

Opko Health, Inc.  
Form S-4/A  
July 16, 2013  
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As filed with the Securities and Exchange Commission on July 15, 2013

Registration No. 333-189640

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

**Pre-Effective**  
**Amendment No. 2**  
**to**  
**Form S-4**  
**REGISTRATION STATEMENT**  
*UNDER*  
*THE SECURITIES ACT OF 1933*

**OPKO HEALTH, INC.**

(Exact Name of Registrant as Specified in Its Charter)

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<p><b>Delaware</b> (State or Other Jurisdiction of Incorporation or Organization)</p>	<p><b>2834</b> (Primary Standard Industrial Classification Code Number) <b>4400 Biscayne Boulevard</b>  <b>Miami, Florida 33137</b>  <b>(305) 575-4100</b></p>	<p><b>75-2402409</b> (I.R.S. Employer Identification Number)</p>
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(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

**Kate Inman, Esq.**  
  
**Deputy General Counsel and Secretary**  
  
**OPKO Health, Inc.**  
  
**4400 Biscayne Boulevard**  
  
**Miami, Florida 33137**  
  
**(305) 575-4100**

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

*Copies to:*

<p><b>Teddy D. Klinghoffer, Esq.</b>   <b>Esther L. Moreno, Esq.</b>   <b>Akerman Senterfitt</b>   <b>One S.E. Third Avenue</b>   <b>25th Floor</b>   <b>Miami, Florida 33131</b>   <b>Telephone: (305) 374-5600</b>   <b>Fax: (305) 374-5095</b></p>	<p><b>Shai Novik</b>   <b>President</b>   <b>PROLOR Biotech, Inc.</b>   <b>7 Golda Meir Street</b>   <b>Weizmann Science Park</b>   <b>Nes-Ziona, Israel L3 74140</b>   <b>Telephone: (866) 644-7811</b>   <b>Fax: (305) 500-2104</b></p>	<p><b>Robert L. Grossman, Esq.</b>   <b>Greenberg Traurig, P.A.</b>   <b>333 Avenue of the Americas</b>   <b>Suite 4400</b>   <b>Miami, Florida 33131</b>   <b>Telephone: (305) 579-0500</b>   <b>Fax: (305) 579-0717</b></p>	<p><b>Jacqueline Hodes, Esq.</b>   <b>Michael P. Reed, Esq.</b>   <b>DLA Piper LLP (US)</b>   <b>200 S. Biscayne Boulevard</b>   <b>Suite 2500</b>   <b>Miami, Florida 33131</b>   <b>Telephone: (305) 423-8500</b>   <b>Fax: (305) 437-8131</b></p>
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**Approximate date of commencement of proposed sale of the securities to the public:** As soon as practicable following the effective date of this registration statement and the effective time of the merger of POM Acquisition, Inc., a Nevada corporation and a wholly owned subsidiary of OPKO Health, Inc., with and into PROLOR Biotech, Inc., a Nevada corporation, as described in the Agreement and Plan of Merger, dated as of April 23, 2013, attached as Annex A to the joint proxy statement/prospectus forming part of this registration statement.

If the securities being registered on this form are being offered in connection with the formation of a holding company and there is compliance with General Instruction G, check the following box.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act.

(Check one):

Large accelerated filer <input type="checkbox"/>	Accelerated filer <input type="checkbox"/>
Non-accelerated filer <input type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company <input type="checkbox"/>

If applicable, place an  in the box to designate the appropriate rule provision relied upon in conducting this transaction:

Exchange Act Rule 13e-4(i) (Cross-Border Issuer Tender Offer)

Exchange Act Rule 14d-1(d) (Cross-Border Third-Party Tender Offer)

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until this Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

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**The information in this joint proxy statement/prospectus is not complete and may be changed. OPKO Health, Inc. may not offer these securities until the registration statement filed with the Securities and Exchange Commission, of which this joint proxy statement/prospectus is a part, is effective. This joint proxy statement/prospectus is not an offer to sell these securities, and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.**

**SUBJECT TO COMPLETION, DATED JULY 15, 2013**

**PRELIMINARY JOINT PROXY STATEMENT/PROSPECTUS**

**PROPOSED MERGER YOUR VOTE IS VERY IMPORTANT**

On April 23, 2013, OPKO Health, Inc., or OPKO, a Delaware corporation, POM Acquisition, Inc., or POM, a Nevada corporation and a wholly owned subsidiary of OPKO, and PROLOR Biotech, Inc., or PROLOR, a Nevada corporation, entered into an Agreement and Plan of Merger, or the Merger Agreement, pursuant to which, subject to the satisfaction of the terms and conditions contained in the Merger Agreement, POM will merge with and into PROLOR with PROLOR surviving as a wholly owned subsidiary of OPKO, which we refer to as the Merger. The Board of Directors of each of PROLOR and OPKO (with Phillip Frost, M.D., Jane H. Hsiao, Ph.D. and Steven D. Rubin, each of whom serves as a director of both PROLOR and OPKO, abstaining) have approved and adopted the Merger Agreement and the transactions contemplated thereby, including the Merger.

If the Merger is completed, holders of PROLOR's common stock, par value \$0.00001 per share, or the PROLOR common stock, will be entitled to receive 0.9951 of a share of OPKO's common stock, par value \$0.01 per share, or the OPKO common stock, for each share of PROLOR common stock they own, which we refer to as the Exchange Ratio. This Exchange Ratio will not be adjusted for changes in the price per share of PROLOR's or OPKO's common stock before the Merger is completed. Based on the number of shares of PROLOR common stock outstanding and the number of shares of PROLOR common stock that may be issued pursuant to outstanding stock options and warrants as of \_\_\_\_\_, 2013, the latest practicable date before the printing of this joint proxy statement/prospectus, OPKO estimates that an aggregate of \_\_\_\_\_ shares of OPKO common stock will be issued in connection with the Merger. The OPKO common stock is listed on the New York Stock Exchange, or the NYSE, and trades under the symbol OPK. The PROLOR common stock is listed on the NYSE MKT and the Tel Aviv Stock Exchange and trades under the symbol PBTH. Upon completion of the Merger, shares of PROLOR common stock will be delisted from the NYSE MKT and the Tel Aviv Stock Exchange and there will no longer be a public trading market for the PROLOR common stock. In addition, promptly following the closing of the Merger, the PROLOR common stock will be deregistered under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and PROLOR will no longer file periodic reports with the Securities and Exchange Commission, or the SEC. Following the completion of the Merger, the OPKO common stock will continue to be traded on the NYSE under the symbol OPK. Additionally, OPKO intends to apply to list its shares on the Tel Aviv Stock Exchange prior to the closing of the Merger.

Based on the closing price of the OPKO common stock on April 23, 2013, the date prior to the announcement of the Merger Agreement, the Exchange Ratio represented an implied value of approximately \$7.00 per share of PROLOR common stock, as compared to the closing price of the PROLOR common stock of \$5.83 per share on that date. Based on the closing price of the OPKO common stock on \_\_\_\_\_, 2013, the latest practicable date before the printing of this joint proxy statement/prospectus, the Exchange Ratio represented an implied value of approximately \$ \_\_\_\_\_ per share of PROLOR common stock, as compared to the closing price of the PROLOR common stock of \$ \_\_\_\_\_ per share on that date. You are urged to obtain current market quotations for the OPKO common stock and the PROLOR common stock.

