

**FORM 4****UNITED STATES SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**OMB APPROVAL**

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 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

|                                                                                |         |          |                                                                               |  |                                                                                                                                                                                                                                                                                                                            |  |
|--------------------------------------------------------------------------------|---------|----------|-------------------------------------------------------------------------------|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| 1. Name and Address of Reporting Person<br><b>FROST PHILLIP M.D.<br/>ET AL</b> |         |          | 2. Issuer Name and Ticker or Trading Symbol<br><b>OPKO Health, Inc. [OPK]</b> |  | 5. Relationship of Reporting Person(s) to Issuer<br>(Check all applicable)<br><br><input checked="" type="checkbox"/> Director <input checked="" type="checkbox"/> 10% Owner<br><input checked="" type="checkbox"/> Officer (give title below) <input type="checkbox"/> Other (specify below)<br><b>CEO &amp; Chairman</b> |  |
| (Last)                                                                         | (First) | (Middle) | 3. Date of Earliest Transaction (Month/Day/Year)<br><b>05/23/2019</b>         |  |                                                                                                                                                                                                                                                                                                                            |  |
| OPKO Health, Inc.<br>4400 Biscayne Blvd.                                       |         |          |                                                                               |  |                                                                                                                                                                                                                                                                                                                            |  |
| (Street)                                                                       |         |          | 4. If Amendment, Date Original Filed (Month/Day/Year)                         |  | 6. Individual or Joint/Group Filing (Check Applicable Line)<br><input type="checkbox"/> Form filed by One Reporting Person<br><input checked="" type="checkbox"/> Form filed by More than One Reporting Person                                                                                                             |  |
| Miami                                                                          | FL      | 33137    |                                                                               |  |                                                                                                                                                                                                                                                                                                                            |  |
| (City)                                                                         | (State) | (Zip)    |                                                                               |  |                                                                                                                                                                                                                                                                                                                            |  |

**Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned**

| 1. Title of Security<br>(Instr. 3) | 2. Transaction<br>Date<br>(Month/Day/Year) | 2A. Deemed<br>Execution Date, if<br>any<br>(Month/Day/Year) | 3. Transaction<br>Code<br>(Instr. 8) |   | 4. Securities Acquired (A)<br>or Disposed of (D)<br>(Instr. 3, 4 and 5) |               |         | 5. Amount of Securities<br>Beneficially Owned Following<br>Reported Transaction(s)<br>(Instr. 3 and 4) | 6. Ownership<br>Form:<br>Direct (D)<br>or Indirect<br>(I)<br>(Instr. 4) | 7. Nature of<br>Indirect<br>Beneficial<br>Ownership<br>(Instr. 4) |
|------------------------------------|--------------------------------------------|-------------------------------------------------------------|--------------------------------------|---|-------------------------------------------------------------------------|---------------|---------|--------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------|
|                                    |                                            |                                                             | Code                                 | V | Amount                                                                  | (A) or<br>(D) | Price   |                                                                                                        |                                                                         |                                                                   |
| Common Stock                       |                                            |                                                             |                                      |   |                                                                         |               |         | 3,068,951                                                                                              | D                                                                       |                                                                   |
| Common Stock                       | 05/23/2019                                 |                                                             | P                                    |   | 38,622                                                                  | A             | \$1.915 | 28,660,799                                                                                             | I                                                                       | See<br>Footnote<br>(1)                                            |
| Common Stock                       | 05/23/2019                                 |                                                             | P                                    |   | 161,378                                                                 | A             | \$1.92  | 28,822,177                                                                                             | I                                                                       | See<br>Footnote<br>(1)                                            |
|                                    |                                            |                                                             |                                      |   |                                                                         |               |         |                                                                                                        |                                                                         | See                                                               |

|              |  |  |  |  |  |  |  |             |   |                        |
|--------------|--|--|--|--|--|--|--|-------------|---|------------------------|
| Common Stock |  |  |  |  |  |  |  | 164,234,443 | I | Footnote<br>(2)        |
| Common Stock |  |  |  |  |  |  |  | 20,091,062  | I | See<br>Footnote<br>(3) |

**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 | (A)                                                                                     | (D) | Date Exercisable                                         | Expiration Date | Title                                                         | Amount or Number of Shares |                                            |                                                                                                    |                                                                                  |                                                        |

| Reporting Owner Name / Address                                                          | Relationships |           |                |       |
|-----------------------------------------------------------------------------------------|---------------|-----------|----------------|-------|
|                                                                                         | Director      | 10% Owner | Officer        | Other |
| FROST PHILLIP M.D. ET AL<br>OPKO Health, Inc.<br>4400 Biscayne Blvd.<br>Miami, FL 33137 | X             | X         | CEO & Chairman |       |
| Frost Nevada Investments Trust<br>4400 Biscayne Blvd.<br>Miami, FL 33137                |               | X         |                |       |

**Explanation of Responses:**

- (1) 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 five limited partners of Frost-Nevada, L.P. and the sole shareholder of Frost-Nevada Corporation, the sole general partner of Frost-Nevada, L.P. 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.
- (2) 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 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.

- (3) 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 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.

Phillip Frost, M.D., Individually and as Trustee

\*\*Signature of Reporting Person

05/24/2019

Date

\* 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).

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.

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JOINT FILER INFORMATION

Name: Frost Nevada 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: May 23, 2019

Relationship to Issuer: 10% Owner

FROST NEVADA INVESTMENTS TRUST

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