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

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**SCHEDULE 13G**

(Amendment No. 4)\*

Under the Securities Exchange Act of 1934

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**MABVAX THERAPEUTICS HOLDINGS, INC.**  
(Name of Issuer)

Common Stock, \$0.01 par value per share  
(Titles of Class of Securities)

55414P702  
(CUSIP Number)

May 9, 2019  
(Date of Event Which Requires Filing of this Statement)

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Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

- ☐ Rule 13d-1(b)  
☒ Rule 13d-1(c)  
☐ Rule 13d-1(d)

\* The remainder of this cover page shall be filled out of 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 in 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 "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	NAME OF REPORTING PERSON  OPKO Health, Inc.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3	SEC USE ONLY	
4	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:	5	SOLE VOTING POWER  488,131 (1)
	6	SHARED VOTING POWER  0
	7	SOLE DISPOSITIVE POWER  488,131 (1)
	8	SHARED DISPOSITIVE POWER  0
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  488,131 (1)	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9  4.99% (2)	
12	TYPE OF REPORTING PERSON  CO	

- (1) Comprised of (i) 135,371 shares of common stock, par value \$0.01 (the "Common Stock"), of Mabvax Therapeutics Holdings, Inc. (the "Issuer") and (ii) 277,778 shares of Common Stock into which shares of Series L Preferred Stock of the Issuer could be converted and 74,982 shares of Common Stock into which Series I Preferred Stock of the Issuer could be converted. Excludes (i) 32,625 shares of Common Stock into which Class I Preferred Stock of the Issuer cannot currently be converted due to a provision that precludes OPKO from converting such preferred stock as applicable, if such conversion would result in OPKO or any of its affiliates beneficially owning in excess of 4.99% of the shares of Common Stock, and (ii) 150,150 shares of Common Stock into which Class E Preferred Stock of the Issuer cannot currently be converted due to a provision that precludes OPKO from converting such preferred stock as applicable, if such conversion would result in OPKO or any of its affiliates beneficially owning in excess of 4.99% of the shares of Common Stock.

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- (2) Calculated based on (i) 9,429,582 shares of Common Stock outstanding as of April 24, 2019, as reported in the Issuer's amended quarterly report on Form 10-Q for the fiscal quarter ended September 30, 2018, filed with the Securities and Exchange Commission on April 24, 2019 (the Quarterly Report"), and (ii) 352,760 shares of Common Stock underlying currently convertible preferred stock.

1	NAME OF REPORTING PERSON	
	Phillip Frost, M.D.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3	SEC USE ONLY	
4	CITIZENSHIP OR PLACE OF ORGANIZATION	
	United States	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:	5	SOLE VOTING POWER
		0
	6	SHARED VOTING POWER
		487,855 (2)
	7	SOLE DISPOSITIVE POWER
		0
	8	SHARED DISPOSITIVE POWER
		487,855 (2)
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON	
	487,855 (2)	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input checked="" type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9	
	4.99% (1)	
12	TYPE OF REPORTING PERSON	
	IN	

- (1) Calculated based on 9,429,582 shares of the Common Stock outstanding as of April 24, 2019, as reported in the Quarterly Report.
- (2) Represents (i) 140,778 shares of common stock held by Frost Gamma Investments Trust ("FGIT"), (ii) 69,299 shares of common stock underlying Series D Convertible Preferred Stock and (iii) 277,778 shares of common stock underlying Series L Convertible Preferred Stock. Excludes (i) 129,388 shares of common stock underlying Series D Convertible Preferred Stock which contains a 4.99% beneficial ownership blocker and (ii) 107,607 shares of common stock underlying Series I Convertible Preferred Stock held by FGIT which contains a 4.99% beneficial ownership blocker. Dr. Frost is the trustee of FGIT. Frost Gamma L.P. is the sole and exclusive beneficiary of FGIT. Dr. Frost is one of two limited partners of Frost Gamma L.P. The general partner of Frost Gamma L.P. is Frost Gamma, Inc., and the sole shareholder of

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Frost Gamma, Inc. is Frost-Nevada Corporation. Dr. Frost is the sole shareholder of Frost-Nevada Corporation. The reporting person disclaims beneficial ownership of these securities, except to the extent of any pecuniary interest therein and this report shall not be deemed an admission that the reporting person is the beneficial owner of these securities for purposes of Section 16 or for any other purpose.