OPKO is soliciting proxies for use at its 2013 annual meeting of stockholders, or the OPKO annual meeting, at which OPKO's stockholders will be asked to consider and vote upon: (1) a proposal to elect as directors the ten nominees named in this joint proxy statement/prospectus for a term of office expiring at the 2014 annual meeting of stockholders and until their respective successors are duly elected and qualified; (2) a proposal to approve an amendment to the OPKO Health, Inc. 2007 Equity Incentive Plan, or the 2007 Plan, to increase the aggregate number of shares of OPKO common stock authorized for issuance pursuant to the 2007 Plan from 35 million shares to 55 million shares of OPKO common stock, which we refer to as the OPKO Plan Amendment Proposal; (3) a proposal to approve an amendment to OPKO's amended and restated certificate of incorporation, or the OPKO Charter, to increase the authorized number of shares of the OPKO common stock that OPKO may issue from 500 million shares to 750 million shares, which we refer to as the OPKO Authorized Share Increase Proposal; (4) a proposal to approve the issuance of shares of OPKO common stock and other securities exercisable for shares of OPKO common stock to PROLOR's stockholders in connection with the Merger, which we refer to as the OPKO Share Issuance Proposal; and (5) a proposal to adjourn the OPKO annual meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the foregoing proposals, which we refer to the OPKO Adjournment Proposal. **OPKO's Board of Directors recommends that OPKO's stockholders vote FOR the election of the ten director nominees named in this joint proxy statement/prospectus and FOR each of the other proposals described above. The approval of the OPKO Share Issuance Proposal is required for the completion of the Merger.**

PROLOR is soliciting proxies for use at a special meeting of PROLOR's stockholders, or the PROLOR special meeting, at which PROLOR's stockholders will be asked to: (1) consider and vote upon a proposal to approve and adopt the Merger Agreement and the transactions contemplated thereby, including the Merger, which we refer to as the PROLOR Merger Proposal, (2) cast an advisory vote to approve the golden parachute compensation that PROLOR's named executive

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officers may potentially receive in connection with the Merger, which we refer to as the PROLOR Compensation Advisory Vote Proposal, and (3) consider and vote upon a proposal to adjourn the PROLOR special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the proposal to approve and adopt the Merger Agreement and the transactions contemplated thereby, including the Merger, which we refer to as the PROLOR Adjournment Proposal. **PROLOR's Board of Directors recommends that PROLOR's stockholders vote FOR each of the foregoing proposals. The adoption and approval by PROLOR's stockholders of the PROLOR Merger Proposal is required for the completion of the Merger.**

**YOUR VOTE IS VERY IMPORTANT.** The Merger cannot be completed unless OPKO's stockholders approve the issuance of OPKO common stock in connection with the Merger **and** PROLOR's stockholders approve and adopt the Merger Agreement and the transactions contemplated thereby, including the Merger. Whether or not you plan to attend the OPKO annual meeting or the PROLOR special meeting, as applicable, please submit your proxy as soon as possible to make sure that your shares are represented at the applicable meeting.

This joint proxy statement/prospectus provides you with detailed information about the OPKO annual meeting, the PROLOR special meeting, the Merger Agreement and the Merger and the other business to be considered by each company's stockholders. In addition to being a proxy statement for the meetings to be held by OPKO and PROLOR, this document is also a prospectus to be used by OPKO when offering shares of OPKO common stock to PROLOR's stockholders in connection with the Merger. **OPKO and PROLOR encourage you to read this entire document carefully. Please pay particular attention to the section titled Risk Factors, beginning on page 36, for a discussion of the risks related to the Merger and to the ownership of OPKO common stock after the Merger is completed.**

**Phillip Frost, M.D.**  
Chairman and Chief Executive Officer  
OPKO Health, Inc.

**Abraham Havron, Ph.D.**  
Chief Executive Officer  
PROLOR Biotech, Inc.

**Neither the SEC nor any state securities commission has approved or disapproved of the securities to be issued in connection with the Merger or determined if this joint proxy statement/prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

This joint proxy statement/prospectus is dated \_\_\_\_\_, 2013 and, together with the accompanying proxy card, is first being mailed to stockholders of OPKO and PROLOR on or about \_\_\_\_\_, 2013.

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**REFERENCES TO ADDITIONAL INFORMATION**

This joint proxy statement/prospectus incorporates by reference important business and financial information about OPKO and PROLOR from other documents that each company has filed with the SEC, but that have not been included in or delivered with this joint proxy statement/prospectus. For a listing of the documents incorporated by reference into this joint proxy statement/prospectus, see the section titled "Where You Can Find Additional Information" beginning on page 176. You can obtain the documents incorporated by reference into this joint proxy statement/prospectus through the SEC's website at [www.sec.gov](http://www.sec.gov) or by requesting them in writing or by telephone at the appropriate address below.

OPKO will provide you with copies of such documents relating to OPKO, without charge, upon written or oral request to:

OPKO Health, Inc.  
4400 Biscayne Boulevard  
Miami, Florida 33137  
Attn: Secretary  
(305) 575-4100

PROLOR will provide you with copies of such documents relating to PROLOR, without charge, upon written or oral request to:

PROLOR Biotech, Inc.  
7 Golda Meir Street  
Weizmann Science Park  
Nes-Ziona, Israel L3 74140  
Attn: Finance Director  
(866) 644-7811

**In order for you to receive timely delivery of the documents in advance of the OPKO annual meeting or the PROLOR special meeting, you must request the information no later than August 23, 2013.**

**ABOUT THIS JOINT PROXY STATEMENT/PROSPECTUS**

This joint proxy statement/prospectus, which forms a part of a registration statement on Form S-4 filed with the SEC by OPKO (File No. 333-189640), constitutes a prospectus of OPKO under Section 5 of the Securities Act of 1933, as amended, or the Securities Act, with respect to the shares of OPKO common stock to be issued to PROLOR's stockholders in connection with the Merger.

This joint proxy statement/prospectus also constitutes a notice of meeting and a proxy statement under Section 14(a) of the Exchange Act with respect to (1) the OPKO annual meeting, at which OPKO stockholders will be asked to consider and vote upon certain proposals, including a proposal to approve the issuance of shares of OPKO common stock in connection with the Merger, and (2) the PROLOR special meeting, at which PROLOR stockholders will be asked to consider and vote upon certain proposals, including a proposal to approve and adopt the Merger Agreement and the transactions contemplated thereby, including the Merger, and a proposal to approve, on an advisory basis, the compensation that PROLOR's named executive officers may potentially receive in connection with the Merger.

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**OPKO HEALTH, INC.**

**4400 Biscayne Boulevard**

**Miami, FL 33137**

**NOTICE OF 2013 ANNUAL MEETING OF STOCKHOLDERS TO BE HELD AUGUST 28, 2013**

To the Stockholders of OPKO Health, Inc.:

You are invited to attend the 2013 annual meeting of stockholders of OPKO Health, Inc., or OPKO, a Delaware corporation, or the OPKO annual meeting, which will be held on Wednesday, August 28, 2013, at 10:00 a.m., local time, at OPKO's headquarters located at 4400 Biscayne Boulevard, Miami, FL 33137, for the following purposes:

1. To consider and vote on a proposal to elect as directors the ten nominees named in this joint proxy statement/prospectus for a term of office expiring at the 2014 annual meeting of stockholders and until their respective successors are duly elected and qualified.
  2. To consider and vote on a proposal to approve an amendment to the OPKO Health, Inc. 2007 Equity Incentive Plan, or the 2007 Plan, to increase the aggregate number of shares of common stock, par value \$0.01 per share, of OPKO, or the OPKO common stock, authorized for issuance pursuant to the 2007 Plan from 35 million shares to 55 million shares of OPKO common stock, which we refer to as the OPKO Plan Amendment Proposal.
  3. To consider and vote on a proposal to approve an amendment to OPKO's amended and restated certificate of incorporation, to increase the authorized number of shares of the OPKO common stock that OPKO may issue from 500 million shares to 750 million shares, which we refer to as the OPKO Authorized Share Increase Proposal.
  4. To consider and vote on a proposal to approve the issuance of shares of OPKO common stock and other securities exercisable for shares of OPKO common stock to the stockholders of PROLOR Biotech, Inc., or PROLOR, a Nevada corporation, in connection with the transactions contemplated by the Agreement and Plan of Merger, or the Merger Agreement, dated as of April 23, 2013, among PROLOR, OPKO and POM Acquisition, Inc., or POM, a Nevada corporation and a wholly owned subsidiary of OPKO formed for the purpose of facilitating the merger of POM with and into PROLOR, or the Merger, which we refer to as the OPKO Share Issuance Proposal.
  5. To consider and vote on a proposal to approve the adjournment of the OPKO annual meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the foregoing proposals.
  6. To conduct any other business as may properly come before the OPKO annual meeting or any adjournment or postponement thereof.
- OPKO's Board of Directors recommends that OPKO's stockholders vote FOR the election of the ten director nominees named in this joint proxy statement/prospectus and FOR each of the other proposals described above. The approval of the OPKO Share Issuance Proposal is required for the completion of the Merger.**

OPKO's Board of Directors has fixed July 22, 2013 as the record date for the determination of stockholders entitled to notice of, and to vote at, the OPKO annual meeting and any adjournment or postponement thereof. Only holders of record of shares of OPKO common stock at the close of business on the record date are entitled to notice of, and to vote at, the OPKO annual meeting. At the close of business on the record date, there were issued and outstanding \_\_\_\_\_ shares of OPKO common stock. A list of the holders of OPKO common stock entitled to vote at the OPKO annual meeting will be available for examination by any OPKO stockholder, for any purpose germane to the OPKO annual meeting, at OPKO's principal executive offices at 4400 Biscayne Blvd., Miami, Florida 33137, for ten days before the OPKO annual meeting, during normal

business hours, and at the time and place of the OPKO annual meeting as required by law.



