

PROSPECTUS SUPPLEMENT NO. 4
(to Prospectus dated August 12, 2021)



Sema4 Holdings Corp.
236,223,401 Shares of Common Stock
7,236,667 Warrants to Purchase Shares of Common Stock
21,995,000 Shares of Common Stock Underlying Warrants

This prospectus supplement supplements the prospectus dated August 12, 2021 (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 current report on Form 8-K, filed with the Securities and Exchange Commission (the "SEC") on January 10, 2022 (the "Current Report"). Accordingly, we have attached the Current Report 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 the Prospectus (the "Selling Securityholders") of (A) up to 236,223,401 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 35,000,000 shares of our Class A common stock issued in a private placement pursuant to subscription agreements each entered into on February 9, 2021; (ii) up to 11,068,750 shares of our Class A common stock issued in connection with the consummation of the Business Combination (as defined in the Prospectus), in exchange for shares of our Class B common stock originally issued in a private placement to CMLS Holdings LLC (the "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 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 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 14,758,333 shares of our Class A common stock that are issuable by us upon the exercise of 14,758,333 warrants (the "public warrants") originally issued in our initial public offering ; 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 symbols "SMFR" and "SMFRW," respectively. On January 7, 2022, the last reported sales price of our common stock was \$4.11 per share and the last reported sales price of our public warrants was \$0.76 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.

Investing in our securities involves risks. See the section entitled "Risk Factors" beginning on page 10 of the Prospectus to read about factors you should consider before buying our securities.

Neither the SEC nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the Prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is January 10, 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): **January 10, 2022**

sema4

Sema4 Holdings Corp.

(Exact name of registrant as specified in its charter)

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

Item 7.01 Regulation FD Disclosure.

On January 10, 2022, Sema4 Holdings Corp. (the "Company") issued a press release announcing its expectations on revenue with respect to the previously announced guidance for the three and twelve months ended December 31, 2021. A copy of the press release is included with this Form 8-K for convenience and attached hereto as Exhibit 99.1.

The information in this current report on Form 8-K and the exhibit attached hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, regardless of any general incorporation language in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

**Exhibit
Number**

Description

99.1	<u>Press Release, dated January 10, 2022, regarding the Registrant's Preliminary Revenue for the Fourth Quarter and Fiscal Year 2021</u>
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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: January 10, 2022

By: /s/ Eric Schadt

Name: Eric Schadt

Title: Chief Executive Officer