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

SCHEDULE 13D

Under the Securities Exchange Act of 1934  
(Amendment No. 1)\*

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**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)

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

(Title of Class of Securities)

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**18978W109**

(CUSIP Number)

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**January 14, 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).

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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
	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)(4)
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) 7.3% (5)
14	Type of Reporting Person (See Instructions) HC, OO

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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)(4)
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)	7.3% (5)
14	Type of Reporting Person (See Instructions)	HC, OO

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1	Names of Reporting Persons	
	M-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)(4)	
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)	
	7.3% (5)	
14	Type of Reporting Person (See Instructions)	
	HC, OO	

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1 Names of Reporting Persons  
 ELI CASDIN

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

(a)

(b)

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3 SEC Use Only

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4 Source of Funds: OO

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

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6 Citizenship or Place of Organization  
 United States of America

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Number of Units Beneficially Owned by Each Reporting Person With:	7	Sole Voting Power 0
	8	Shared Voting Power 22,730,419 (1)(2)(3)(6)
	9	Sole Dispositive Power 0
	10	Shared Dispositive Power 22,730,419 (1)(2)(3)(6)

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11 Aggregate Amount Beneficially Owned by Each Reporting Person  
 22,730,419 (1)(2)(3)(4)(6)

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

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13 Percent of Class Represented by Amount in Row (11)  
 9.4% (5)

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

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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	
Number of Units Beneficially Owned by Each Reporting Person With:	7	Sole Voting Power 4,500,000 (7)
	8	Shared Voting Power 17,730,419 (1)(2)(3)
	9	Sole Dispositive Power 4,500,000 (7)
	10	Shared Dispositive Power 17,730,419 (1)(2)(3)
11	Aggregate Amount Beneficially Owned by Each Reporting Person 22,230,419 (1)(2)(3)(4)(7)	
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) 9.2% (5)	
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 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 242,578,824 shares of Common Stock outstanding as of December 31, 2021, as disclosed in the Agreement and Plan of Merger and Reorganization, dated as of January 14, 2022, by and among the Issuer, Orion Merger Sub I Inc., Orion Merger Sub II, LLC, GeneDx, Inc., GeneDx Holding 2, Inc. and OPKO Health, Inc., filed as Exhibit 2.1 to the Issuers' current report on Form 8-K, filed with the SEC on January 18, 2022.
- (5) The shares of Common Stock to be acquired pursuant to the Subscription Agreements described in Item 4 below are not included in the number of shares reported as beneficially owned herein.
- (6) Casdin Partners Master Fund, LP is the record holder of the 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.
- (7) The shares reflected as beneficially owned by Mr. Meister consist of 4,500,000 shares of Common Stock. Such securities are owned by investment funds advised by Corvex Management, L.P., and 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. 1 (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, 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. Items 4, 6 and 7 to the Schedule 13D are supplementally amended as follows, and Item 5 to the Schedule 13D is amended and restated as follows.

### **Item 4 Purpose of Transaction**

On January 14, 2022, the Issuer entered into an Agreement and Plan of Merger and Reorganization (the "Merger Agreement") with GeneDx, Inc. ("GeneDx"), a wholly-owned subsidiary of OPKO Health, Inc. ("OPKO"), OPKO and the other parties thereto, pursuant to which the Issuer will acquire GeneDx. Concurrently with the execution of the Merger Agreement, the Issuer entered into subscription agreements (collectively, the "Subscription Agreements") with certain institutional investors (collectively, the "PIPE Investors") governing the issuance and sale of 50 million shares of Common Stock (the "PIPE Shares") at \$4.00 per share, for an aggregate gross purchase price of \$200 million. Casdin Partners Master Fund, LP, an investment fund advised by Casdin Capital, LLC, of which Mr. Casdin is the managing member, executed a Subscription Agreement with respect to 11,437,500 PIPE Shares and investments funds advised by Corvex Management LP, the general partner of which is controlled by Mr. Meister, executed Subscription Agreements with respect to an aggregate of 11,437,500 PIPE Shares.

Pursuant to, and on the terms and subject to the conditions of, the Subscription Agreements, the Issuer agreed to issue and sell the PIPE Shares to the PIPE Investors, in private placements to close substantially concurrently with the closing of the transactions contemplated by the Merger Agreement. The Subscription Agreements provide for certain customary registration rights for the PIPE Investors. The Subscription Agreements will terminate with no further force and effect upon the earliest to occur of: (a) such date and time as the Merger Agreement is terminated in accordance with its terms; (b) upon the mutual written agreement of the parties to such Subscription Agreement; (c) if any of the conditions to closing of the PIPE Investment set forth in Section 2 of the Subscription Agreement are not satisfied (or waived, to the extent waivable) on or prior to the earlier of the closing date of the Acquisition (the "Closing Date") or October 14, 2022 (the "Outside Date"), or become incapable of being satisfied on or prior to the earlier of the Closing Date or the Outside Date, and, as a result thereof, the transactions contemplated by the Subscription Agreements are not consummated at the closing of the PIPE Investment, and (d) the Outside Date. Each PIPE Investor may, by written notice to the Issuer, extend the Outside Date beyond October 14, 2022.