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**Your vote is important. All OPKO stockholders are cordially invited to attend the OPKO annual meeting in person. However, even if you plan to attend the OPKO annual meeting in person, OPKO requests that you sign and return the enclosed proxy card or vote over the Internet or by telephone as instructed on the enclosed proxy card to ensure that your shares of OPKO common stock will be represented at the OPKO annual meeting if you are unable to attend. If you fail to return your proxy card or to vote by telephone or over the Internet, the effect will be that your shares will not be counted for purposes of determining whether a quorum is present at the OPKO annual meeting. Such action will also have the same effect as a vote AGAINST the OPKO Authorized Share Increase Proposal but will have no effect on the outcome of any of the other proposals to be voted on at the OPKO annual meeting, except to the extent that there are insufficient shares voted at the meeting to meet the New York Stock Exchange requirements applicable to the approval of the OPKO Share Issuance Proposal and the OPKO Plan Amendment Proposal. None of the proposals to be considered at the OPKO annual meeting can be approved unless a quorum is present at the meeting.**

OPKO is first mailing these proxy solicitation materials on or about \_\_\_\_\_, 2013 to all stockholders of record entitled to vote at the OPKO annual meeting.

This joint proxy statement/prospectus provides you with detailed information about the OPKO annual meeting, the Merger Agreement and the Merger and the other business to be considered by the OPKO stockholders at the OPKO annual meeting. **OPKO encourages you to read this entire document carefully, including the Merger Agreement, a copy of which is attached as Annex A to this joint proxy statement/prospectus and is incorporated by reference into this joint proxy statement/prospectus. Please pay particular attention to the section titled Risk Factors, beginning on page 36, for a discussion of the risks related to the Merger and to ownership of OPKO common stock after the Merger is completed.**

By Order of the OPKO Board of Directors,

Kate Inman

*Secretary*

, 2013

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**PROLOR BIOTECH, INC.**

**7 Golda Meir Street**

**Weizmann Science Park**

**Nes-Ziona, Israel L3 74140**

**NOTICE OF A SPECIAL MEETING OF STOCKHOLDERS TO BE HELD AUGUST 28, 2013**

To the Stockholders of PROLOR Biotech, Inc.:

You are invited to attend the special meeting of stockholders of PROLOR Biotech, Inc., or PROLOR, a Nevada corporation, or the PROLOR special meeting, which will be held on Wednesday, August 28, 2013, at 10:00 a.m., local time, at PROLOR's headquarters located at 7 Golda Meir Street, Weizmann Science Park, Nes-Ziona, Israel L3 74140 for the following purposes:

1. To consider and vote on a proposal to approve and adopt the Agreement and Plan of Merger, or the Merger Agreement, dated as of April 23, 2013, among PROLOR, OPKO Health, Inc., or OPKO, a Delaware corporation, and POM Acquisition, Inc., a wholly owned subsidiary of OPKO formed for the purpose of facilitating the merger of POM Acquisition, Inc. with and into PROLOR, or the Merger, and the transactions contemplated by such agreement, including the Merger, which we refer to as the PROLOR Merger Proposal.
2. To consider and vote on a proposal to approve, on an advisory basis, the golden parachute compensation that PROLOR's named executive officers may potentially receive in connection with the Merger.
3. To consider and vote on a proposal to approve the adjournment of the PROLOR special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the PROLOR Merger Proposal.
4. To conduct any other business as may properly come before the PROLOR special meeting or any adjournment or postponement thereof.

**PROLOR's Board of Directors recommends that PROLOR stockholders vote FOR each of the foregoing proposals. The approval by PROLOR's stockholders of the PROLOR Merger Proposal is required for the completion of the Merger.**

PROLOR's Board of Directors has fixed July 22, 2013 as the record date for the determination of stockholders entitled to notice of, and to vote at, the PROLOR special meeting and any adjournment or postponement thereof. Only holders of record of shares of PROLOR common stock at the close of business on the record date are entitled to notice of, and to vote at, the PROLOR special meeting. At the close of business on the record date, PROLOR had outstanding and entitled to vote \_\_\_\_\_ shares of common stock.

**Your vote is important. All PROLOR stockholders are cordially invited to attend the PROLOR special meeting in person. However, even if you plan to attend the PROLOR special meeting in person, PROLOR requests that you sign and return the enclosed proxy card or vote over the Internet or by telephone as instructed on the enclosed proxy card and thus ensure that your shares of PROLOR common stock will be represented at the PROLOR special meeting if you are unable to attend. If you fail to return your proxy card or to vote by telephone or over the Internet, the effect will be that your shares will not be counted for purposes of determining whether a quorum is present at the PROLOR special meeting. Such action will also have the same effect as a vote AGAINST the approval of the PROLOR Merger Proposal but will have no effect on the outcome of any of the other proposals to be voted on at the PROLOR special meeting. None of the proposals to be considered at the PROLOR special meeting can be approved unless a quorum is present at the meeting.**

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PROLOR is first mailing these proxy solicitation materials on or about \_\_\_\_\_, 2013 to all stockholders of record entitled to vote at the PROLOR special meeting.

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This joint proxy statement/prospectus provides you with detailed information about the PROLOR special meeting, the Merger Agreement and the Merger and the other business to be considered by PROLOR's stockholders at the PROLOR special meeting. **PROLOR encourages you to read this entire document carefully, including the Merger Agreement, a copy of which is attached as Annex A to this joint proxy statement/prospectus and is incorporated by reference into this joint proxy statement/prospectus. Please pay particular attention to the section titled Risk Factors, beginning on page 36, for a discussion of the risks related to the Merger and to ownership of common stock, par value \$0.01 per share, of OPKO, after the Merger is completed.**

By Order of the PROLOR Board of Directors,

Abraham Havron

Chief Executive Officer

, 2013

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**QUESTIONS AND ANSWERS ABOUT THE MERGER,**

**THE OPKO ANNUAL MEETING AND THE PROLOR SPECIAL MEETING**

*The following are some questions that you, as a stockholder of OPKO and/or PROLOR, may have regarding the Merger, the OPKO annual meeting and/or the PROLOR special meeting, together with brief answers to those questions. OPKO and PROLOR urge you to carefully read this joint proxy statement/prospectus in its entirety, including the annexes and other documents attached and/or referred to in this joint proxy statement/prospectus, because the information in this section does not provide all of the information that will be important to you with respect to the Merger, the OPKO annual meeting and/or the PROLOR special meeting.*

*Q: Why am I receiving these materials?*

A: OPKO and PROLOR are sending these materials to their respective stockholders to help them decide how to vote their shares of OPKO common stock and/or PROLOR common stock, as the case may be, with respect to the proposed Merger and the other matters to be considered at their respective stockholder meetings.

This document constitutes both a joint proxy statement of OPKO and PROLOR and a prospectus of OPKO. It is a joint proxy statement because the boards of directors of both companies are soliciting proxies from their respective stockholders. It is a prospectus of OPKO because OPKO will use it in connection with the offering of shares of OPKO common stock to PROLOR stockholders in exchange for their shares of PROLOR common stock in connection with the Merger. You should read this document carefully as it contains important information about the Merger Agreement and the Merger, the OPKO annual meeting and the PROLOR special meeting.

*Q: What will happen in the Merger?*

A: OPKO and PROLOR entered into the Merger Agreement on April 23, 2013. The Merger Agreement contains the terms and conditions of the proposed business combination of OPKO and PROLOR. Under the Merger Agreement, POM, a wholly owned subsidiary of OPKO, will merge with and into PROLOR, with PROLOR surviving as a wholly owned subsidiary of OPKO. As promptly as practicable after the completion of the Merger, PROLOR will merge with and into a Delaware limited liability company, wholly owned by OPKO, with the Delaware limited liability company surviving as a wholly owned subsidiary of OPKO, which we refer to as the PROLOR-LLC Merger. We refer to the Merger and the PROLOR-LLC Merger collectively as the Mergers. A complete copy of the Merger Agreement is attached as Annex A to this joint proxy statement/prospectus and is incorporated by reference into this joint proxy statement/prospectus.

*Q: Why are OPKO and PROLOR proposing to effect the Merger?*

A: OPKO's and PROLOR's respective Boards of Directors each believe that the Merger will provide strategic and financial benefits to their respective stockholders. The transaction also will deliver value to PROLOR's stockholders, who will receive merger consideration representing a 40% premium over the trading price of PROLOR common stock on April 8, 2013 and will have an opportunity to participate in the growth and opportunities of the combined company through their ownership of OPKO common stock received in connection with the Merger. To review the reasons for the Merger in greater detail, see The Merger Recommendation of OPKO's Board of Directors and its Reasons for the Merger and The Merger Recommendation of PROLOR's Board of Directors and its Reasons for the Merger beginning on pages 53 and 56, respectively.