1	NAME OF REPORTING PERSON	
	Frost Gamma Investments Trust	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3	SEC USE ONLY	
4	CITIZENSHIP OR PLACE OF ORGANIZATION	
	Florida	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:	5	SOLE VOTING POWER
		0
	6	SHARED VOTING POWER
		487,855 (2)
	7	SOLE DISPOSITIVE POWER
		0
	8	SHARED DISPOSITIVE POWER
		487,855 (2)
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON	
	487,855 (2)	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input checked="" type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9	
	4.99% (1)	
12	TYPE OF REPORTING PERSON	
	OO	

- (1) Calculated based on 9,429,582 shares of the Common Stock outstanding as of April 24, 2019, as reported in the Quarterly Report.
- (2) Represents (i) 140,778 shares of common stock held by Frost Gamma Investments Trust ("FGIT"), (ii) 69,299 shares of common stock underlying Series D Convertible Preferred Stock and (iii) 277,778 shares of common stock underlying Series L Convertible Preferred Stock. Excludes (i) 129,388 shares of common stock underlying Series D Convertible Preferred Stock which contains a 4.99% beneficial ownership blocker and (ii) 107,607 shares of common stock underlying Series I Convertible Preferred Stock held by FGIT which contains a 4.99% beneficial ownership blocker. Dr. Frost is the trustee of FGIT. Frost Gamma L.P. is the sole and exclusive beneficiary of FGIT. Dr. Frost is one of two limited partners of Frost Gamma L.P. The general partner of Frost Gamma L.P. is Frost Gamma, Inc., and the sole shareholder of

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## EXPLANATORY NOTE

This Schedule 13G (the “Statement”) is filed (i) by OPKO Health, Inc. (“OPKO”) and (ii) to amend the Schedule 13G filed by Phillip Frost, M.D. and Frost Gamma Investments Trust (“FGIT”) on April 10, 2015 (the “Original 13G”), as amended on February 8, 2016, February 3, 2017 and January 31, 2018.

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. Frost.

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. 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 Securities Exchange Act of 1934 (the “Exchange Act”), a claim that requires no showing of scienter, and to pay a civil monetary penalty, which has been paid. OPKO also agreed, within certain stipulated time periods, to: (i) establish a Management Investment Committee (“MIC”) that will make recommendations to an Independent Investment Committee (“IIC”) of OPKO’s board of directors in connection with existing and future strategic minority investments; and (ii) retain an Independent Compliance Consultant (“ICC”) on a time-limited basis to, among other things, advise OPKO on whether filings pursuant to Section 13(d) of the Exchange Act for previous strategic minority investments made at the suggestion of or in tandem with Dr. Frost and his related persons or entities should be made or amended to reflect group membership with Dr. Frost.

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, claims which may be satisfied by strict liability and negligence, respectively, and Section 13(d) of 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.

The ICC has concluded his work, determined that certain prior investments in the Issuer by OPKO and Dr. Frost should have been grouped under Section 13(d) of the Exchange Act, and recommended the filing of this form.

OPKO has now established the MIC and IIC, and following the establishment of these committees, any group between OPKO, Dr. Frost and affiliated entities with respect to investments in the Issuer has ceased to exist.



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**Item 1(a). Name of Issuer:**

Mabvax Therapeutics Holdings, Inc.

**Item 1(b). Address of Issuer's Principal Executive Offices:**

11535 Sorrento Valley Road, Suite 400, San Diego, CA 92121

**Item 2(a). Name of Person Filing:**

This statement is being filed by:

- (i) OPKO Health, Inc., a corporation incorporated under the laws of the State of Delaware;
- (ii) Phillip Frost, M.D.; and
- (iii) Frost Gamma Investments Trust, a trust organized under the laws of the State of Florida.

