
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

SCHEDULE 13D/A

Under the Securities Exchange Act of 1934
(Amendment No. 21)*

OPKO Health, Inc.

(Name of Issuer)

Common Stock, par value \$0.01 per share

(Title of Class of Securities)

68375N103

(CUSIP Number)

Camielle Green
Associate General Counsel, Secretary
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)

February 10, 2023

(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(b) 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		
	Frost Gamma Investments Trust		
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>		
3	SEC USE ONLY		
4	SOURCE OF FUNDS		
	WC,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		
	Florida		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER	
		213,891,935 Shares ⁽¹⁾	
	8	SHARED VOTING POWER	
		0	
	9	SOLE DISPOSITIVE POWER	
		213,891,935 Shares ⁽¹⁾	
	10	SHARED DISPOSITIVE POWER	
		0	
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON		
	213,891,935 Shares ⁽¹⁾		
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>		
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)		
	27.2% ⁽²⁾		
14	TYPE OF REPORTING PERSON		
	OO		

⁽¹⁾Includes approximately 15,060,241 shares of Common Stock underlying \$25,000,000 of the Issuer's 5% Convertible Promissory Notes (the "Notes"), which Notes were originally issued on February 27, 2018 and amended on February 10, 2023, and mature on January 31, 2025 and may be redeemed at any time prior to maturity upon 30 days' notice at a conversion price of \$1.66, subject to adjustment.

⁽²⁾Calculated based on (i) 772,650,812 shares outstanding as of February 10, 2023, as communicated by the Issuer to the Reporting Person; and (ii) 15,060,241 shares of Common Stock underlying the Notes.

1	NAME OF REPORTING PERSONS Frost Nevada Investments Trust	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS WC, 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 Florida	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 30,127,177 Shares
	8	SHARED VOTING POWER 0 Shares
	9	SOLE DISPOSITIVE POWER 30,127,177 Shares
	10	SHARED DISPOSITIVE POWER 0 Shares
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 30,127,177 Shares	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 3.9% ⁽¹⁾	
14	TYPE OF REPORTING PERSON OO	

⁽¹⁾ Calculated based on 772,650,812 shares outstanding as of February 10, 2023, as communicated by the Issuer to the Reporting Person.

1	NAME OF REPORTING PERSONS	
	Phillip Frost, M.D.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS	
	N/A	
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	
	United States	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER
		249,575,563 Shares
	8	SHARED VOTING POWER
		2,851,830 Shares
	9	SOLE DISPOSITIVE POWER
		249,575,563 Shares
	10	SHARED DISPOSITIVE POWER
		2,851,830 Shares
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON	
	252,427,393 Shares ⁽¹⁾	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)	
	31.9% ⁽²⁾	
14	TYPE OF REPORTING PERSON IN	

⁽¹⁾ Includes (i) 3,068,951 shares of Common Stock held individually by Dr. Frost; (ii) 30,127,177 shares of Common Stock held by the Frost Nevada Investments Trust, which is controlled by Dr. Frost as sole trustee; (iii) options to acquire 2,487,500 shares of Common Stock, which are exercisable within 60 days; (iv) 198,831,694 shares of Common Stock held by the Gamma Trust, which is controlled by Dr. Frost as sole trustee; (v) 15,060,241 shares of Common Stock underlying the Notes; and (vi) 2,851,830 shares of Common Stock held by the Phillip and Patricia Frost Philanthropic Foundation, Inc., which is controlled by Dr. Frost and his wife.

⁽²⁾ Calculated based on (i) 772,650,812 shares outstanding as of February 10, 2023, as communicated by the Issuer to the Reporting Person; (ii) options to acquire 2,487,500 shares of Common Stock, which are exercisable within 60 days; and (iii) 15,060,241 shares of Common Stock underlying the Notes held by the Gamma Trust.