*Q: What will PROLOR stockholders receive in the Merger?*

A:

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As a result of the Merger, holders of PROLOR common stock will have the right to receive 0.9951 of a share of OPKO common stock in exchange for each share of PROLOR common stock they own, rounded up to the nearest whole share number. For example, if you own 1,000 shares of PROLOR common stock, upon completion of the Merger, you will have the right to receive 996 shares of OPKO common stock (995.1 shares, rounded up to the nearest share). Based on the number of shares of OPKO common stock and

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PROLOR common stock outstanding as of \_\_\_\_\_, 2013, the latest practicable date before the printing of this joint proxy statement/prospectus, if the Merger had been completed on such date, the holders of PROLOR common stock would have been entitled to receive shares of OPKO common stock representing approximately \_\_\_\_\_% of all shares of OPKO common stock outstanding immediately following the completion of the Merger. OPKO stockholders would have continued to own their existing shares, which would not have been affected by the Merger, and such shares would have represented approximately \_\_\_\_\_% of all shares of OPKO common stock outstanding immediately following the completion of the Merger. For a more complete discussion of what PROLOR's stockholders will receive in connection with the Merger, see the sections titled "The Merger - What PROLOR Stockholders Will Receive in the Merger" and "The Merger - Ownership of OPKO After the Completion of the Merger" beginning on pages 46 and 47, respectively.

*Q: Is the Exchange Ratio subject to adjustment based on changes in the prices of OPKO and/or PROLOR common stock?*

A: No. The Exchange Ratio is fixed and no adjustments to the Exchange Ratio will be made based on changes in the price of either OPKO common stock or PROLOR common stock prior to the completion of the Merger. As a result of any such changes in stock price, the aggregate market value of the shares of OPKO common stock that a PROLOR stockholder is entitled to receive at the time that the Merger is completed could vary significantly from the value of such shares on the date of this joint proxy statement/prospectus, the date of the OPKO annual meeting, the date of the PROLOR special meeting or the date on which such PROLOR stockholder actually receives its shares of OPKO common stock. For a more complete discussion of the Exchange Ratio, see the section titled "The Merger - What PROLOR Stockholders Will Receive in the Merger" beginning on page 46.

*Q: How does the Exchange Ratio impact the ownership of OPKO after the completion of the Merger?*

A: Because the Exchange Ratio is fixed, to the extent that the number of shares of outstanding OPKO common stock or PROLOR common stock changes prior to the completion of the Merger, whether due to any new issuance of shares of OPKO common stock or PROLOR common stock, any exercise of any outstanding options or warrants to purchase shares of OPKO common stock or PROLOR common stock, or otherwise, there will automatically occur a corresponding change in the relative ownership percentages of the combined company by the current OPKO stockholders and the current PROLOR stockholders.

For a more complete discussion of the ownership of OPKO after the completion of the Merger, see the section titled "The Merger - Ownership of OPKO After the Completion of the Merger" beginning on page 47.

*Q: What will holders of PROLOR stock options and warrants receive in the Merger?*

A: Upon completion of the Merger, each option to purchase one share of PROLOR common stock that is outstanding and unexercised immediately prior to the effective time of the Merger, or the Effective Time, will be converted into an option to purchase OPKO common stock and (1) the number of shares of OPKO common stock subject to such option will be adjusted to an amount equal to the product of (a) the number of shares of PROLOR common stock subject to such option immediately before the Effective Time and (b) the Exchange Ratio, rounded down to the nearest whole share, and (2) the per share exercise price of such option will be adjusted to a price equal to the quotient of (a) the per share exercise price of such option and (b) the Exchange Ratio, rounded up to the nearest whole cent. OPKO will assume each such stock option in accordance with the terms and conditions of the applicable PROLOR equity incentive plan and stock option agreement relating to such PROLOR stock option, subject to the adjustments described in the preceding sentence and the substitution of OPKO and its Compensation Committee for PROLOR and its Compensation Committee with respect to the administration of each PROLOR equity incentive plan. In addition, pursuant to the stock option agreements governing PROLOR's outstanding stock option awards, each PROLOR stock option will become fully vested and exercisable upon the consummation of the Merger. Abraham Havron, Ph.D., PROLOR's Chief Executive Officer and a Director, Shai Novik,

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PROLOR's President and a Director, and Eyal Fima, PROLOR's Chief Operating Officer, have each executed waiver agreements with PROLOR whereby they have waived their right to the acceleration of the vesting of the stock options that were granted to each of them in February 2013 upon the closing of the Merger.

For example, if you hold an option to purchase up to 1,000 shares of PROLOR common stock at an exercise price of \$2.00 per share, upon completion of the Merger, such option will be converted into an option to purchase up to 995 shares of OPKO common stock (995.1 shares rounded down to the nearest whole share) at an exercise price of \$2.01 per share (\$2.009 rounded up to the nearest whole cent).

Similarly, upon completion of the Merger and subject to the consent of the holder thereof, each warrant to purchase one share of PROLOR common stock that is outstanding and unexercised immediately prior to the Effective Time will be converted into a warrant to purchase OPKO common stock and (1) the number of shares of OPKO common stock subject to such warrant will be adjusted to an amount equal to the product of (a) the number of shares of PROLOR common stock subject to such warrant immediately before the Effective Time and (b) the Exchange Ratio, rounded up to the nearest whole share, and (2) the per share exercise price of such warrant will be adjusted to a price equal to the quotient of (a) the per share exercise price of such warrant and (b) the Exchange Ratio, rounded up to the nearest whole cent. OPKO will assume each such warrant in accordance with the terms and conditions thereof, subject to the conditions and adjustments described in the preceding sentence.

For example, if you hold a warrant to purchase up to 1,000 shares of PROLOR common stock at an exercise price of \$2.00 per share, upon completion of the Merger, such warrant will be converted into a warrant to purchase up to 996 shares of OPKO common stock (995.1 shares rounded up to the nearest whole share) at an exercise price of \$2.01 per share (\$2.009 rounded up to the nearest whole cent).

For a more complete discussion of what holders of PROLOR stock options and warrants will receive in connection with the Merger, see the section titled "The Merger Treatment of PROLOR Stock Options and Warrants" beginning on page 47.

*Q: What is required to complete the Merger?*

A: In order for the Merger to be completed:

OPKO's stockholders must approve the OPKO Share Issuance Proposal;

PROLOR's stockholders must approve the PROLOR Merger Proposal; and

each of the other conditions to the completion of the Merger contained in the Merger Agreement (including the receipt of required regulatory approvals) must be satisfied or waived on or prior to the completion of the Merger.

For a more complete discussion of the conditions to the completion of the Merger under the Merger Agreement, see the section titled "The Merger Agreement Conditions to the Completion of the Merger" beginning on page 96.

*Q: How will OPKO's stockholders be affected by the Merger and the issuance of shares of OPKO common stock to PROLOR's stockholders in connection with the Merger?*

A: Immediately after the completion of the Merger, each OPKO stockholder will have the same number of shares of OPKO common stock that such stockholder held immediately prior to the completion of the Merger. However, upon issuance of the shares of OPKO common stock to PROLOR stockholders in connection with the Merger, each share of OPKO common stock outstanding immediately prior to the completion of the Merger will represent a smaller percentage of the aggregate number of shares of OPKO common stock (and therefore a smaller percentage of the outstanding voting power and equity value) outstanding after the completion of the Merger than it did immediately prior to completion of the Merger.



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*Q: When do OPKO and PROLOR expect to complete the Merger?*

A: OPKO and PROLOR currently expect to complete the Merger in the second half of 2013. Completion of the Merger will only be possible, however, if all conditions to the completion of the Merger contained in the Merger Agreement are satisfied or waived, including approval of the OPKO Share Issuance Proposal and the PROLOR Merger Proposal and receipt of the required regulatory approvals. Therefore, factors outside of either company's control could delay or prevent the completion of the Merger.

*Q: What risks should I consider in deciding whether to vote in favor of the proposals described herein, including if applicable the OPKO Share Issuance Proposal and/or the PROLOR Merger Proposal?*

A: You should carefully review the section of this joint proxy statement/prospectus titled "Risk Factors" beginning on page 36, which presents risks and uncertainties related to the Merger, the combined company and the business and operations of each of OPKO and PROLOR.

