
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 13D

Under the Securities Exchange Act of 1934

Sema4 Holdings, Corp.

(Name of Issuer)

Class A Common Stock, par value \$0.0001 per share

(Title of Class of Securities)

81663L101

(CUSIP Number)

Steven D. Rubin
Executive Vice President - Administration
OPKO Health, Inc.
4400 Biscayne Boulevard
Miami, Florida 33137
Telephone: (305) 575-4100

(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 which is the subject of this Schedule 13D, and is filing this schedule because of Rule 13d-1(e), Rule 13d-1(f) or Rule 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 Rule 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 the 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 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	NAME OF REPORTING PERSONS OPKO Health, Inc.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (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 checked="" type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 80,000,000
	8	SHARED VOTING POWER —
	9	SOLE DISPOSITIVE POWER 80,000,000
	10	SHARED DISPOSITIVE POWER —
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 80,000,000	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 21.2 % ⁽¹⁾	
14	TYPE OF REPORTING PERSON CO	

⁽¹⁾Based on 377,249,186 shares of Class A Common Stock, par value \$0.0001 per share, of Sema4 Holdings Corp., a Delaware corporation (the “Issuer”), outstanding as of April 30, 2022, as set forth in the Issuer’s Registration Statement on Form S-1 (File No. 333-264626) filed with the SEC on May 2, 2022.

ITEM 1. Security and Issuer.

This Schedule 13D is filed with respect to the Class A common stock, par value \$0.0001 per share (“Sema4 Common Stock”), of Sema4 Holdings Corp., a Delaware corporation (“Sema4” or the “Issuer”). The principal executive offices of the Issuer are located at 333 Ludlow Street, North Tower, 8th Floor, Stamford, Connecticut 06902.

ITEM 2. Identity and Background.

(a), (f) This Schedule 13D is filed by OPKO Health, Inc., a Delaware corporation (the “Company”, “OPKO” or the “Reporting Person”). Set forth on Schedule I to this Schedule 13D are the name, business address and present principal occupation or employment and citizenship of each executive officer and director of the Company.

(b) The address of the Company’s principal executive office is 4400 Biscayne Blvd., Miami, Florida 33137.

(c) The Company is a diversified healthcare company that seeks to establish industry-leading positions in large and rapidly growing medical markets.

(d), (e) Except as described herein, during the last five years, neither the Reporting Persons nor any of the persons listed on Schedule I hereto (i) has been convicted in a criminal proceeding (excluding traffic violations or similar misdemeanors) or (ii) was a party to a civil proceeding of a judicial or administrative body of competent jurisdiction and as a result of such proceeding was or is subject to a judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violations with respect to such laws.

On September 7, 2018, the Securities and Exchange Commission (the “SEC”) filed a civil complaint in the Southern District of New York (the “Complaint”), against a number of individuals and entities, including OPKO and its CEO and Chairman, Dr. Phillip Frost and Frost Gamma Investments Trust (“FGIT”), an entity of which Dr. Frost is trustee. In December 2018, OPKO, Dr. Frost and FGIT entered into settlements with the SEC, which, upon approval by the court in January 2019, resolved the claims against OPKO, Dr. Frost and FGIT. Under the terms of the settlement between the SEC, Dr. Frost and FGIT, and without admitting or denying any of the allegations in the Complaint, Dr. Frost agreed to injunctions from violations of Sections 5(a) and (c) and 17(a)(2) of the Securities Act of 1933, as amended (the “Securities Act”), claims which may be satisfied by strict liability and negligence, respectively, and Section 13(d) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), also a strict liability claim; to pay a civil monetary penalty, disgorgement and pre-judgment interest, which have been paid; and to be prohibited, with certain exceptions, from trading in penny stocks. Pursuant to the settlement between OPKO and the SEC, and without admitting or denying any of the allegations of the Complaint, OPKO agreed to be enjoined from future violations of Section 13(d) of the Exchange Act, a claim that requires no showing of scienter, and to pay a civil monetary penalty, which has been paid.

ITEM 3. Source and Amount of Funds or Other Consideration.

On January 14, 2022, the Company entered into an Agreement and Plan of Merger and Reorganization (the “Merger Agreement”) with Sema4, its two wholly owned subsidiaries, Orion Merger Sub I, Inc., a Delaware corporation, and Orion Merger Sub II, LLC, a Delaware limited liability company, GeneDx Inc., a New Jersey corporation and an indirect wholly owned subsidiary of the Company (“GeneDx”), and GeneDx Holding 2, Inc., a Delaware corporation and wholly owned subsidiary of the Company.