EXPLANATORY NOTE

This Amendment No. 21 (the “Amendment”) amends and supplements the statement on Schedule 13D filed on February 15, 2007, as amended by Amendment No. 1 to the Schedule 13D filed on April 6, 2007, as amended by Amendment No. 2 to the Schedule 13D filed on August 2, 2007, as amended by Amendment No. 3 to the Schedule 13D filed on February 14, 2008, as amended by Amendment No. 4 to Schedule 13D filed on August 21, 2008, as amended by Amendment No. 5 to the Schedule 13D filed on February 26, 2009, as amended by Amendment No. 6 to the Schedule 13D filed on March 19, 2009, as amended by Amendment No. 7 to the Schedule 13D filed on October 1, 2009, as amended by Amendment No. 8 to the Schedule 13D filed on March 28, 2011, as amended by Amendment No. 9 to the Schedule 13D filed on October 24, 2011, as amended by Amendment No. 10 to the Schedule 13D filed on October 11, 2012, as amended by Amendment No. 11 to the Schedule 13D filed on March 21, 2013, as amended by Amendment No. 12 to the Schedule 13D filed on September 16, 2013, as amended by Amendment No. 13 to the Schedule 13D filed on February 17, 2015, as amended by Amendment No. 14 to the Schedule 13D filed on December 18, 2015, as amended by Amendment No. 15 to Schedule 13-D filed on September 20, 2017, as amended by Amendment No. 16 to Schedule 13-D filed on November 20, 2018, as amended by Amendment No. 17 to Schedule 13-D filed on March 20, 2019, as amended by Amendment No. 18 to Schedule 13-D filed on March 22, 2019, as amended by Amendment No. 19 to Schedule 13-D filed on November 1, 2019, as amended by Amendment No. 20 to Schedule 13-D filed on August 19, 2022 (collectively, the “Original Schedule 13D”), by The Frost Group, LLC (the “Frost Group”), a previously reporting entity, Frost Gamma Investments Trust (“Gamma Trust”), Frost Nevada Investments Trust (“Frost Nevada”), and Phillip Frost, M.D. (“Dr. Frost”). This Amendment is filed pursuant to the Joint Filing Agreement as executed by the reporting persons listed on the cover pages to this Amendment. The Joint Filing Agreement, filed as Exhibit 1 to Amendment No. 15 to the Schedule 13D filed on September 20, 2017, is hereby incorporated by this reference. This Amendment is filed with respect to the common stock, par value \$0.01 per share (“Common Stock”), of OPKO Health, Inc., a Delaware corporation (the “Issuer”).

ITEM 3. Source and Amount of Funds or Other Consideration.**Item 3 is amended by adding the following paragraph to the end of the item:**

On February 27, 2018, the Issuer issued a series of 5% Convertible Promissory Notes (the “Original Notes”) in the aggregate principal amount of \$55 million, including a note to Gamma Trust in the principal amount of \$25 million, with a conversion price of \$5.00 and a maturity date of February 27, 2023. On or about February 10, 2023, the Issuer amended the Original Notes to extend the maturity to January 31, 2025, and to reset the conversion price to the 10 day volume weighted average price immediately preceding the date of the amended note, plus a 25% conversion premium, or \$1.66 (the “Amended Notes”). The Amended Notes can be converted into shares of Common Stock at any time prior to the maturity date. In addition, under the terms of the Amended Note, interest will accrue from the most recent date to which interest has been paid or, if no interest has been paid, from the date of issuance, until the principal and accrued and unpaid interest, are paid in full. Gamma Trust used working capital to purchase the Original Note.

ITEM 4. Purpose of Transaction.**Item 4 is amended by adding the following paragraph to the end of the item:**

On February 27, 2018, the Issuer issued the Original Notes including a note to Gamma Trust in the principal amount of \$25 million with a conversion price of \$5.00 and a maturity date of February 27, 2023. On or about February 10, 2023, the Issuer issued the Amended Notes. The Amended Note can be converted into shares of Common Stock at any time prior to the maturity date.