*Q: If I am a PROLOR stockholder, what are the material U.S. federal income tax consequences of the Merger to me?*

A: OPKO and PROLOR intend for the Mergers to qualify as a reorganization within the meaning of Section 368(a) of the Internal Revenue Code of 1986, as amended, or the Code. Assuming the Mergers qualify as a reorganization, PROLOR's stockholders will not recognize gain or loss for U.S. federal income tax purposes upon the exchange of their shares of PROLOR common stock for shares of OPKO common stock in connection with the Merger or upon the closing of the PROLOR-LLC Merger.

**Tax matters are very complicated, and the tax consequences of the Mergers to a particular stockholder will depend on such stockholder's individual circumstances. Accordingly, OPKO and PROLOR urge you to consult your tax advisor for a full understanding of the tax consequences of the Mergers to you, including the applicability and effect of federal, state, local and foreign income and other tax laws. For a more complete discussion of the material U.S. federal income tax consequences of the Mergers, see the section titled "Material United States Federal Income Tax Consequences of the Mergers" beginning on page 77.**

*Q: If I am a PROLOR stockholder, what are the material Israeli income tax consequences of the Merger to me?*

A: As a condition to the obligations of PROLOR to consummate the Merger, PROLOR is seeking a ruling from the Israeli Income Tax Authority, or the ITA, whereby the Merger will be treated as a tax-exempt transaction under Israeli law. Pursuant to the Merger Agreement, PROLOR may waive such condition and, absent an interim arrangement with the ITA, the consideration paid to PROLOR stockholders that are Israeli tax payors will be subject to Israeli tax. For a more complete discussion of the anticipated effects of such tax ruling, if received, see "Israeli Income Tax Treatment of the Merger" beginning on page 80.

*Q: Do I have appraisal rights in connection with the Merger?*

A: No. Neither OPKO stockholders nor PROLOR stockholders will be entitled to exercise any appraisal rights in connection with the Merger under Delaware law, Nevada law or otherwise.

*Q: When and where will the OPKO annual meeting take place?*

A:

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The OPKO annual meeting will be held on August 28, 2013, at 10:00 a.m., local time, at OPKO's headquarters located at 4400 Biscayne Boulevard, Miami FL 33137.

*Q: When and where will the PROLOR special meeting take place?*

A: The PROLOR special meeting will be held on August 28, 2013, at 10:00 a.m., local time, at PROLOR's headquarters located at 7 Golda Meir Street, Weizmann Science Park, Nes-Ziona, Israel L3 74140.

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*Q: Who can attend and vote at the OPKO annual meeting?*

A: All holders of record of OPKO's common stock as of the close of business on July 22, 2013, the record date for the OPKO annual meeting, are entitled to receive notice of and to vote at the OPKO annual meeting.

*Q: Who can attend and vote at the PROLOR special meeting?*

A: All holders of record of PROLOR's common stock as of the close of business on July 22, 2013, the record date for the PROLOR special meeting, are entitled to receive notice of and to vote at the PROLOR special meeting.

*Q: If I am an OPKO stockholder, what am I being asked to vote on at the OPKO annual meeting?*

A: If you are a holder of record of OPKO common stock as of the close of business on July 22, 2013, you will be asked to consider and vote upon the following proposals at the OPKO annual meeting:

a proposal to elect as directors the ten nominees named in this joint proxy statement/prospectus for a term of office expiring at the 2014 annual meeting of stockholders and until their respective successors are duly elected and qualified;

the OPKO Plan Amendment Proposal;

the OPKO Authorized Share Increase Proposal;

the OPKO Share Issuance Proposal;

the OPKO Adjournment Proposal; and

such other matters as may properly come before the OPKO annual meeting or any adjournment or postponement thereof.

**OPKO's Board of Directors recommends that OPKO's stockholders vote FOR the election of the ten director nominees named in this joint proxy statement/prospectus and FOR each of the other proposals described above. The approval of the OPKO Share Issuance Proposal is required for the completion of the Merger.**

*Q: What vote is required for the approval of each of the proposals to be voted on at the OPKO annual meeting?*

A: If a quorum is present, the following votes will be required for the approval of the proposals to be voted on at the OPKO annual meeting:

*Election of directors.* A nominee for director will be elected to OPKO's Board of Directors if the votes cast in favor of such nominee by the holders of shares of OPKO common stock present in person or represented by proxy and entitled to vote at the



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OPKO annual meeting exceed the votes cast against such nominee.

*OPKO Plan Amendment Proposal.* The OPKO Plan Amendment Proposal will be approved if the votes cast in favor of such proposal by the holders of shares of OPKO common stock present in person or represented by proxy and entitled to vote at the OPKO annual meeting exceed the votes cast against such proposal; provided that, pursuant to the NYSE's shareholder approval policy, the total votes cast on the proposal must represent over 50% of all securities entitled to vote on the proposal.

*OPKO Authorized Share Increase Proposal.* The OPKO Authorized Share Increase Proposal will be approved if the holders of a majority of the shares of OPKO common stock outstanding and entitled to vote at the OPKO annual meeting vote in favor of the proposal.

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*OPKO Share Issuance Proposal.* The OPKO Share Issuance Proposal will be approved if the votes cast in favor of such proposal by the holders of shares of OPKO common stock present in person or represented by proxy and entitled to vote at the OPKO annual meeting exceed the votes cast against such proposal; provided that, pursuant to the NYSE's shareholder approval policy, the total votes cast on the proposal must represent over 50% of all securities entitled to vote on the proposal.

*OPKO Adjournment Proposal.* The OPKO Adjournment Proposal will be approved if the votes cast in favor of such proposal by the holders of shares of OPKO common stock present in person or represented by proxy and entitled to vote at the OPKO annual meeting exceed the votes cast against such proposal.

*Q: Do OPKO's or PROLOR's officers and directors own shares of OPKO common stock that are entitled to be voted at the OPKO annual meeting?*

A: Yes. At the close of business on July 22, 2013, OPKO's directors and executive officers and their affiliates had the right to vote approximately \_\_\_\_\_ million shares of the then-outstanding OPKO common stock (excluding any shares of OPKO common stock deliverable upon exercise of outstanding stock options or warrants or underlying unvested restricted stock awards) at the OPKO annual meeting, which shares represented approximately \_\_\_\_\_ % of the OPKO common stock outstanding and entitled to vote at the OPKO annual meeting. Excluding shares of OPKO common stock held by PROLOR officers and directors who are also directors and executive officers of OPKO, at the close of business on July 22, 2013, PROLOR's directors and executive officers and their affiliates had the right to vote approximately \_\_\_\_\_ million shares of the then-outstanding OPKO common stock, which shares represented approximately \_\_\_\_\_ % of the OPKO common stock outstanding and entitled to vote at the OPKO annual meeting. OPKO expects that its and PROLOR's directors and executive officers will vote their shares FOR approval of each of the proposals to be voted on at the OPKO annual meeting, including the OPKO Share Issuance Proposal. As a result, the OPKO Share Issuance Proposal and the other proposals to be voted on at the OPKO annual meeting may be approved even if a majority of OPKO's unaffiliated stockholders vote against such proposal.

*Q: If I am a PROLOR stockholder, what am I being asked to vote on at the PROLOR special meeting?*

A: If you are a holder of record of PROLOR common stock as of the close of business on July 22, 2013, you will be asked to consider and vote upon the following proposals at the PROLOR special meeting:

the PROLOR Merger Proposal;

the PROLOR Compensation Advisory Vote Proposal;

the PROLOR Adjournment Proposal; and

such other matters as may properly come before the PROLOR special meeting or any adjournment or postponement thereof.

**PROLOR's Board of Directors recommends that PROLOR stockholders vote FOR each of the foregoing proposals. The approval by PROLOR's stockholders of the PROLOR Merger Proposal is required for the completion of the Merger.**

*Q: What vote is required for the approval of each of the proposals to be voted on at the PROLOR special meeting?*

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- A: If a quorum is present, the following votes will be required for the approval of the proposals to be voted on at the PROLOR special meeting:

*PROLOR Merger Proposal.* The PROLOR Merger Proposal will be approved if the holders of a majority of the shares of PROLOR common stock outstanding and entitled to vote at the PROLOR special meeting vote in favor of the proposal.

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*PROLOR Compensation Advisory Vote Proposal.* The PROLOR Compensation Advisory Vote Proposal will be approved if the holders of a majority of the shares of PROLOR common stock present in person or represented by proxy and entitled to vote at the PROLOR special meeting vote in favor of the proposal. The PROLOR Compensation Advisory Vote Proposal is advisory in nature and will not be binding on PROLOR or PROLOR's Board of Directors and will not impact whether or not the compensation is paid.

