not purport to be complete and is subject to, and qualified in its entirety by reference to, the full text of the Merger Agreement, which is attached as Exhibit 2.1 hereto and is incorporated herein by reference.

**Item 3.02. Unregistered Sales of Equity Securities.**

Concurrently with the Closing, the Company issued and sold in private placements an aggregate of 50,000,000 shares of the Company's Class A common stock to certain institutional investors (the "PIPE Investors") at \$4.00 per share (the "PIPE Investment") pursuant to subscription agreements entered into on January 14, 2022 (collectively, the "PIPE Subscription Agreements") as previously disclosed on the Company's Current Report on Form 8-K filed on January 18, 2022 (the "January 18, 2022 8-K") with the Securities and Exchange Commission (the "SEC").

This summary is qualified in its entirety by reference to the PIPE Subscription Agreements, the form of which is attached as Exhibit 10.1 to the January 18, 2022 8-K and is incorporated herein by reference.

The disclosure contained in Item 2.01 of this Report related to the issuance of the Stock Consideration is also incorporated herein by reference.

The Company issued the shares of Class A common stock pursuant to the Acquisition and the PIPE Investment under Section 4(a)(2) of the Securities Act of 1933, as amended (the "Securities Act"), and/or Rule 506 of Regulation D promulgated under the Securities Act, as a transaction by an issuer not involving a public offering. OPKO and the PIPE Investors represented their intentions to acquire the shares for investment only and not with a view to or for sale in connection with any distribution, and appropriate restrictive legends were affixed to the certificates representing all of the shares issued in the Acquisition and the PIPE Investment (or reflected in restricted book entry with the Company's transfer agent). The parties also had adequate access, through business or other relationships, to information about the Company.

**Item 5.02. Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.**

Effective as of April 29, 2022, Nat Turner resigned from his position on the Board of Directors of the Company and all committees thereof (the "Board of Directors" or the "Board").

As contemplated by the Merger Agreement, the Board expanded the size of the Board of Directors to eleven (11) members effective as of April 29, 2022, and in connection with the Special Meeting, Katherine Stueland and Richard P. Pfenniger were each elected to the Board of Directors as Class III directors effective as of April 29, 2022 to serve until the 2024 annual meeting of stockholders, each until such director's respective successor is duly elected and qualified, subject to such director's earlier death, resignation, disqualification or removal.

In connection with the Closing, Eric Schadt was appointed President and Chief Research & Development Officer of the Company and ceased serving as the Chief Executive Officer effective as of April 29, 2022. Dr. Schadt will remain as an executive officer and director of the Company.

In addition, in connection with the Closing and effective as of April 29, 2022, Katherine Stueland was appointed as Co-Chief Executive Officer of the Company. Ms. Stueland has entered into an employment agreement with the Company dated January 14, 2022, as amended on April 29, 2022 (the “Stueland Employment Agreement”), which provides for at-will employment and includes a base salary of \$675,000, a discretionary incentive bonus opportunity with a target amount of 100% of the annual base salary, an initial grant of stock options and restricted stock units with an aggregate grant-date value of \$9,000,000, and standard employee benefit plan participation.

Pursuant to the Stueland Employment Agreement, if Ms. Stueland is terminated without “cause” or resigns for “good reason” (as such terms are defined in such employment agreement) other than in connection with a change in control, she will be entitled to receive 24 months of base salary continuation, 12 months of continued coverage under the Company’s group health plans, and accelerated vesting of a portion of her initial stock option grant, subject to her execution of a release of claims. If instead such termination occurs within the period commencing three months prior to (or the date on which the Company has commenced engagement with a change in control counterparty, if later) and ending 12 months following a change in control, Ms. Stueland will be entitled to receive 24 months of base salary continuation, a lump sum payment equal to two times her target annual bonus, 24 months of continued coverage under the Company’s group health plans, and accelerated vesting of her outstanding equity-based compensation awards, subject to her execution of a release of claims.

In addition, pursuant to the Stueland Employment Agreement, Ms. Stueland agreed that, during the nine-month period following the Closing, 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 Securities Exchange Act of 1934, as amended (the “Exchange Act”), with respect to any shares of the Company’s 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). The Stueland Employment Agreement also includes restrictive covenants that would prohibit Ms. Stueland from soliciting the Company’s employees and exclusive consultants or competing with the Company during the 12-month period following her termination of employment. The summary of the Stueland Employment Agreement is qualified in its entirety by reference to the Stueland Employment Agreement, which is attached as Exhibit 10.2 hereto and is incorporated herein by reference.

Except as described in this Report, there is no arrangement or understanding between Dr. Schadt or Ms. Stueland and any other persons pursuant to which Dr. Schadt or Ms. Stueland was selected as a director or officer or between Mr. Pfenniger and any other persons pursuant to which Mr. Pfenniger was selected as a director, and, except as described in this Report, there are no related party transactions involving Dr. Schadt, Ms. Stueland or Mr. Pfenniger that are reportable under Item 404(a) of Regulation S-K. The Company’s transactions with Dr. Schadt are described under “Certain Relationships and Related Party Transactions—Sema4 Related Party Transactions” beginning on page 249 of the Company’s definitive proxy statement filed with the SEC on March 31, 2022 (the “Proxy Statement”), which descriptions are incorporated herein by reference. The Company’s transactions with OPKO, the former employer of Ms. Stueland and where Mr. Pfenniger serves as a director, are described under “The Acquisition—The Merger Agreement,” “The Acquisition—Support Agreements” and “The Acquisition—Shareholder Agreements” beginning on pages 106, 134 and 135, respectively, of Proxy Statement, as well as in the disclosure contained in Item 1.01 of this Report, which descriptions and disclosure are incorporated herein by reference. Further, Mr. Pfenniger is expected to receive compensation for his service on the Board consistent with the Company’s standard compensation arrangements for non-employee directors. Such compensation arrangements are described under “Executive Compensation of Sema4—Director

Compensation” beginning on page 226 of the Proxy Statement, which description is incorporated herein by reference. Mr. Pfenniger, as a non-employee director, was not appointed to serve on any committee of the Board of Directors.