The Reporting Persons have entered into a joint filing agreement, dated as of May 9, 2019, a copy of which is attached hereto as Exhibit 1.

**Item 2(b). Address of Principal Business Office or, if none, Residence:**

The principal business address of each of the Reporting Persons is as follows:

OPKO Health, Inc.  
4400 Biscayne Blvd.  
Miami, Florida 33137

Phillip Frost, M.D.  
Frost Gamma Investments Trust  
4400 Biscayne Blvd, Suite 1500  
Miami, Florida 33137

**Item 2(c). Citizenship:**

See response to Item 4 of each of the cover pages.

**Item 2(d). Titles of Classes of Securities:**

Common Stock, \$0.01 par value per share

**Item 2(e). CUSIP Number:**

55414P702

**Item 3. If This Statement is Filed Pursuant to Rule 13d-1(b), or 13d-2(b) or (c), Check Whether the Person Filing is a(n):**

- (a) ☐ Broker or dealer registered under Section 15 of the Exchange Act (15 U.S.C. 78o).
- (b) ☐ Bank as defined in Section 3(a)(6) of the Exchange Act (15 U.S.C. 78c).
- (c) ☐ Insurance company as defined in Section 3(a)(19) of the Exchange Act (15 U.S.C. 78c).

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- (d) ☐ Investment company registered under Section 8 of the Investment Company Act of 1940 (15 U.S.C 80a-8).
  - (e) ☐ Investment adviser in accordance with §240.13d-1(b)(1)(ii)(E).
  - (f) ☐ Employee benefit plan or endowment fund in accordance with §240.13d-1(b)(1)(ii)(F).
  - (g) ☐ Parent holding company or control person in accordance with §240.13d-1(b)(1)(ii)(G).
  - (h) ☐ Savings association as defined in Section 3(b) of the Federal Deposit Insurance Act (13 U.S.C. 1813).
  - (i) ☐ Church plan that is excluded from the definition of an investment company under Section 3(c)(14) of the Investment Company Act (15 U.S.C. 80a-3).
  - (j) ☐ Non-U.S. institution in accordance with §240.13d-1(b)(1)(ii)(J).
  - (k) ☐ Group in accordance with §240.13d-1(b)(1)(ii)(K).

If filing as a non-U.S. institution in accordance with §240.13d-1(b)(1)(ii)(J), please specify the type of institution: \_\_\_\_\_

**Item 4. Ownership**

(a) **Amount Beneficially Owned:**

See responses to Item 9 on each cover page.

(b) **Percent of Class:**

See responses to Item 11 on each cover page.

(c) Number of shares as to which such person has:

(i) **Sole power to vote or to direct the vote:**

See responses to Item 5 on each cover page.

(ii) **Shared power to vote or to direct the vote:**

See responses to Item 6 on each cover page.

(iii) **Sole power to dispose or to direct the disposition of:**

See responses to Item 7 on each cover page.

(iv) **Shared power to dispose or to direct the disposition of:**

See responses to Item 8 on each cover page.

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**Item 5. Ownership of Five Percent or Less of a Class.**

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following ☒.

OPKO ceased to be a member of a group with Dr. Frost no later than the establishment of the IIC and MIC on February 1, 2019. None of the Reporting Persons are the beneficial owner of more than 5% of the outstanding Common Stock

**Item 6. Ownership of More than Five Percent on Behalf of Another Person.**

Not Applicable.

**Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company.**

See response to Item 2(a) above.

**Item 8. Identification and Classification of Members of the Group.**

The information set forth under the heading "Explanatory Note" and Item 5 is incorporated by reference in its entirety into this Item 8.

**Item 9. Notice of Dissolution of Group.**

The information set forth under the heading "Explanatory Note" and Item 5 is incorporated by reference in its entirety into this Item 9.

**Item 10. Certification.**

By signing below each of the undersigned certifies that, to the best of its or his knowledge and belief, the securities referred to above were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the Issuer and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect, other than activities solely in connection with a nomination under § 240.14a-11.