*PROLOR Adjournment Proposal.* The PROLOR Adjournment Proposal will be approved if the holders of a majority of the shares of PROLOR common stock present in person or represented by proxy and entitled to vote at the PROLOR special meeting vote in favor of the proposal.

*Q: Do PROLOR's or OPKO's officers and directors own shares of PROLOR common stock that are entitled to be voted at the PROLOR special meeting?*

A: Yes. At the close of business on July 22, 2013, PROLOR's directors and executive officers and their affiliates had the right to vote approximately \_\_\_\_\_ million shares of the then-outstanding PROLOR common stock (excluding any shares of PROLOR common stock deliverable upon exercise of outstanding stock options or warrants) at the PROLOR special meeting, which shares represented approximately \_\_\_\_\_ % of the PROLOR common stock outstanding and entitled to vote at the PROLOR special meeting. Excluding shares of PROLOR common stock held by OPKO officers and directors who are also directors and executive officers of PROLOR, at the close of business on July 22, 2013, OPKO's directors and executive officers and their affiliates had the right to vote approximately \_\_\_\_\_ million shares of the then-outstanding PROLOR common stock, which shares represented approximately \_\_\_\_\_ % of the PROLOR common stock outstanding and entitled to vote at the PROLOR special meeting. PROLOR expects that its and OPKO's directors and executive officers will vote their shares FOR approval of each of the PROLOR Merger Proposal and the PROLOR Compensation Advisory Vote Proposal. As a result, the PROLOR Merger Proposal and the PROLOR Compensation Advisory Vote Proposal may be approved even if a majority of PROLOR's unaffiliated stockholders vote against such proposals.

*Q: Why is PROLOR asking its stockholders to vote on the PROLOR Compensation Advisory Vote Proposal?*

A: PROLOR is asking its stockholders to cast an advisory (non-binding) vote to approve the PROLOR Compensation Advisory Vote Proposal because SEC rules require a company that is being acquired to seek an advisory (non-binding) vote of its stockholders with respect to certain compensation that its named executive officers may potentially receive as a result of the acquisition.

*Q: What will happen if PROLOR's stockholders do not approve the PROLOR Compensation Advisory Vote Proposal?*

A: The advisory approval by PROLOR's stockholders of the PROLOR Compensation Advisory Vote Proposal is not a condition to the completion of the Merger. Because the vote is advisory in nature, it will not be binding on either PROLOR or OPKO and will have no effect on whether the Merger is completed or whether the compensation subject to such vote is paid.

*Q: What do I need to do now and how do I vote?*

A: OPKO and PROLOR urge you to carefully read this joint proxy statement/prospectus in its entirety, including the annexes and other documents attached and/or referred to in this joint proxy statement/prospectus, and to consider how the Merger may affect you. If you are an OPKO stockholder, you may vote your shares in any of the following ways:

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by completing, executing and mailing your signed OPKO proxy card in the enclosed postage paid return envelope;

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by calling the toll-free number listed on the enclosed OPKO proxy card and following the instructions provided;

by accessing the website indicated on the enclosed OPKO proxy card and following the instructions provided; or

by attending the OPKO annual meeting and voting in person.

If you are a PROLOR stockholder, you may vote your shares in any of the following ways:

by completing, executing and mailing your signed PROLOR proxy card in the enclosed postage paid return envelope;

by calling the toll-free number listed on the enclosed PROLOR proxy card and following the instructions provided;

by accessing the website indicated on the enclosed PROLOR proxy card and following the instructions provided; or

by attending the PROLOR special meeting and voting in person.

If you elect to vote by telephone or on the Internet, please have your OPKO proxy card or PROLOR proxy card (as applicable) available when you submit your vote.

*Q: What procedures must I follow if I wish to vote in person?*

A: If your shares of OPKO common stock or PROLOR common stock are registered directly in your name with OPKO's or PROLOR's transfer agent, respectively, you are considered, with respect to those shares, the stockholder of record, and you will receive your proxy materials and proxy card directly from OPKO and/or PROLOR, as applicable. If you are an OPKO or PROLOR stockholder of record, you will be permitted to attend the meeting and vote in person upon presentation of a valid government-issued identification verifying your identity.

If your shares of OPKO common stock or PROLOR common stock are held in a brokerage account or by another nominee, you are considered the beneficial owner of shares held in street name, and you will receive your proxy materials and proxy card from the broker or nominee holding your shares. As the beneficial owner, you are also invited to attend the OPKO annual meeting and/or the PROLOR special meeting, as applicable. However, because a beneficial owner is not the stockholder of record, you may not vote these shares in person at the OPKO annual meeting or PROLOR special meeting, as applicable, unless you obtain a legal proxy from the broker or other nominee that holds your shares giving you the right to vote the shares in person at the applicable meeting.

*Q: May I revoke or change my vote after I have provided proxy instructions?*

A: Yes. You may revoke or change your vote at any time before your proxy is voted at the OPKO annual meeting or the PROLOR special meeting, as applicable. If you are a stockholder of record, you may revoke or change your vote by:

sending a written notice stating that you would like to revoke your proxy to the address specified below;

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submitting new proxy instructions on a new proxy card with a later date;

granting a subsequent proxy by telephone or over the Internet; or

attending the meeting and voting in person.

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Your attendance alone at the applicable stockholder meeting will not revoke your proxy. If you wish to revoke or change your vote by providing written notice to the applicable company, such notice should be addressed as follows:

with respect to votes relating to matters to be voted on at the OPKO annual meeting: 4400 Biscayne Boulevard, Miami, Florida 33137, Attn: Secretary.

with respect to votes relating to matters to be voted on at the PROLOR special meeting: 7 Golda Meir Street, Weizmann Science Park, Nes-Ziona, Israel 74140, Attn: Finance Director.

If you have instructed a broker or other nominee to vote your shares, you must follow directions received from your broker or other nominee in order to change those instructions.

*Q: What happens if I do not return a proxy card or otherwise provide proxy instructions?*

A: If you are an OPKO stockholder and you do not submit a proxy card, provide proxy instructions by telephone or over the Internet or vote in person at the OPKO annual meeting, your shares will not be counted as present for the purpose of determining the presence of a quorum, which is required to transact business at the OPKO annual meeting. If a quorum is present, your actions will have the same effect as a vote AGAINST the OPKO Authorized Share Increase Proposal but will have no effect on the outcome of any of the other proposals to be voted on at the OPKO annual meeting, except to the extent that there are insufficient shares voted at the meeting to meet the NYSE requirements applicable to the approval of the OPKO Share Issuance Proposal and the OPKO Plan Amendment Proposal.

If you are a PROLOR stockholder and you do not submit a proxy card, provide proxy instructions by telephone or over the Internet or vote in person at the PROLOR special meeting, your shares will not be counted as present for the purpose of determining the presence of a quorum, which is required to transact business at the PROLOR special meeting. If a quorum is present, your actions will have no effect on the outcomes of the PROLOR Adjournment Proposal and the PROLOR Compensation Advisory Vote Proposal. However, because the approval of the PROLOR Merger Proposal requires the affirmative vote of a majority of the shares of PROLOR common stock outstanding and entitled to vote at the PROLOR special meeting, your failure to submit a proxy card or otherwise vote your shares at the meeting will have the same effect as a vote AGAINST the PROLOR Merger Proposal.

*Q: What happens if I submit a proxy without indicating how I wish to vote or abstain from voting with respect to any matter?*

A: If you are an OPKO stockholder and you sign, date and mail your proxy card without indicating how you wish to vote, your proxy will be counted as present for the purpose of determining the presence of a quorum for the OPKO annual meeting and all of your shares will be voted FOR the election of each of the director nominees named in this joint proxy statement/prospectus and FOR the approval of each of the other proposals to be voted on at the OPKO annual meeting. However, if you submit a proxy card or provide proxy instructions by telephone or over the Internet and affirmatively elect to abstain from voting, your proxy will be counted as present for the purpose of determining the presence of a quorum for the OPKO annual meeting, but will not be voted at the OPKO annual meeting. Your abstention will have the same effect as a vote AGAINST the OPKO Authorized Share Increase Proposal. In addition, under guidance issued by the NYSE, your abstention will have the same effect as a vote AGAINST the OPKO Plan Amendment Proposal and the OPKO Share Issuance Proposal. Your abstention will have no effect on the outcome of any of the other proposals to be voted on at the OPKO annual meeting.