On April 29, 2022, the transactions contemplated by the Merger Agreement closed (the “Closing”), with GeneDx (now a Delaware limited liability company) surviving the mergers contemplated thereby as a wholly owned indirect subsidiary of Sema4.

At Closing, Sema4 paid to the Company aggregate consideration of \$150.0 million in cash (before deduction of transaction expenses and other customary purchase price adjustments), together with 80.0 million shares of Sema4 Common Stock (the “Closing Shares”). Additionally, Sema4 has agreed to pay the Company up to an additional \$150.0 million, which may be paid in Sema4 Common Stock, cash or a combination thereof in Sema4’s discretion, subject to GeneDx achieving certain revenue targets for the fiscal years ending December 31, 2022 and 2023 (the “Milestone Consideration”). If the Milestone Consideration in respect of the year ending December 31, 2022

becomes payable in full, then the Milestone Consideration conditionally payable in respect of the year ending December 31, 2023 is subject to acceleration in the event of a change in control of Sema4.

ITEM 4. Purpose of Transaction.

All Common Shares beneficially owned by the Company are held solely for investment purposes. The Company has no present plan or proposal that relates to, or could result in, any of the events referred to in paragraphs (a) through (j), inclusive, of Item 4 of Schedule 13D. Pursuant to the terms of the Merger Agreement, the Company designated one of its current independent directors, Richard C. Pfenniger, Jr., as a director designee to serve on Sema4's board of directors (the "Sema4 Board"). At a special meeting of Sema4's stockholders held on April 27, 2022, Mr. Pfenniger was elected to serve as a director on the Sema4 Board for a term expiring at Sema4's 2024 annual meeting of stockholders.

The Reporting Person may, at any time or from time to time, formulate plans or proposals regarding the Issuer or its securities to the extent deemed advisable by the Reporting Person in light of its general investment policies, market conditions, subsequent developments affecting the Issuer, the general business and future prospects of the Issuer, or other factors. The Reporting Person intends to review its investment in the Issuer on a continuing basis. Depending on various factors, including, without limitation, the Issuer's financial position and strategic direction, actions taken by the Sema4 Board, price levels of shares of the Sema4 Common Stock, other investment opportunities available to the Reporting Person, concentration of positions in the portfolios managed by the Reporting Person, market conditions and general economic and industry conditions, the Reporting Person may in the future take such actions with respect to its investments in the Issuer as it deems appropriate (subject to the terms of the Shareholder Agreement, as defined in Item 6 of this Schedule 13D), including, without limitation, purchasing additional shares of the Sema4 Common Stock or other financial instruments related to the Issuer or selling some or all of its beneficial or economic holdings, engaging in hedging or similar transactions with respect to the securities relating to the Issuer and/or otherwise changing its intention with respect to any and all matters referred to in this Item 4 of Schedule 13D.

ITEM 5. Interest in Securities of the Issuer.

- (a) The Company's beneficial ownership of Sema4 Common Stock is as set forth in the table below:

Name and Title of Beneficial Owner	Number of Outstanding Shares Beneficially Owned	Percentage of Outstanding Common Shares ⁽¹⁾
OPKO Health, Inc.	80,000,000	21.2%

⁽¹⁾ Based on 377,249,186 shares of Sema4 Common Stock outstanding as of April 30, 2022, as set forth in the Issuer's Registration Statement on Form S-1 (File No. 333-264626) filed with the SEC on May 2, 2022.

- (b) Items 7-10, inclusive, set forth on the cover page to this Schedule 13D are hereby incorporated by reference in this Item 5.

- (c) The information contained in Item 3 of this Schedule 13D is incorporated by reference in this Item 5.
- (d) Not applicable.
- (e) Not applicable.

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

The information contained in Item 3 of this Schedule 13D is incorporated by reference in this Item 6.

