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

SCHEDULE 13D
Under the Securities Exchange Act of 1934
(Amendment No. 2)*

SEMA4 HOLDINGS CORP.

(Name of Issuer)

Class A Common Stock

(Title of Class of Securities)

81663L101

(CUSIP Number)

Mount Sinai Health System, Inc.
150 East 42nd Street
Suite 2-B.17
New York, NY 10017
212.659.8105

(Name, Address and Telephone Number of Person
Authorized to Receive Notices and Communications)

April 29, 2022

(Date of Event which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

Note: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See §240.13d-7 for other parties to whom copies are to be sent.

* The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section of the Exchange Act but shall be subject to all other provisions of the Exchange Act (however, see the Notes).

| | | |
|--|--|---|
| 1 | NAMES OF REPORTING PERSONS ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI | |
| 2 | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (SEE INSTRUCTIONS) (a) <input type="checkbox"/> (b) <input type="checkbox"/> | |
| 3 | SEC USE ONLY | |
| 4 | SOURCE OF FUNDS OO | |
| 5 | CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E) <input type="checkbox"/> | |
| 6 | CITIZENSHIP OR PLACE OF ORGANIZATION New York | |
| NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH | 7 | SOLE VOTING POWER 94,605,473 |
| | 8 | SHARED VOTING POWER 0 |
| | 9 | SOLE DISPOSITIVE POWER 94,605,473 |
| | 10 | SHARED DISPOSITIVE POWER 0 |
| 11 | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 94,605,473 ¹ | |
| 12 | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS) <input checked="" type="checkbox"/> See Items 3 and 5 below. | |
| 13 | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 25.1% ² | |
| 14 | TYPE OF REPORTING PERSON (SEE INSTRUCTIONS) CO | |

¹ The shares do not include (a) up to 11,597,198 Earn-Out Shares (as described in Item 3 of Reporting Persons' Schedule 13D filed October 13, 2021).

² Based on the number of shares of Class A Common Stock of Issuer (as defined below) issued and outstanding at April 29, 2022.

| | | |
|--|---|--------------------------------------|
| 1 | NAMES OF REPORTING PERSONS MOUNT SINAI HEALTH SYSTEM, INC | |
| 2 | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (SEE INSTRUCTIONS) (a) <input type="checkbox"/> (b) <input type="checkbox"/> | |
| 3 | SEC USE ONLY | |
| 4 | SOURCE OF FUNDS OO | |
| 5 | CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E) <input type="checkbox"/> | |
| 6 | CITIZENSHIP OR PLACE OF ORGANIZATION New York | |
| NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH | 7 | SOLE VOTING POWER 0 |
| | 8 | SHARED VOTING POWER 0 |
| | 9 | SOLE DISPOSITIVE POWER 0 |
| | 10 | SHARED DISPOSITIVE POWER 0 |
| 11 | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 0 | |
| 12 | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS) <input type="checkbox"/> | |
| 13 | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 0% | |
| 14 | TYPE OF REPORTING PERSON (SEE INSTRUCTIONS) HC | |

Item 1. Security and Issuer

This Amendment No. 2 ("Amendment No. 2") to Schedule 13D relates to the Class A common stock, par value \$0.0001 per share (the "Class A Common Stock"), of Sema4 Holdings Corp. ("Sema4" or "Issuer"), and amends and supplements the Schedule 13D, filed October 13, 2021, as amended by Amendment No. 1, filed January 21, 2022 ("Amendment No. 1" and as amended, the "Schedule 13D") by Icahn School of Medicine at Mount Sinai ("ISMMS") and Mount Sinai Health System, Inc. ("MSHS"). As of April 29, 2022, following closing of the transactions described in Issuer's Current Report on Form 8-K (referenced in Item 4 below), the issued and outstanding Class A Common Stock of Sema4 totalled 377,249,186 shares. The principal executive office of Sema4 is located at 333 Ludlow Street, North Tower, 8th Floor, Stamford, Connecticut 06902.

Item 2. Identity and Background

Item 2 of this Amendment No. 2 incorporates herein by reference the information set forth in Item 2 of the Schedule 13D.

Item 3. Source and Amount of Funds or Other Consideration

Item 3 of the Schedule 13D is hereby amended and supplemented as follows:

The information set forth in Item 4 of this Amendment No. 2 is hereby incorporated by reference into this Item 3.