If you are a PROLOR stockholder and you sign, date and mail your proxy card without indicating how you wish to vote, your proxy will be counted as present for the purpose of determining the presence of a quorum for the PROLOR special meeting and all of your shares will be voted FOR each of the proposals to be voted on at the PROLOR special meeting. However, if you submit a proxy card or provide proxy instructions by telephone or over the Internet and affirmatively elect to abstain from voting, your proxy will



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be counted as present for the purpose of determining the presence of a quorum for the PROLOR special meeting, but will not be voted at the PROLOR special meeting. As a result, your abstention will have the same effect as a vote AGAINST each of the PROLOR Merger Proposal, the PROLOR Adjournment Proposal and the PROLOR Compensation Advisory Vote Proposal.

*Q: If a broker or other nominee holds my shares in street name, will my broker or nominee vote my shares for me?*

A: If your shares are held in street name in a stock brokerage account or by another nominee, you must provide the record holder of your shares with instructions on how to vote your shares. Please follow the voting instructions provided by your broker or other nominee. Please note that you may not vote shares held in street name by returning a proxy card directly to OPKO or PROLOR or by voting in person at your special meeting, as the case may be, unless you provide a legal proxy, which you must obtain from your broker or other nominee.

*Q: What happens if I hold my shares in street name but do not provide voting instructions to my broker or other nominee?*

A: Brokers or other nominees who hold shares in street name for a beneficial owner typically have the authority to vote in their discretion on routine proposals, even when they have not received instructions from the beneficial owner. However, brokers or other nominees are not allowed to exercise their voting discretion on matters that are determined to be non-routine without specific instructions from the beneficial owner. A broker non-vote occurs when a broker or other nominee does not receive such voting instructions from its customer on non-routine matters. Broker non-votes will not be counted for purposes of determining the presence of a quorum at the OPKO annual meeting, but will be counted for purposes of determining the presence of a quorum at the PROLOR special meeting.

OPKO and PROLOR believe that, other than the OPKO Authorized Share Increase Proposal, the OPKO Adjournment Proposal and the PROLOR Adjournment Proposal, each of the matters presented by it in this joint proxy statement/prospectus are non-routine matters. For this reason, OPKO and PROLOR urge you to give voting instructions to your broker or other nominee. If any routine matters are properly brought before the OPKO annual meeting or the PROLOR special meeting, then brokers and other nominees holding shares in street name will be permitted to vote those shares in their discretion for any such routine matters.

Broker non-votes will have the same effect as a vote AGAINST the PROLOR Merger Proposal. In addition, pursuant to the NYSE's interpretations of its shareholder approval policies, broker non-votes will also have the effect of votes against each of the OPKO Plan Amendment Proposal and the OPKO Share Issuance Proposal unless holders of more than 50% of the shares of OPKO common stock entitled to vote on such proposal cast votes, in which case, broker non-votes will have no effect on the result of the vote. Broker non-votes will not have any effect on any of the OPKO director election proposal, the OPKO Authorized Share Increase Proposal, the OPKO Adjournment Proposal, the PROLOR Compensation Advisory Vote Proposal and the PROLOR Adjournment Proposal.

*Q: What constitutes a quorum for the OPKO annual meeting and the PROLOR special meeting?*

A: Stockholders who hold a majority of the voting power of all the outstanding shares of OPKO common stock entitled to vote, present in person or represented by proxy at the OPKO annual meeting, constitute a quorum to conduct business at the meeting. Stockholders who hold a majority of the shares of PROLOR common stock entitled to vote, present in person or represented by proxy at the PROLOR special meeting, constitute a quorum to conduct business at the meeting.

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*Q: Who is paying for this proxy solicitation?*

A: Each of OPKO and PROLOR will bear its own expenses under the Merger Agreement, except that OPKO and PROLOR have agreed to share equally the expenses associated with the printing, filing and mailing of this joint proxy statement/prospectus, and any amendments or supplements to this joint proxy statement/prospectus.

OPKO and PROLOR may reimburse brokerage houses and other custodians, nominees and fiduciaries for their costs of soliciting and obtaining proxies from beneficial owners, including the costs of forwarding this joint proxy statement/prospectus and other solicitation materials to beneficial owners.

Each of OPKO and PROLOR may also retain the services of a professional proxy solicitor and, if so, will pay for the fees and expenses of its respective proxy solicitor's services.

*Q: Whom should I contact if I have any questions about the Merger, the OPKO annual meeting or the PROLOR special meeting?*

A: If you have any questions about the Merger, the OPKO annual meeting or the PROLOR special meeting, or if you need assistance in submitting your proxy or voting your shares or need additional copies of this joint proxy statement/prospectus or the enclosed proxy card, you should contact:

OPKO Health, Inc.

4400 Biscayne Boulevard

Miami, Florida 33137

Attn: Secretary

(305) 575-4100

PROLOR Biotech, Inc.

7 Golda Meir Street

Weizmann Science Park

Nes-Ziona, Israel 74140

Attn: Finance Director

(866) 644-7811

*Q: What do I do if I receive more than one joint proxy statement/prospectus or set of voting instructions?*

A: If you hold shares directly as a record holder and also in street name or otherwise through a nominee, or if you hold both shares of OPKO common stock and PROLOR common stock, you may receive more than one joint proxy statement/prospectus and/or set of voting instructions relating to the OPKO annual meeting or PROLOR special meeting, as applicable. These should each be voted and/or returned separately in order to ensure that all of your shares are voted. A vote as a PROLOR stockholder will not constitute a vote as an OPKO stockholder on any matter, nor will a vote as an OPKO stockholder constitute a vote as a PROLOR stockholder on any matter.

*Q: What happens if I sell my shares after the applicable record date, but before the OPKO annual meeting or the PROLOR special meeting, as applicable?*

A: If you transfer your OPKO common stock or PROLOR common stock after the applicable record date, but before the date of the applicable meeting, you will retain your right to vote at the OPKO annual meeting or the PROLOR special meeting, as applicable. However, if you are a PROLOR stockholder, you will not have the right to receive any shares of OPKO common stock in exchange for

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your former shares of PROLOR common stock if and when the Merger is completed. In order to receive shares of OPKO common stock in exchange for your shares of PROLOR common stock, you must hold your PROLOR common stock through the completion of the Merger.

*Q: Should I send in my stock certificates now?*

**A: No. Please do not send any stock certificates with your proxy card.**

If you are a holder of PROLOR common stock, after the Merger is completed you will receive written instructions from American Stock Transfer & Trust Company, LLC, the exchange agent for the Merger, regarding how to exchange your PROLOR stock certificates for certificates representing shares of OPKO common stock.

OPKO stockholders will not be required to exchange their stock certificates in connection with the Merger and should not send in their stock certificates for exchange either now or after the Merger is completed.

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**SUMMARY**

*This summary highlights selected information from this joint proxy statement/prospectus. It does not contain all of the information that is important to you with respect to the OPKO Share Issuance Proposal, the PROLOR Merger Proposal, the PROLOR Compensation Advisory Vote Proposal or any other matter described in this joint proxy statement/prospectus. OPKO and PROLOR urge you to carefully read this joint proxy statement/prospectus in its entirety, including the annexes and other documents attached and/or referred to in this joint proxy statement/prospectus, to fully understand the Merger. In particular, you should read the Merger Agreement, which is described elsewhere in this joint proxy statement/prospectus and attached as Annex A hereto. In addition, OPKO and PROLOR encourage you to read the information incorporated by reference into this joint proxy statement/prospectus, which includes important business and financial information about OPKO and PROLOR that has been filed with the SEC. You may obtain the information incorporated by reference into this joint proxy statement/prospectus without charge by following the instructions in the section titled *Where You Can Find Additional Information* beginning on page 176.*

*When this joint proxy statement/prospectus refers to the combined company, it means OPKO and its subsidiaries and PROLOR and its subsidiaries, collectively.*

**The Companies**

***OPKO Health, Inc.***

OPKO is a multi-national biopharmaceutical and diagnostics company that seeks to establish industry-leading positions in large and rapidly growing medical markets by leveraging its discovery, development and commercialization expertise and its novel and proprietary technologies. OPKO is developing a range of solutions to diagnose, treat and prevent various conditions, including molecular diagnostics tests, laboratory developed tests, or LDTs, point-of-care tests and proprietary pharmaceuticals and vaccines. OPKO plans to commercialize these solutions on a global basis in large and high growth markets, including emerging markets.