ITEM 5. Interest in Securities of the Issuer.**Item 5 is deleted in its entirety and replaced with the following text:**

(a)-(b) Gamma Trust directly beneficially owns 213,891,935 shares of Common Stock, which includes approximately 15,060,241 shares of Common Stock underlying \$25,000,000 of the Amended Notes, which notes were originally issued on February 27, 2018 with a conversion price of \$5.00 and maturity date of February 27, 2023. The Original Notes were amended and restated to reflect a conversion price of \$1.66 and an extended maturity date of January 31, 2025. The Amended Note may be redeemed at any time prior to maturity upon 30 days’ notice at a conversion price of \$1.66, subject to adjustment. The 213,891,935 total shares of Common Stock beneficially owned by Gamma Trust constitute approximately 27.2% of the Issuer’s outstanding shares of Common Stock, based

upon (i) 772,650,812 shares of Common Stock outstanding as of February 10, 2023 as communicated by the Issuer to the Reporting Person; and (ii) 15,060,241 shares of the Common Stock underlying the Notes. Dr. Frost is the sole trustee of Gamma Trust and holds sole voting and dispositive power with respect to 213,891,935 shares of Common Stock.

Frost Nevada directly beneficially owns 30,127,177 shares of Common Stock. The 30,127,177 total shares of Common Stock beneficially owned by Frost Nevada constitute approximately 3.9% of the Issuer's outstanding shares of Common Stock, based upon 772,650,812 shares of Common Stock outstanding as of February 10, 2023 as communicated by the Issuer to the Reporting Person. Dr. Frost is the sole trustee of Frost Nevada and holds sole voting and dispositive power with respect to 30,127,177 shares of Common Stock.

Dr. Frost, as the sole trustee of Gamma Trust, may be deemed to beneficially own the 213,891,935 shares of Common Stock beneficially owned by Gamma Trust. Dr. Frost, as the sole trustee of Frost Nevada may be deemed to beneficially own the 30,127,177 shares of Common Stock beneficially owned by Frost Nevada. In addition, the Phillip and Patricia Frost Philanthropic Foundation, Inc., which is controlled by Dr. Frost and his wife, owns 2,851,830 shares of Common Stock. Dr. Frost individually owns 3,068,951 shares of Common Stock and options to acquire 2,487,500 shares of Common Stock, which are exercisable within 60 days, and has sole voting and dispositive power over each. The 252,427,393 shares of Common Stock beneficially owned by Dr. Frost constitute approximately 31.9% of the Issuer's outstanding shares of Common Stock, based upon (i) 772,650,812 shares of Common Stock outstanding as of February 10, 2023 as communicated by the Issuer to the Reporting Person; (ii) options to acquire 2,487,500 shares of Common Stock, which are exercisable within 60 days; and (iii) 15,060,241 shares of the Common Stock underlying the Amended Notes. Dr. Frost, as sole trustee of Gamma Trust, has sole voting and dispositive power over 213,891,935 shares of Common Stock. Dr. Frost, as sole trustee of Frost Nevada, has sole voting and dispositive power over 30,127,177 shares of Common Stock. Dr. Frost has shared voting and dispositive power with respect to 2,851,830 shares of Common Stock owned by the Phillip and Patricia Frost Philanthropic Foundation, Inc.

(c) In the last 60 days prior to the filing of this Amendment No. 21, Gamma Trust, Frost Nevada, and Dr. Frost have not effected any transactions in the shares of Common Stock.

(d) Except as described herein, no other person is known by any Reporting Person to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, any shares of the Issuer beneficially owned by them.

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.

Frost Gamma Investments Trust

Dated: February 21, 2023

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

Name: Phillip Frost, M.D.

Title: Sole Trustee

Frost Nevada Investments Trust

Dated: February 21, 2023

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

Name: Phillip Frost, M.D.

Title: Sole Trustee

Dated: February 21, 2023

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

Name: Phillip Frost, M.D.

Title: Phillip Frost, M.D., Individually