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

| OMB APPROVAL | | | | | |
|-------------------------|-----------|--|--|--|--|
| OMB Number: | 3235-0287 | | | | |
| Stimated average burden | | | | | |
| ours per respons | e 0.5 | | | | |

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

| Check all applicables Chec | (Print or Ty | pe Response | es) | | | | | | | | | | | | | | |
|--|--|---|---|--|----------------------------|-------------|--|--------|---|----------|------------------------------------|--------------------------|--------------------------------|------------------------|--|---|-----------------------------------|
| CEO & Chairman CEO & CEO & Chairman | 1. Name and Address of Reporting Person * FROST PHILLIP MD ET AL | | | | | | | | | | (Check all applicable) | | | | | | |
| MIAMI, FL 33137 | | | | | | | st Tran | sactio | on (M | Ionth/Da | y/Year) | | X Office | | ow) | Other (specify | below) |
| MAMI_FL 33137 Close Clos | | | | 4. If Amendment, Date Original Filed(Month/Day/Year) | | | | | | | Form filed by One Reporting Person | | | | | | |
| 1. Title of Security Date 2. Transaction Date Execution Date (Month/Day/Year) (Month/Day/Yea | MIAMI, FL 33137 | | | | | | | | | | | | | | | | |
| Date Month/Day/Year Code | (City | ·) | (State) | (Zip) | | Ta | ble I - | - Non- | -Deri | vative S | ecuritie | s Acqui | ired, Disp | osed of, or | Beneficially | Owned | |
| Month/Day/Year) any Month/Day/Year) (Instr. 3) (Instr. 3, 4 and 5) (Instr. 3 and 4) (Instr. 3 and 4) (Instr. 3 and 4) (Instr. 3 and 4) (Instr. 3) Form: (Instr. 3 and 4) (Instr. 3) Form: (Instr. 3) (Instr. 3) (Instr. 3) (Instr. 4) (| | Security | | | | | | ction | | | | | | | | | |
| Common Stock | (IIIsti. 3) | | | 77.7.5 | any | , | (Instr. 8 | | | | | | Reported Transaction(s) | | | Form: | Beneficial |
| Common Stock | | | | | (Month | /Day/Yea | | ode | v | Amoun | | Price | (Instr. 3 a | 3 and 4) | | or Indirect | Ownership (Instr. 4) |
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| Common Stock 01/11/2016 P 1,500 A 8.52 158,568,843 I Founded (1) Common Stock 01/11/2016 P 1,500 A 8.52 158,568,843 I Founded (1) Common Stock 1 | Common | Stock | | 01/11/2016 | | | | P | | 600 | A | \$ 8.515 | 158,567 | ,343 | | I | Footnote |
| Reminder: Report on a separate line for each class of securities beneficially owned directly or ndirectly. 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. Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) Security Securities | Common | Stock | | 01/11/2016 | | | | P | | 1,500 | A | \$ 8.52 | 158,568 | 3,843 | | I | Footnote |
| Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) I. Title of Derivative Conversion Date (Instr. 3) Price of Derivative Security (Month/Day/Year) 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. Table II - Derivative Securites Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) I. Title of Derivative Conversion Date (Month/Day/Year) 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. Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) I. Title of Derivative (Month/Day/Year) 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. I. Title of Derivative (Month/Day/Year) I. Title of Derivati | Common | Stock | | | | | | | | | | | 20,091,0 | 062 | | I | Footnote |
| Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) 1. Title of 2. Derivative Conversion Date or Exercise (Instr. 3) Price of Derivative Security Price of Derivative Security OExecurity Price of Derivative Security Security Security Code V (A) (D) Code V (A) (D) Contained in this form are not required to respond unless the form displays a currently valid OMB control number. 7. Title and Amount of Derivative Derivative Derivative Securities Securities Securities Securities Securities (Instr. 3 and 4) 7. Title and Amount of Derivative Owner Shep of Instr. 3 and 4) Omnet Transaction(s) (Instr. 4) | Reminder: indirectly. | Report on a | separate line | for each class of seco | urities be | eneficially | owne | | | | | | | | | | |
| 1. Title of Derivative Security Security (e.g., puts, calls, warrants, options, convertible securities) 3. Transaction Date Exercise (Month/Day/Year) (Instr. 3) (Month/Day/Year) (Month/Day/Year) (Instr. 4) | | | | | | | | | cont | ained i | n this f | orm ar | e not req | uired to re | espond un | less | EC 1474 (9- 02) |
| Derivative Security Or Exercise (Instr. 3) Date Or Exercise (Instr. 3) Date Or Exercise (Instr. 3) Derivative Security Or Exercise (Instr. 3) Derivative Security Or Exercise (Instr. 4) Derivative Securities Or Exercise (Instr. 4) Or Indirect (Instr. 4) Or Instr. 4) | | | | | | | | • | | • | | | • | i | | | |
| Code V (A) (D) Code V (A) (D) (D) Code V (A) (D) Code V (A) (D) Code V (A) (D) (D) (D) Code V (A) (D) (D) (D) Code V (A) (D) (D) (D) (D) (D) (D) (D) (D) (D) (D | Derivative Security | Conversion or Exercise Price of Derivative | rsion Date Execution Day/ f (Month/Day/Year) any (Month/Day/ | | te, if Transaction Code | | of Derivative Securities Acquired (A) or Disposed | | and Expiration Date (Month/Day/Year) | | | Am Und Sec (Ins | ount of derlying urities | Derivative Security | Derivative Securities Beneficially Owned Following Reported | Owners Form o y Derivat Security Direct (or Indir | Benefici Ownersh (Instr. 4) |
| Code V (A) (D) Exercisable Expiration Date Expiration Date Title Number of Shares | | | | | | | (Inst | r. 3, | | | | | | | | | |
| Zanarting Owners | | | | | | Code V | (A) | (D) | | | | Titl | e Number of | | | | |
| | Range | ting (| wnore | | | | | | | | | | | | | | |

| Daniel Communication (Addison | Relationships | | | | | | |
|---|---------------|-----------|----------------|-------|--|--|--|
| Reporting Owner Name / Address | 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 | 01/12/2016 |
|--|------------|
| **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 owned directly by The Frost Group, LLC. Frost Gamma Investments Trust is a principal member of The Frost Group, LLC. The reporting person (2) 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.

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

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: January 11, 2016

Relationship to Issuer: 10% Owner

FROST GAMMA INVESTMENTS TRUST

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