Each of Ms. Stueland and Mr. Pfenniger entered into an indemnification agreement with the Company in the form previously filed as Exhibit 10.4 to the Company’s Current Report on Form 8-K filed with the SEC on July 28, 2021 (the “July 28, 2021 8-K”). The indemnification agreements provide, among other things, that the Company will indemnify the director or executive officer, as applicable, against any and all expenses incurred by that director or executive officer because of his or her status as one of the Company’s directors, executive officers, or other key employees, to the fullest extent permitted by Delaware law, the Amended and Restated Certificate of Incorporation (the “Certificate of Incorporation”) and the Company’s bylaws.

The foregoing description of the form of indemnification agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the form of indemnification agreement, a copy of which is attached as Exhibit 10.4 to the July 28, 2021 8-K and is incorporated herein by reference.

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

As previously disclosed, the Company’s stockholders voted and approved, among other things, Proposal No. 4 – The Charter Amendment Proposal, which is described in greater detail in the Proxy Statement.

The Certificate of Amendment (the “Certificate of Amendment”) to the Certificate of Incorporation to increase the authorized shares of Class A common stock from 380,000,000 to 1,000,000,000 shares of Class A common stock became effective immediately upon filing with the Secretary of State of the State of Delaware on April 29, 2022.

A copy of the Certificate of Amendment is attached hereto as Exhibit 3.1, and is incorporated herein by reference.

### **Item 8.01 Other Events.**

#### ***Amendment to the Merger Agreement***

On April 29, 2022, the Company, Merger Subs, GeneDx, Holdco and OPKO entered into an immaterial amendment to the Merger Agreement (the “Amendment”) in connection with the Closing to provide for the Closing to be effective as of 11:59 pm Eastern Time on April 29, 2022. Other than as expressly modified by the Amendment, the Merger Agreement remains in full force and effect as originally executed on January 14, 2022.

The foregoing description of the Amendment is not complete and is subject to, and qualified in its entirety by reference to the Amendment, a copy of which is included as Exhibit 99.2 to this Report.

### **Item 9.01 Financial Statements and Exhibits.**

#### ***(a) Financial Statements of Businesses Acquired.***

The audited combined carve out balance sheets of GeneDx and subsidiary as of December 31, 2021 and 2020, the related audited combined carve out statements of comprehensive loss, equity and cash flows for each of the two years in the period ended December 31, 2021, and the related

notes are included in the Proxy Statement beginning on page F-41 and are incorporated herein by reference.

In addition, the consent of Ernst & Young, LLP, Independent Auditors for GeneDx, Inc., is attached as Exhibit 23.1 to this Report.

(b) *Pro Forma Financial Information.*

The unaudited pro forma combined financial information of the Company giving effect to the Acquisition as of and for the year ended December 31, 2021, and the related notes are attached as Exhibit 99.3 to this Report and are incorporated herein by reference.

(d) *Exhibits.*

Exhibit Number	Description	Incorporated by Reference			Filed Herewith
		Form	Exhibit	Filing Date	
2.1*	<a href="#">Agreement and Plan of Merger and Reorganization, dated as of January 14, 2022, by and among, Sema4 Holdings Corp., Orion Merger Sub I, Inc., Orion Merger Sub II, LLC, GeneDx, Inc., GeneDx Holding 2, Inc. and OPKO Health, Inc.</a>	DEFM	Annex A	March 31, 2022	
3.1	<a href="#">Certificate of Amendment to the Third Amended and Restated Certificate of Incorporation of Sema4 Holdings Corp.</a>				X
10.1*	<a href="#">Transition Services Agreement, dated as of April 29, 2022, by and between GeneDx, Inc. and OPKO Health, Inc.</a>				X
10.2	<a href="#">Employment Agreement, dated as of January 14, 2022, as amended April 29, 2022, by and between Sema4 Holdings Corp. and Katherine Stueland.</a>				X
23.1	<a href="#">Consent of Ernst &amp; Young, LLP, Independent Auditors for GeneDx, Inc.</a>				X
99.2	<a href="#">Amendment to Agreement and Plan of Merger and Reorganization, dated as of April 29, 2022, by and among, Sema4 Holdings Corp., Orion Merger Sub I, Inc., Orion Merger Sub II, LLC, GeneDx, Inc., GeneDx Holding 2, Inc. and OPKO Health, Inc.</a>				X
99.3	<a href="#">Unaudited Pro Forma Combined Financial Information of the Company as of and the year ended December 31, 2021.</a>				X
104	Cover Page Interactive Data File (embedded within the Inline XBRL Document)				X

\* The schedules and exhibits to this exhibit have been omitted from this filing pursuant to Item 601(a)(5) of Regulation S-K. Sema4 will furnish copies of any such schedules and exhibits to the Securities and Exchange Commission upon request.



**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**Sema4 Holdings Corp.**

Date: May 2, 2022

By: /s/ Katherine Stueland  
Name: Katherine Stueland  
Title: Chief Executive Officer