Item 4. Purpose of Transaction

Item 4 is hereby amended and supplemented as follows:

As disclosed by Issuer in a Current Report on Form 8-K filed May 2, 2022 (the "Form 8-K"), Issuer closed the mergers described in that certain Agreement and Plan of Merger and Reorganization, dated January 14, 2021, with GeneDx, Inc. ("GeneDx"), a wholly-owned subsidiary of OPKO Health, Inc. ("OPKO"), GeneDx Holding 2, Inc., and OPKO (the "GeneDx Merger Agreement"), and as contemplated thereby, GeneDx became a wholly-owned indirect subsidiary of Issuer (the "Closing").

As described in Amendment No. 1, concurrently with the Closing, as part of a \$200 million private placement of Class A Common Stock (the "PIPE") of Issuer, ISMMS purchased from Issuer 6,250,000 shares of Class A Common Stock (the "PIPE Shares") at a purchase price of \$4.00 per share for the aggregate purchase price of \$25 million.

The information in Item 3 of this Amendment No. 2 is incorporated by reference into this Item 4. The Reporting Persons expect to evaluate on an ongoing basis the Issuer's financial condition and prospects and their respective interests in, and intentions with respect to, the Issuer and their respective investments in the securities of Issuer, which review may be based on various factors, including Issuer's business and financial condition, results of operations and prospects, general economic and industry conditions, the securities markets in general and those for Issuer's securities in particular, as well as other developments and other investment opportunities. Accordingly, each Reporting Person reserves the right to change its intentions, as it deems appropriate. In particular, each Reporting Person may, at any time and from time to time, in the open market, in privately negotiated transactions or otherwise, increase its holdings in Issuer or dispose of all or a portion of the securities of Issuer that such Reporting Person now owns or may hereafter acquire, including sales pursuant to the exercise of the registration rights provided for in the Subscription Agreements described in Amendment No. 1.

Except as described in this Amendment No. 2, the Reporting Persons do not have any present plans or proposals that relate to or would result in any of the actions described in subparagraphs (a) through (j) of Item 4 of Schedule 13D, although, subject to the agreements described herein, the Reporting Persons, at any time and from time to time, may review, reconsider and change their position and/or change their purpose and/or develop such plans and may seek to influence management or the board of Issuer with respect to the business and affairs of Issuer and may from time to time consider pursuing or proposing such matters with advisors, Issuer or other persons.

Item 5. Interest in Securities of the Issuer

Item 5 of the Schedule 13D is hereby amended and restated as follows:

(a) and (b) Items 7 through 11 and 13 of each of the cover pages of this Amendment No. 2 are incorporated herein by reference. Calculation of the percentage of shares of Class A Common Stock beneficially owned assumes that there were 377,249,186 shares of Class A Common Stock issued and outstanding following the Closing and the PIPE, as reported by Issuer in the Registration Statement on Form S-1 filed on May 3, 2022. Shares of Class A Common Stock owned by ISMMS include the following:

| | | |
|------------|--|---|
| 88,355,473 | | Shares Reported in the Schedule 13D |
| 6,250,000 | | PIPE Shares Acquired as of April 29, 2022 |

The information set forth in Item 4 of this Amendment No. 2 is hereby incorporated by reference into this Item 5.

MSSH disclaims beneficial ownership over all Shares beneficially owned by ISMMS, other than for the purpose of determining obligations under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the filing of this Amendment No. 2 shall not be deemed an admission that MSSH is the beneficial owner of such securities for any other purpose.

- (c) Except as described in Item 4 of this Amendment No. 2, which is incorporated herein by reference, during the past 60 days, none of the Reporting Persons conducted transactions in the securities of the Issuer.
- (d) To the knowledge of the Reporting Persons, no one other than the Reporting Persons has the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the securities of the Issuer reported as beneficially owned by the Reporting Persons herein.
- (e) Not applicable.

Item 6. Contracts, Arrangements, Understandings or Relationships With Respect to Securities of the Issuer

The information set forth in Items 2, 3, 4 and 5 is hereby incorporated by reference into this Item 6. The Subscription Agreements described in Amendment No. 1 provide for certain customary registration rights for the PIPE investors.

Item 7. Material to Be Filed as Exhibits

None.

Signature

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Dated: May 6, 2022

ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI

By: /s/ Stephen Harvey

Name: Stephen Harvey

Title: Chief Financial Officer Icahn School of Medicine at Mount Sinai

Dated: May 6, 2022

MOUNT SINAI HEALTH SYSTEM, INC.

By: /s/ Stephen Harvey

Name: Stephen Harvey

Title: Chief Financial Officer Mount Sinai Health System, Inc.

Attention: Intentional misstatements or omissions of fact constitute Federal criminal violations (See 18 U.S.C. 1001)