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**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 9, 2019

OPKO Health, Inc.

By: /s/ Kate Inman  
Kate Inman  
General Counsel, Secretary

Phillip Frost, M.D.

By: \*

Frost Gamma Investments Trust

By: \*  
Phillip Frost, M.D.  
Trustee

By: /s/ Steven D. Rubin  
Attorney-in-Fact

\* This Schedule 13G was executed by Steven D. Rubin on behalf of the individuals listed above pursuant to a Power of Attorney, a copy of which is attached as Exhibit 2.

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**Exhibit Index**

Exhibit 1	Agreement of Joint Filing as required by Rule 13d-1(k)(1) under the Act.
Exhibit 2	Power of Attorney.

**JOINT FILING AGREEMENT**

In accordance with Rule 13d-1(k)(1) under the Securities Exchange Act of 1934, as amended, each of the undersigned hereby agrees to the joint filing, along with all other such undersigned, on behalf of the Reporting Persons (as defined in the joint filing), of a statement on Schedule 13G (including amendments thereto) with respect to Mabvax Therapeutics Holdings, Inc. and that this agreement be included as an Exhibit 1 to such joint filing. This agreement may be executed in any number of counterparts, all of which taken together shall constitute one and the same instrument. The undersigned acknowledge that each shall be responsible for the timely filing of any amendments, and for the completeness and accuracy of the information concerning him or it contained herein and therein, but shall not be responsible for the completeness and accuracy of the information concerning the others, except to the extent that he or it knows or has reason to believe that such information is inaccurate.

*[Signature Page Follows]*

IN WITNESS WHEREOF, each of the undersigned hereby executes this agreement as of May 9, 2019.

OPKO Health, Inc.

By: /s/ Kate Inman

Kate Inman  
General Counsel, Secretary

Phillip Frost, M.D.

By: \*

Frost Gamma Investments Trust

By: \*

Phillip Frost, M.D.  
Trustee

By: /s/ Steven D. Rubin

Attorney-in-Fact

\* This Schedule 13G was executed by Steven D. Rubin on behalf of the individuals listed above pursuant to a Power of Attorney, a copy of which is attached as Exhibit 2.

• POWER OF ATTORNEY

The undersigned hereby constitutes and appoints Steven D. Rubin, with full power to act singly, his true and lawful attorney-in-fact to: (i) sign any and all instruments, certificates and documents that may be necessary, desirable or appropriate to be executed on behalf of himself as an individual or in his capacity as a general partner of any partnership or limited liability company, pursuant to Section 13 or 16 of the Securities Exchange Act of 1934, as amended, and any and all regulations promulgated thereunder, (ii) file the same (including any amendments thereto), with all exhibits thereto, and any other documents in connection therewith, with the Securities and Exchange Commission, and any stock exchange or similar authority and (iii) take any other action of any type whatsoever in connection with the foregoing which, in the opinion of such attorney-in-fact, may be of benefit to, in the best interest of, or legally required by, the undersigned, it being understood that the documents executed by such attorney-in-fact on behalf of the undersigned pursuant to this power of attorney shall be in such form and shall contain such terms and conditions as such attorney-in-fact may approve in such attorney-in-fact's discretion, granting unto said attorney-in-fact full power and authority to do and perform each and every act and thing necessary, desirable or appropriate.

The undersigned hereby grants to the attorney-in-fact full power and authority to do and perform any and every act and thing whatsoever requisite, necessary or proper to be done in the exercise of any of the rights and powers herein granted, as fully to all intents and purposes as the undersigned might or could do if personally present with full power of substitution or revocation, hereby ratifying and confirming all that such attorney-in-fact or such attorney-in-fact's substitute or substitutes, shall lawfully do or cause to be done by virtue of this power of attorney and the rights and powers herein granted.

This power of attorney shall remain in full force and effect until revoked by the undersigned in a signed writing delivered to the attorney-in-fact.

IN WITNESS WHEREOF, this Power of Attorney has been signed as of the 9th day of May, 2019.

Phillip Frost, M.D.

By: /s/ Phillip Frost, M.D.