

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)

**CMLS Holdings LLC
Eli Casdin and Keith Meister
c/o Corvex Management LP
667 Madison Avenue
New York, New York 10065
(212) 474-6745**

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

Class A common stock, \$0.0001 par value per share

(Title of Class of Securities)

18978W109

(CUSIP Number)

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 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

1	Names of Reporting Persons CMLS HOLDINGS LLC	
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 if disclosure of legal proceedings is required pursuant to Items 2(d) or 2(e): <input type="checkbox"/>	
6	Citizenship or Place of Organization Delaware	
Number of Units Beneficially Owned by Each Reporting Person With:	7	Sole Voting Power 0
	8	Shared Voting Power 17,730,419 (1)(2)(3)
	9	Sole Dispositive Power 0
	10	Shared Dispositive Power 17,730,419 (1)(2)(3)
11	Aggregate Amount Beneficially Owned by Each Reporting Person 17,730,419 (1)(2)(3)	
12	Check if the Aggregate Amount in Row (11) Excludes Certain Units (See Instructions) <input type="checkbox"/>	
13	Percent of Class Represented by Amount in Row (11) 4.6% (4)	
14	Type of Reporting Person (See Instructions) HC, OO	

1	Names of Reporting Persons C-LSH LLC
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 if disclosure of legal proceedings is required pursuant to Items 2(d) or 2(e): <input type="checkbox"/>
6	Citizenship or Place of Organization Delaware
	7 Sole Voting Power 0
Number of Units Beneficially Owned by Each Reporting Person With:	8 Shared Voting Power 17,730,419 (1)(2)(3)
	9 Sole Dispositive Power 0
	10 Shared Dispositive Power 17,730,419 (1)(2)(3)
11	Aggregate Amount Beneficially Owned by Each Reporting Person 17,730,419 (1)(2)(3)
12	Check if the Aggregate Amount in Row (11) Excludes Certain Units (See Instructions) <input type="checkbox"/>
13	Percent of Class Represented by Amount in Row (11) 4.6% (4)
14	Type of Reporting Person (See Instructions) HC, OO

1 Names of Reporting Persons
M-LSH LLC

2 Check the Appropriate Box if a Member of a Group (See Instructions)
(a)
(b)

3 SEC Use Only

4 Source of Funds: OO

5 Check if disclosure of legal proceedings is required pursuant to Items 2(d) or 2(e):

6 Citizenship or Place of Organization
Delaware

7 Sole Voting Power
0

Number of
Units
Beneficially
Owned by
Each
Reporting
Person With:

8 Shared Voting Power
17,730,419 (1)(2)(3)

9 Sole Dispositive Power
0

10 Shared Dispositive Power
17,730,419 (1)(2)(3)

11 Aggregate Amount Beneficially Owned by Each Reporting Person
17,730,419 (1)(2)(3)

12 Check if the Aggregate Amount in Row (11) Excludes Certain Units (See Instructions)

13 Percent of Class Represented by Amount in Row (11)
4.6% (4)

14 Type of Reporting Person (See Instructions)
HC, OO

1	Names of Reporting Persons	ELI CASDIN
<hr/>		
2	Check the Appropriate Box if a Member of a Group (See Instructions)	(a) <input type="checkbox"/>
		(b) <input type="checkbox"/>
<hr/>		
3	SEC Use Only	
<hr/>		
4	Source of Funds: OO	
<hr/>		
5	Check if disclosure of legal proceedings is required pursuant to Items 2(d) or 2(e):	<input type="checkbox"/>
<hr/>		
6	Citizenship or Place of Organization	United States of America
<hr/>		
7	Sole Voting Power	0
<hr/>		
8	Shared Voting Power	34,167,919 (1)(2)(3)(5)
<hr/>		
9	Sole Dispositive Power	0
<hr/>		
10	Shared Dispositive Power	34,167,919 (1)(2)(3)(5)
<hr/>		
11	Aggregate Amount Beneficially Owned by Each Reporting Person	34,167,919 (1)(2)(3)(5)
<hr/>		
12	Check if the Aggregate Amount in Row (11) Excludes Certain Units (See Instructions)	<input type="checkbox"/>
<hr/>		
13	Percent of Class Represented by Amount in Row (11)	8.9% (4)
<hr/>		
14	Type of Reporting Person (See Instructions)	HC, IN
<hr/>		

1	Names of Reporting Persons KEITH A. MEISTER
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 if disclosure of legal proceedings is required pursuant to Items 2(d) or 2(e): <input type="checkbox"/>
6	Citizenship or Place of Organization United States of America
	7 Sole Voting Power 15,937,500 (6)
Number of Units Beneficially Owned by Each Reporting Person With:	8 Shared Voting Power 17,730,419 (1)(2)(3)
	9 Sole Dispositive Power 15,937,500 (6)
	10 Shared Dispositive Power 17,730,419 (1)(2)(3)
11	Aggregate Amount Beneficially Owned by Each Reporting Person 33,667,919 (1)(2)(3)(6)
12	Check if the Aggregate Amount in Row (11) Excludes Certain Units (See Instructions) <input type="checkbox"/>
13	Percent of Class Represented by Amount in Row (11) 8.8% (4)
14	Type of Reporting Person (See Instructions) HC, IN

