

PROSPECTUS SUPPLEMENT NO. 1  
(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 our Form 8-K, filed with the Securities and Exchange Commission (the “SEC”) on April 27, 2022. Accordingly, we have attached the form 8-K 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 26, 2022, the last reported sales price of our common stock was \$2.18 per share and the last reported sales price of our public warrants was \$0.52 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 April 27, 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): **April 27, 2022**

**sema4**

**Sema4 Holdings Corp.**

(Exact name of registrant as specified in its charter)

<b>Delaware</b> <hr/> (State or other jurisdiction of incorporation or organization)	<b>001-39482</b> <hr/> (Commission File Number)	<b>85-1966622</b> <hr/> (I.R.S. Employer Identification No.)
<b>333 Ludlow Street, North Tower, 8th Floor</b> <b>Stamford, Connecticut</b> <hr/> (Address of Principal Executive Offices)	<b>(800) 298-6470</b>	<b>06902</b> <hr/> (Zip Code)

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:

<b>Title of each class</b>	<b>Trading Symbol(s)</b>	<b>Name of each exchange on which registered</b>
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.

**Item 5.07 Submission of Matters to a Vote of Security Holders.**

On April 27, 2022, Sema4 Holdings Corp. (“Sema4” or the “Company”) held its Special Meeting of Stockholders (the “Special Meeting”). At the Special Meeting, the Company’s stockholders (the “Stockholders”) considered and voted on the matters listed below. The proposals are described in detail in the Company’s Definitive Proxy Statement filed with the Securities and Exchange Commission on March 31, 2022 (the “Proxy Statement”).

There were 245,016,425 shares of Class A common stock, par value \$0.0001 per share, of the Company (“Class A common stock”), issued and outstanding on March 22, 2022, the record date (the “Record Date”) for the Special Meeting.

The final voting results from the Special Meeting are set forth below.

**Proposal N. 1 – The Stock Consideration Issuance Proposal**

The Stockholders approved, for purposes of complying with the applicable listing rules of the Nasdaq Stock Market (“Nasdaq”), the issuance of the Company’s Class A common stock in connection with the Company’s acquisition of GeneDx, Inc. (“GeneDx”) (the “Acquisition”), as contemplated by the Agreement and Plan of Merger and Reorganization dated January 14, 2022 (the “Merger Agreement”), by and among the Company, 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., which will own 100% of GeneDx at the Effective Time (as defined in the Proxy Statement). The votes were as follows:

<b>For</b>	<b>Against</b>	<b>Abstain</b>	<b>Broker Non-Votes</b>
178,157,301	104,365	154,244	16,922,114

**Proposal N. 2 – The PIPE Investment Issuance Proposal**

The Stockholders approved, for purposes of complying with the applicable listing rules of Nasdaq, the issuance of the Company’s Class A common stock in connection with the PIPE Investment, as defined and described in the Company’s Proxy Statement, and as contemplated by the Subscription Agreements, each dated as of January 14, 2022 with certain institutional investors (including affiliates of the Company and existing investors in Sema4). The votes were as follows:

<b>For</b>	<b>Against</b>	<b>Abstain</b>	<b>Broker Non-Votes</b>
178,106,518	153,719	155,673	16,922,114

**Proposal N. 3 – The Special Designee Director Proposal**

The Stockholders appointed two directors who will become directors of the Company effective upon the consummation of the Acquisition of GeneDx, to serve until the 2024 annual meeting of stockholders. The votes were as follows:

<b>For</b>	<b>Against</b>	<b>Abstain</b>	<b>Broker Non-Votes</b>
177,922,126	192,188	301,596	16,922,114

**Proposal N. 4 – The Charter Amendment Proposal**

The Stockholders approved the amendment to the Company’s Third Amended and Restated Certificate of Incorporation increasing the number of authorized shares of Class A common stock from 380,000,000 to 1,000,000,000. The votes were as follows:

<b>For</b>	<b>Against</b>	<b>Abstain</b>	<b>Broker Non-Votes</b>
186,861,884	8,303,721	172,419	-

**Proposal N. 5 – The Class I Director Election Proposal**

The Stockholders elected three Class I directors of the Company, each to serve a three-year term expiring at the Company’s 2025 annual meeting of stockholders and until such director’s successor is duly elected and qualified. The votes were as follows:

<b>For</b>	<b>Against</b>	<b>Abstain</b>	<b>Broker Non-Votes</b>
177,477,299	780,173	158,438	-

**Proposal N. 6 – The Auditor Ratification Proposal**

The Stockholders approved the ratification of the appointment of Ernst & Young LLP as the Company’s independent registered public accounting firm for the fiscal year ending December 31, 2022. The votes were as follows:

<b>For</b>	<b>Against</b>	<b>Abstain</b>	<b>Broker Non-Votes</b>
194,934,705	222,807	180,512	-

**Proposal N. 7 – The Adjournment Proposal**

The Stockholders approved the adjournment of the Special Meeting to a later date or dates, if necessary, to permit further solicitation and votes of proxies in the event that there were insufficient votes for, or otherwise in connection with the of the proposals described herein and presented at the Special Meeting. The votes were as follows:

<b>For</b>	<b>Against</b>	<b>Abstain</b>	<b>Broker Non-Votes</b>
192,469,434	2,684,200	184,390	-

**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: April 27, 2022

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