Additionally, on January 14, 2022, the Issuer and OPKO entered into Support Agreements (the "Support Agreements") with certain stockholders of the Issuer, including Casdin Partners Master Fund LP and Corvex Management LP on behalf of the investment funds it advises that currently own Common Stock.

On the terms and subject to the conditions set forth in the Support Agreements, Casdin Partners Master Fund LP, Corvex Management LP and the other signing stockholders have agreed to, among other things: (a) vote at any meeting of the stockholders of the Issuer all of their shares of Common Stock held of record: (i) to approve the issuance of the stock consideration to be issued pursuant to Merger Agreement and the issuance of PIPE Shares pursuant to the Subscription Agreements; (ii) to approve the appointment of the certain designees to the Issuer's board of directors (the "Board"); (iii) to approve an amendment to the Issuer's current Third Amended and Restated Certificate of Incorporation to increase the authorized shares of Common Stock from 380,000,000 to 1,000,000,000; (iv) to approve any other proposal included in the proxy statement related to the Merger Agreement that is recommended by the Board as necessary to consummate the transactions contemplated by the Merger Agreement; (v) to approve any proposal that is recommended by the Board to adjourn the stockholder meeting related to the Merger Agreement to a later date, if there are not sufficient affirmative votes (in person or by proxy) to obtain the requested approvals on the date on which such meeting is held; and (vi) against any and all other proposals that could reasonably be expected to delay or impair the ability of the Issuer to consummate the transactions contemplated by the Merger Agreement; (b) provide, as contemplated therein, a proxy to the Issuer to vote such shares accordingly (subject to the condition that a proxy statement has been filed with the SEC and provided to the stockholders of the Issuer); (c) be bound by certain other covenants and agreements; and (d) be bound by certain transfer restrictions with respect to all or a percentage of their shares of Common Stock prior to the meeting.



Effective as of January 14, 2022, Keith Meister was appointed to the Board as a Class III director of the Issuer, whose term expires at the Issuer's 2024 annual meeting of stockholders.

The foregoing descriptions of the Subscription Agreements and the Support Agreements above do not purport to be complete, and are qualified in their entirety by reference to the full text of the Subscription Agreements and the Support Agreements, forms of which are filed as Exhibit 1 and Exhibit 2, respectively, to this Amendment.

The purpose of the transaction was to acquire securities of the Issuer for investment purposes. Except as set forth in this Item 4, the Reporting Persons have no present plans or proposals that relate to, or that would result in, any of the actions specified in clauses (a) through (j) of Item 4 of Schedule 13D under the Act. Mr. Casdin and Mr. Meister currently serve as directors of the Issuer and, in connection with such roles, may consider such activities referred to in clauses (a) through (j). The Reporting Persons do, however, reserve the right in the future to adopt such plans or proposals subject to compliance with applicable regulatory requirements.

#### **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 the 242,578,824 shares of Common Stock stated to be outstanding as of December 31, 2021 in the Merger Agreement, filed as Exhibit 2.1 to the Issuer's current report on Form 8-K, filed with the SEC on January 18, 2022. 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 22,730,419 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 4,500,000 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 shares of Common Stock to be acquired 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.

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

The information set forth in Item 4 above is hereby incorporated by reference into this Item 6.

#### **Item 7 Material to be Filed as Exhibits**

<u>Exhibit No.</u>	<u>Description</u>
1	<a href="#">Form of Subscription Agreement (incorporated by reference to Exhibit 10.1 of the Issuer's current report on Form 8-K, filed with the SEC on January 18, 2022).</a>
2	<a href="#">Form of Support Agreement (incorporated by reference to Exhibit 10.3 of the Issuer's current report on Form 8-K, filed with the SEC on January 18, 2022).</a>

**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: January 19, 2022

CMLS HOLDINGS LLC

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

Date: January 19, 2022

C-LSH LLC

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

Date: January 19, 2022

M-LSH LLC

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

Date: January 19, 2022

/s/ Eli Casdin  
Eli Casdin

Date: January 19, 2022

/s/ Keith A. Meister  
Keith A. Meister

EXHIBIT INDEX

**Ex.**

- 1 [Form of Subscription Agreement \(incorporated by reference to Exhibit 10.1 of the Issuer's current report on Form 8-K, filed with the SEC on January 18, 2022\).](#)
- 2 [Form of Support Agreement \(incorporated by reference to Exhibit 10.3 of the Issuer's current report on Form 8-K, filed with the SEC on January 18, 2022\).](#)