- (1) Includes 10,993,750 shares of Class A common stock of Sema4 Holdings Corp. (the “Issuer”), par value \$0.0001 per share (“Common Stock”).
- (2) Includes 6,736,669 shares of Common Stock issuable upon the exercise of 6,736,669 private placement warrants of the Issuer. On September 3, 2021, each private placement warrant became exercisable to purchase one share of Common Stock at a price of \$11.50 per share, subject to adjustment, as described in the definitive proxy statement of the Issuer (File No. 001-39482) filed with the U.S. Securities Exchange Commission (the “SEC”) on July 2, 2021.
- (3) CMLS Holdings LLC is the record holder of the shares reported herein. The Board of Managers of CMLS Holdings LLC is comprised of Mr. Casdin and Mr. 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.
- (4) Based on 377,249,186 shares of Common Stock outstanding as of April 29, 2022, as provided by the Issuer.
- (5) Casdin Partners Master Fund, LP is the record holder of 16,437,500 shares reported herein. Casdin Capital, LLC is the investment adviser to Casdin Partners Master Fund, LP and Casdin Partners GP, LLC is the general partner of Casdin Partners Master Fund LP. Eli Casdin is the managing member of Casdin Capital, LLC and Casdin Partners GP, LLC. As such, each of the foregoing may be deemed to have or share beneficial ownership of the Common Stock held directly by Casdin Partners Master Fund, LP.
- (6) The shares reflected as beneficially owned by Mr. Meister include 15,937,500 shares of Common Stock owned by investment funds advised by Corvex Management, L.P., which may be deemed to be indirectly beneficially owned by Keith Meister by virtue of Mr. Meister’s control of the general partner of Corvex Management, L.P.

SCHEDULE 13D

This Amendment No. 2 (the "Amendment") supplements the information set forth in the Schedule 13D (the "Schedule 13D") filed with the United States Securities and Exchange Commission (the "SEC") on August 2, 2021, as amended as of January 19, 2022, by CMLS Holdings LLC, Keith Meister, Eli Casdin and the other Reporting Persons named therein, relating to the shares of common stock, par value \$0.0001 per share ("Common Stock"), of Sema4 Holdings Corp. (the "Issuer"). Capitalized terms used but not defined herein shall have the meanings ascribed to them in the Schedule 13D.

The information set forth in response to each separate Item below shall be deemed to be a response to all Items where such information is relevant. Item 3 to the Schedule 13D is supplementally amended as follows, and Item 5 to the Schedule 13D is amended and restated as follows.

Item 3 Source and Amount of Funds or Other Consideration

On April 29, 2022, Casdin Partners Master Fund, LP, an investment fund advised by Casdin Capital, LLC, of which Mr. Casdin is the managing member, acquired 11,437,500 shares of Common Stock for an aggregate purchase price of \$45,750,000, funded by cash on hand. On April 29, 2022, investment funds advised by Corvex Management LP, the general partner of which is controlled by Mr. Meister, acquired 11,437,500 shares of Common Stock for an aggregate purchase price of \$45,750,000, funded by cash on hand.

Such 22,875,000 shares were acquired in connection with the consummation of the Issuer's acquisition of GeneDx, Inc. pursuant to the previously disclosed subscription agreements (collectively, the "Subscription Agreements") entered into between the Issuer and Casdin Partners Master Fund, LP and between the Issuer and Corvex Management LP, as investment advisor to the investment funds advised by Corvex Management LP, as of January 14, 2022.

Item 5 Interest in the Securities of the Issuer

The information set forth in the facing pages of this Schedule 13D with respect to the shared beneficial ownership of Common Stock by the Reporting Persons is incorporated by reference into this Item 5.

The information set forth in Items 2, 3 and 4 is hereby incorporated by reference into this Item 5.

(a) The aggregate number of shares of Common Stock and the percentage of total outstanding shares of Common Stock beneficially owned by the Reporting Persons is set forth below.

References to percentage ownerships of shares of Common Stock in this Statement are based upon 377,249,186 shares of Common Stock outstanding as of April 29, 2022, as provided by the Issuer. The filing of this Statement shall not be construed as an admission that a Reporting Person beneficially owns those shares held by any other Reporting Person.

(b) Eli Casdin has shared power to vote or to direct the vote and shared power to dispose or to direct the disposition of the 34,167,919 shares of Common Stock reported in (a) above. Keith Meister has the sole power to vote or to direct the vote and sole power to dispose or to direct the disposition of 15,937,500 shares of Common Stock reported in (a) above and shared power to vote or direct the vote and shared power to dispose or to direct the disposition of 17,730,419 shares of Common Stock reported in (a) above.

Except with respect to the 22,875,000 shares of Common Stock acquired as of April 29, 2022 in connection with the Subscription Agreements, the Reporting Persons have not effected any transactions in the Issuer's Common Stock during the past 60 days.

No person other than the Reporting Persons is known to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the Common Stock beneficially owned by the Reporting Persons.

As of April 29, 2022, each of CMLS Holdings LLC, C-LSH LLC and M-LSH LLC ceased to be the beneficial owner of more than 5% of Common Stock.

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.

Date: May 3, 2022

CMLS HOLDINGS LLC

By: /s/ Keith A. Meister
Name: Keith A. Meister
Title: Manager

Date: May 3, 2022

C-LSH LLC

By: /s/ Eli Casdin
Name: Eli Casdin
Title: Managing Member

Date: May 3, 2022

M-LSH LLC

By: /s/ Keith A. Meister
Name: Keith A. Meister
Title: Managing Member

Date: May 3, 2022

/s/ Eli Casdin
Eli Casdin

Date: May 3, 2022

/s/ Keith A. Meister
Keith A. Meister