

FORM 4

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

OMB APPROVAL

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☐ Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP OF SECURITIES

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

(Print or Type Responses)

| 1. Name and Address of Reporting Person [*] FROST PHILLIP MD ET AL | | 2. Issuer Name and Ticker or Trading Symbol OPKO HEALTH, INC. [OPK] | | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable) <input type="checkbox"/> Director <input checked="" type="checkbox"/> 10% Owner <input checked="" type="checkbox"/> Officer (give title below) <input type="checkbox"/> Other (specify below) CEO & Chairman | | | | | | |
|--|---|---|-----------------------------------|--|--|------------|--|---|--|------------------|
| (Last) (First) (Middle) OPKO HEALTH, INC., 4400 BISCAYNE BLVD. | | 3. Date of Earliest Transaction (Month/Day/Year) 02/14/2022 | | | | | | | | |
| (Street) MIAMI, FL 33137 | | 4. If Amendment, Date Original Filed(Month/Day/Year) | | 6. Individual or Joint/Group Filing (Check Applicable Line) <input type="checkbox"/> Form filed by One Reporting Person <input checked="" type="checkbox"/> Form filed by More than One Reporting Person | | | | | | |
| (City) (State) (Zip) | | Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned | | | | | | | | |
| 1. Title of Security (Instr. 3) | 2. Transaction Date (Month/Day/Year) | 2A. Deemed Execution Date, if any (Month/Day/Year) | 3. Transaction Code (Instr. 8) | | 4. Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) | | 5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4) | 6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 7. Nature of Indirect Beneficial Ownership (Instr. 4) | |
| | | | Code | V | Amount | (A) or (D) | Price | | | |
| Common Stock | | | | | | | | 3,068,951 | D | |
| Common Stock | 02/14/2022 | | P | | 13,273 | A | \$ 3.015 | 193,684,967 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 1,259 | A | \$ 3.02 | 193,686,226 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 608 | A | \$ 3.025 | 193,686,834 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 1,701 | A | \$ 3.029 | 193,688,535 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 28,759 | A | \$ 3.03 | 193,717,294 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 11,809 | A | \$ 3.035 | 193,729,103 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 18,191 | A | \$ 3.04 | 193,747,294 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 8,200 | A | \$ 3.045 | 193,755,494 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 300 | A | \$ 3.05 | 193,755,794 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 12,400 | A | \$ 3.055 | 193,768,194 | I | See Footnote (1) |
| Common Stock | 02/14/2022 | | P | | 3,500 | A | \$ 3.06 | 193,771,694 | I | See Footnote (1) |
| Common Stock | | | | | | | | 30,127,177 | I | See Footnote (2) |

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB control number.

SEC 1474 (9-02)

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned
(e.g., puts, calls, warrants, options, convertible securities)

| 1. Title of Derivative Security (Instr. 3) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | 3A. Deemed Execution Date, if any (Month/Day/Year) | 4. Transaction Code (Instr. 8) | | 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4, and 5) | 6. Date Exercisable and Expiration Date (Month/Day/Year) | | 7. Title and Amount of Underlying Securities (Instr. 3 and 4) | 8. Price of Derivative Security (Instr. 5) | 9. Number of Derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4) | 10. Ownership Form of Derivative Security: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) |
|--|--|--------------------------------------|--|--------------------------------|---|---|--|-----------------|---|--|--|--|--|
| | | | | Code | V | | Date Exercisable | Expiration Date | Title | | | | |
| | | | | | | (A) (D) | | | Amount or Number of Shares | | | | |

Reporting Owners

| Reporting Owner Name / Address | Relationships | | | |
|---|---------------|-----------|----------------|-------|
| | Director | 10% Owner | Officer | Other |
| FROST PHILLIP MD ET AL OPKO HEALTH, INC. 4400 BISCAYNE BLVD. MIAMI, FL 33137 | X | X | CEO & Chairman | |
| Frost Gamma Investments Trust 4400 BISCAYNE BLVD. MIAMI, FL 33137 | | X | | |

Signatures

| | | |
|--|--|------------|
| Phillip Frost, M.D., Individually and as Trustee | | 02/15/2022 |
| **Signature of Reporting Person | | Date |

Explanation of Responses:

* If the form is filed by more than one reporting person, see Instruction 4(b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations. See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

The securities are held by Frost Gamma Investments Trust, of which Phillip Frost M.D., is the trustee. Frost Gamma L.P. is the sole and exclusive beneficiary of Frost Gamma Investments Trust. 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

(1) shareholder of Frost Gamma, Inc. is Frost-Nevada Corporation. Dr. Frost is also 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.

These securities are held by Frost Nevada Investments Trust, of which the Reporting Person is the trustee and Frost-Nevada, L.P. is the sole and exclusive beneficiary. The Reporting Person is one of seven limited partners of Frost-Nevada, L.P. and the sole shareholder of Frost-Nevada Corporation, the sole general partner of Frost-Nevada, L.P.

(2) 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.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

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JOINT FILER INFORMATION

Name: Frost Gamma Investments Trust

Address:
4400 Biscayne Blvd.
Miami, FL 33137

Designated Filer: Phillip Frost, M.D.

Issuer Name and Ticker Symbol: OPKO Health, Inc. (OPK)

Date of Earliest Transaction: February 14, 2022

Relationship to Issuer: 10% Owner

FROST GAMMA INVESTMENTS TRUST

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