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

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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 FROST PHILLIP MD ET AI | 2. Issuer Name a<br>Opko Health, I | nc. [OPK         | .]          |   |           |   | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable)  X Director X 10% Owner |                                   |                                  |                        |
| OPKO HEALTH, INC., 4400<br>BLVD.                        | 3. Date of Earlies 11/16/2015      | t Transacti      | on (N       | Month/Da  | y/Year]   | X Officer (give title below) Other (specify below)  CEO & Chairman  |   |                                   |                                  |                        |
| (Street)  | 4. If Amendment,                   | Date Orig        | inal l      | Filed(Mon   | h/Day/Ye  | 6. Individual or Joint/Group Filin Form filed by One Reporting Person X_Form filed by More than One Reporting |   | able Line)                        |                                  |                        |
| MIAMI, FL 33137 (City) (State)                          | (Zip)                              | Tal              | ble I - Non | -Der  | ivative S | ecuriti   | es Acqui  | red, Disposed of, or Beneficially |                                  |                        |
| 1.Title of Security<br>(Instr. 3)                       | 2A. Deemed<br>Execution Date, if   |                  |             | 4. Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) |           |   | 5. Amount of Securities Beneficially Owned Following Reported Transaction(s)                    | 6.                                | 7. Nature of Indirect Beneficial |                        |
|   | (Month/Day/Year)                   | (Month/Day/Year) |             |   | (mstr. 5  | (A) or  |   | (Instr. 3 and 4)                  | Direct (D)<br>or Indirect<br>(I) | Ownership              |
| Common Stock  |                                    |                  | Code        | V   | Amount    | (D)   | Price   | 2.069.051                         | (Instr. 4)                       |                        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 2,500     | A   | \$<br>10.32   | 3,068,951<br>158,056,943          | I                                | See<br>Footnote        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 660       | A   | \$<br>10.33   | 158,057,603                       | I                                | See<br>Footnote        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 540       | A   | \$<br>10.335  | 158,058,143                       | I                                | See<br>Footnote<br>(1) |
| Common Stock  | 11/16/2015                         |                  | P           |   | 800       | A   | \$<br>10.34   | 158,058,943                       | Ι                                | See<br>Footnote        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 400       | A   | \$<br>10.365  | 158,059,343                       | I                                | See<br>Footnote        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 100       | A   | \$<br>10.37   | 158,059,443                       | Ι                                | See<br>Footnote        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 1,000     | A   | \$<br>10.38   | 158,060,443                       | I                                | See Footnote (1)       |
| Common Stock  | 11/16/2015                         |                  | P           |   | 1,500     | A   | \$<br>10.39   | 158,061,943                       | I                                | See Footnote (1)       |
| Common Stock  | 11/16/2015                         |                  | P           |   | 1,000     | A   | \$ 10.4   | 158,062,943                       | I                                | See Footnote (1)       |
| Common Stock  | 11/16/2015                         |                  | P           |   | 1,000     | A   | \$<br>10.41   | 158,063,943                       | I                                | See Footnote (1)       |
| Common Stock  | 11/16/2015                         |                  | P           |   | 500       | A   | \$<br>10.44   | 158,064,443                       | I                                | See<br>Footnote        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 500       | A   | \$<br>10.45   | 158,064,943                       | Ι                                | See<br>Footnote        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 500       | A   | \$<br>10.46   | 158,065,443                       | I                                | See<br>Footnote        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 500       | A   | \$<br>10.47   | 158,065,943                       | I                                | See<br>Footnote        |
| Common Stock  | 11/16/2015                         |                  | P           |   | 500       | A   | \$<br>10.49   | 158,066,443                       | I                                | See<br>Footnote        |