In connection with the transactions contemplated by the Merger Agreement, on January 14, 2022, the Company entered into a Shareholder Agreement (the "Shareholder Agreement") with Sema4, pursuant to which the Company has agreed to, among other things, be subject to a lock-up period with respect to its shares of Sema4 Common Stock (the "Lock-Up Shares"), which include the Closing Shares, together with any shares issued in respect of the Milestone Consideration (the "Milestone Shares"). The lock-up period extends from the Closing until (a) in the case

of the Closing Shares, April 29, 2023, (b) if and to the extent earned, in the case of the Milestone Shares for the first payment in respect of the Milestone Consideration, the date that is one (1) year from the date of issuance for such stock and (c) if and to the extent earned, in the case of the Milestone Shares for the second payment in respect of the Milestone Consideration, the date that is six (6) months from the date of issuance for such stock (as applicable, the “Lock-Up Period”). During this Lock-Up Period, the Company may not transfer any Lock-Up Shares or engage in any short sales or other hedging or derivative transactions, subject to certain limited exceptions. Following such Lock-Up Period, the Company has agreed to dispose of its Lock-Up Shares in a marketed sale process under certain circumstances for so long as it continues to hold at least 5% of the outstanding shares of Sema4 Common Stock.

In addition, the Company has further agreed to certain standstill provisions whereby, subject to certain exceptions, it is obligated to refrain from taking certain actions with respect to the Sema4 Common Stock. The Company has also agreed to vote its shares of Sema4 Common Stock in accordance with the recommendations of the Sema4 Board for so long as it continues to hold at least 5% of the outstanding shares of Sema4 Common Stock. Further, Sema4 has also granted the Company certain customary shelf, piggyback and demand registration rights that require Sema4 to register the Company’s Lock-Up Shares for resale under the Securities Act.

ITEM 7. Material to be Filed as Exhibits.

- Exhibit 1. [Agreement and Plan of Merger and Reorganization, dated as of January 14, 2022, by and among the Company, Sema4, Orion Merger Sub I, Inc., Orion Merger Sub II, LLC, GeneDx Inc. and GeneDx Holding 2, Inc. \(incorporated by reference to Exhibit 2.1 to the Company’s Current Report on Form 8-K filed with the SEC on January 18, 2022\).](#)
- Exhibit 2. [Shareholder Agreement, dated as of January 14, 2022, by and among the Company and Sema4 Holdings Corp \(incorporated by reference to Exhibit 10.1 to the Company’s Current Report on Form 8-K filed with the SEC on January 18, 2022\).](#)

SIGNATURES

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.

OPKO Health, Inc.

Date: March 9, 2022

By: /s/ Steven D. Rubin

Name: Steven D. Rubin

Title: Executive Vice President-Administration

SCHEDULE I

Directors of OPKO

Name	Business Address	Principal Occupation or Employment	Citizenship
Phillip Frost, M.D.	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Chairman of the Board and Chief Executive Officer of OPKO Health, Inc.	United States
Jane H. Hsiao, Ph.D, MBA	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Vice Chairman of the Board and Chief Technical Officer of OPKO Health, Inc.	United States
Steven D. Rubin	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Executive Vice President - Administration of OPKO Health Inc.	United States
Jon R. Cohen, M.D.	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Senior Vice President of OPKO Health, Inc. and Chairperson of BioReference Health, LLC	United States
Richard M. Krasno, Ph.D.	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Director of BioCardia, Inc.	United States
Prem A. Lachman, M.D.	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	General Partner of Maximus Capital, LLC	United States
Roger J. Medel, M.D.	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Director of MEDNAX, Inc.	United States
John A. Paganelli	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Former Chairman of the Board of Pharos Systems International	United States
Richard C. Pfenniger, Jr.	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Former Chairman, Chief Executive Officer and President of Continucare Corporation	United State
Alice Lin-Tsing Yu, M.D., Ph.D.	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Emeriti Professor of Pediatrics at University of California in San Diego	United States

Officers of OPKO

Name	Business Address	Principal Occupation or Employment	Citizenship
Phillip Frost, M.D.	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Chief Executive Officer and Chairman of the Board	United States
Jane H. Hsiao, Ph.D, MBA	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Chief Technical Officer and Vice Chairman of the Board	United States
Steven D. Rubin	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Executive Vice President - Administration	United States

Jon R. Cohen, M.D.	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Senior Vice President	United States
Adam Logal	c/o OPKO Health, Inc. 4400 Biscayne Blvd. Miami, Florida 33137	Senior Vice President, Chief Financial Officer, Chief Accounting Officer and Treasurer	United States