| Common Stock | 11/16/2015 | P | 1,000 | A | \$ 10.5      | 158,067,443 | I | See<br>Footnote  |
|--------------|------------|---|-------|---|--------------|-------------|---|------------------|
| Common Stock | 11/16/2015 | P | 500   | A | \$<br>10.52  | 158,067,943 | I | See<br>Footnote  |
| Common Stock | 11/16/2015 | P | 400   | A | \$<br>10.545 | 158,068,343 | I | See<br>Footnote  |
| Common Stock | 11/16/2015 | Р | 100   | A | \$<br>10.55  | 158,068,443 | I | See Footnote (1) |
| Common Stock | 11/16/2015 | Р | 1,800 | A | \$<br>10.56  | 158,070,243 | I | See Footnote (1) |
| Common Stock | 11/16/2015 | P | 650   | A | \$<br>10.57  | 158,070,893 | I | See Footnote (1) |
| Common Stock | 11/16/2015 | Р | 1,150 | A | \$<br>10.58  | 158,072,043 | I | See Footnote (1) |
| Common Stock | 11/16/2015 | Р | 500   | A | \$<br>10.62  | 158,072,543 | I | See Footnote (1) |
| Common Stock | 11/16/2015 | Р | 3,000 | A | \$<br>10.63  | 158,075,543 | I | See Footnote (1) |
| Common Stock | 11/16/2015 | P | 5,500 | A | \$<br>10.64  | 158,081,043 | I | See Footnote (1) |
| Common Stock | 11/16/2015 | Р | 1,900 | A | \$<br>10.65  | 158,082,943 | I | See Footnote (1) |
| Common Stock | 11/16/2015 | Р | 1,500 | A | \$<br>10.68  | 158,084,443 | I | See<br>Footnote  |
| Common Stock |            |   |       |   |              | 20,091,062  | I | See<br>Footnote  |

| deminder: Report on a separate line for each class of securities beneficially owned directly. | ectly or        |  |                     |
|---|-----------------|--|---------------------|
|   | contained in th | respond to the collection of information<br>nis form are not required to respond unless<br>ays a currently valid OMB control number. | SEC 1474 (9-<br>02) |

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

| 1. Title of | 2.          | 3. Transaction   | 3A. Deemed         | 4.         |   | 5. Nu   | mber   | 6. Date Exer | cisable            | 7. Tit | le and     | 8. Price of  | 9. Number of   | 10.         | 11. Nature  |
|-------------|-------------|------------------|--------------------|------------|---|---------|--------|--------------|--------------------|--------|------------|--------------|----------------|-------------|-------------|
| Derivative  | Conversion  | Date             | Execution Date, if | Transactio | n | of      |        | and Expirati | on Date            | Amo    | unt of     | Derivative   | Derivative     | Ownership   | of Indirect |
| Security    | or Exercise | (Month/Day/Year) | any                | Code       | ] | Deriv   | ative  | (Month/Day   | /Year)             | Unde   | rlying     | Security     | Securities     | Form of     | Beneficial  |
| (Instr. 3)  | Price of    |                  | (Month/Day/Year)   | (Instr. 8) | 9 | Secur   | rities |              | Secui              | rities | (Instr. 5) | Beneficially | Derivative     | Ownership   |             |
|             | Derivative  |                  |                    |            | 4 | Acqui   | ired   |              |                    | (Instr | . 3 and    |              | Owned          | Security:   | (Instr. 4)  |
|             | Security    |                  |                    |            | ( | (A) or  | ſ      |              |                    | 4)     |            |              | Following      | Direct (D)  |             |
|             |             |                  |                    |            | ] | Dispo   | sed    |              |                    |        |            |              |                | or Indirect |             |
|             |             |                  |                    |            | • | of (D)  | )      |              |                    |        |            |              | Transaction(s) | (I)         |             |
|             |             |                  |                    |            | ( | (Instr. | . 3,   |              |                    |        |            |              | (Instr. 4)     | (Instr. 4)  |             |
|             |             |                  |                    |            | 4 | 4, and  | l 5)   |              |                    |        |            |              |                |             |             |
|             |             |                  |                    |            |   |         |        |              |                    |        | Amount     |              |                |             |             |
|             |             |                  |                    |            |   |         |        | Date         | Evnination         |        | or         |              |                |             |             |
|             |             |                  |                    |            |   |         |        | Exercisable  | Expiration<br>Date | Title  | Number     |              |                |             |             |
|             |             |                  |                    |            |   |         |        | Exercisable  | Date               |        | of         |              |                |             |             |
|             |             |                  |                    | Code \     | I | (A)     | (D)    |              |                    |        | Shares     |              |                |             |             |

# **Reporting Owners**

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

| 4400 BISCAYNE BLVD.<br>MIAMI, FL 33137 | X |  |
|--|---|--|
| <b>G•</b> 4                            |   |  |

## **Signatures**

| Phillip Frost, M.D., Individually and as Trustee | 11/17/2015 |
|--|------------|
| 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: November 16, 2015

Relationship to Issuer: 10% Owner

FROST GAMMA INVESTMENTS TRUST

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