OPKO is headquartered in Miami, Florida. OPKO's principal offices are located at 4400 Biscayne Boulevard, Miami, Florida 33137 and its phone number is (305) 575-4100. OPKO's principal website is [www.opko.com](http://www.opko.com). The information contained on OPKO's website is not deemed part of this joint proxy statement/prospectus. OPKO common stock is listed on the NYSE and trades under the symbol **OPK**. Additionally, OPKO intends to apply to list its shares on the Tel Aviv Stock Exchange prior to the closing of the Merger.

For a more complete discussion of OPKO's business, see the section titled *Information About the Companies - OPKO Health, Inc.* beginning on page 104. Additional information about OPKO and its subsidiaries is also included in documents incorporated by reference into this joint proxy statement/prospectus. See the section titled *Where You Can Find Additional Information* beginning on page 176.

***PROLOR Biotech, Inc.***

PROLOR is a development stage biopharmaceutical company utilizing patented technology to develop longer-acting, proprietary versions of already-approved therapeutic proteins that currently generate billions of dollars in annual global sales. PROLOR has obtained certain exclusive worldwide rights from Washington University in St. Louis, Missouri to use a short, naturally-occurring amino acid sequence (peptide) that has the effect of slowing the removal from the body of the therapeutic protein to which it is attached. This Carboxyl Terminal Peptide, or CTP, can be readily attached to a wide array of existing therapeutic proteins, stabilizing the therapeutic protein in the bloodstream and extending its life span without additional toxicity or loss of desired biological activity. PROLOR is using the CTP technology to develop new, proprietary versions of certain existing therapeutic proteins that have longer life spans than therapeutic proteins without CTP. PROLOR believes that its products will have greatly improved therapeutic profiles and distinct market advantages.

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PROLOR is headquartered in Nes-Ziona, Israel. Its principal office address is 7 Golda Meir Street, Weizmann Science Park, Nes-Ziona, Israel 74140 and its phone number is (866) 644-7811. PROLOR's principal website is [www.prolor-biotech.com](http://www.prolor-biotech.com). The information contained on PROLOR's website is not deemed part of this joint proxy statement/prospectus. PROLOR's common stock is listed on the NYSE MKT and the Tel Aviv Stock Exchange and trades under the symbol PBTH.

For a more complete discussion of PROLOR's business, see the section titled "Information About the Companies PROLOR Biotech, Inc." beginning on page 106. Additional information about PROLOR and its subsidiaries is also included in documents incorporated by reference into this joint proxy statement/prospectus. See the section titled "Where You Can Find Additional Information" beginning on page 176.

### ***POM Acquisition, Inc.***

POM is a wholly owned subsidiary of OPKO and was incorporated in Nevada in April 2013, solely for the purpose of facilitating the Merger. POM has not carried on any activities to date, except for activities incidental to its formation and activities undertaken in connection with the transactions contemplated by the Merger Agreement.

### **The Merger**

OPKO, POM and PROLOR entered into the Merger Agreement, which provides that, subject to the terms and conditions of the Merger Agreement and in accordance with the Nevada Revised Statutes, or the NRS, upon completion of the Merger, POM will merge with and into PROLOR, with PROLOR continuing as the surviving entity and as a wholly owned subsidiary of OPKO. Each of the boards of directors of OPKO and PROLOR (with Dr. Frost, Dr. Hsiao and Mr. Rubin, each of whom serves as a director of both PROLOR and OPKO, abstaining) approved the combination of the businesses of OPKO and PROLOR. As promptly as practicable after the completion of the Merger, PROLOR will merge with and into a Delaware limited liability company, wholly owned by OPKO, with the Delaware limited liability company surviving as a wholly owned subsidiary of OPKO.

### **What PROLOR Stockholders Will Receive in the Merger**

At the Effective Time, by virtue of the Merger and without any action on the part of the holders of PROLOR common stock, each share of PROLOR common stock that is issued and outstanding as of the Effective Time (other than any shares of PROLOR common stock held by OPKO, POM, PROLOR or any subsidiary of OPKO or PROLOR, which will be cancelled and retired at the Effective Time) will be converted into the right to receive 0.9951 of a share of OPKO common stock, rounded up to the nearest whole share number. The Exchange Ratio is fixed and will not be adjusted based upon changes in the price of PROLOR common stock or OPKO common stock prior to the completion of the Merger. As a result, the value of the shares of OPKO common stock that PROLOR stockholders will receive in connection with the Merger will not be known before the Merger is completed and will fluctuate as the price of OPKO common stock fluctuates.

For a more complete discussion of what PROLOR stockholders will receive in connection with the Merger, see the section titled "The Merger What PROLOR Stockholders Will Receive in the Merger" beginning on page 46.

### **Ownership of OPKO After the Completion of the Merger**

Based on the number of shares of OPKO common stock and PROLOR common stock outstanding as of \_\_\_\_\_, 2013, the latest practicable date before the printing of this joint proxy statement/prospectus, if the Merger had been completed on such date, the holders of PROLOR common stock would have been entitled to receive shares of OPKO common stock representing approximately \_\_\_\_\_% of all shares of OPKO common stock outstanding immediately following the completion of the Merger. OPKO stockholders would have continued to own their existing shares, which would not have been affected by the Merger, and such shares would have

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represented approximately % of all shares of OPKO common stock outstanding immediately following the completion of the Merger. However, because the Exchange Ratio is fixed, to the extent that the number of shares of outstanding OPKO common stock or PROLOR common stock changes prior to the completion of the Merger, there will automatically occur a corresponding change in the relative ownership percentages of the combined company by the current OPKO stockholders and the current PROLOR stockholders. Such changes may occur due to, among other reasons, any new issuance of shares of OPKO common stock or PROLOR common stock, any exercise of any outstanding options or warrants to purchase shares of OPKO common stock or PROLOR common stock, or otherwise. Although the Merger Agreement imposes limits on the ability of each of OPKO and PROLOR to issue additional shares of Common Stock, OPKO may issue shares or equity rights representing up to 20% of the outstanding shares of OPKO common stock outstanding as of the date of the Merger Agreement.

For a more complete discussion of the ownership of OPKO after the completion of the Merger, see the section titled "The Merger Ownership of OPKO After the Completion of the Merger" beginning on page 47.

### **Treatment of PROLOR Stock Options and Warrants**

Upon completion of the Merger, each option to purchase one share of PROLOR common stock that is outstanding and unexercised immediately prior to the Effective Time will be converted into an option to purchase OPKO common stock and (1) the number of shares of OPKO common stock subject to such option will be adjusted to an amount equal to the product of (a) the number of shares of PROLOR common stock subject to such option immediately before the Effective Time and (b) the Exchange Ratio, rounded down to the nearest whole share, and (2) the per share exercise price of such option will be adjusted to a price equal to the quotient of (a) the per share exercise price of such option and (b) the Exchange Ratio, rounded up to the nearest whole cent. OPKO will assume each such stock option in accordance with the terms and conditions of the applicable PROLOR equity incentive plan and stock option agreement relating to such PROLOR stock option, subject to the adjustments described in the preceding sentence and the substitution of OPKO and its Compensation Committee for PROLOR and its Compensation Committee with respect to the administration of each PROLOR equity incentive plan. In addition, pursuant to the stock option agreements governing PROLOR's outstanding stock option awards, each PROLOR stock option will become fully vested and exercisable upon the consummation of the Merger. Dr. Havron and Messrs. Novik and Fima have each executed waiver agreements with PROLOR whereby they have waived their right to acceleration of the vesting of the stock options that were granted to each of them in February 2013 upon the closing of the Merger.

For example, if you hold an option to purchase up to 1,000 shares of PROLOR common stock at an exercise price of \$2.00 per share, upon completion of the Merger, such option will be converted into an option to purchase up to 995 shares of OPKO common stock (995.1 shares rounded down to the nearest whole share) at an exercise price of \$2.01 per share (\$2.009 rounded up to the nearest whole cent).

Similarly, upon completion of the Merger and subject to the consent of the holder thereof, each warrant to purchase one share of PROLOR common stock that is outstanding and unexercised immediately prior to the Effective Time will be converted into a warrant to purchase OPKO common stock and (1) the number of shares of OPKO common stock subject to such warrant will be adjusted to an amount equal to the product of (a) the number of shares of PROLOR common stock subject to such warrant immediately before the Effective Time and (b) the Exchange Ratio, rounded up to the nearest whole share, and (2) the per share exercise price of such warrant will be adjusted to a price equal to the quotient of (a) the per share exercise price of such warrant and (b) the Exchange Ratio, rounded up to the nearest whole cent. OPKO will assume each such warrant in accordance with the terms and conditions thereof, subject to the conditions and adjustments described in the preceding sentence.

For example, if you hold a warrant to purchase up to 1,000 shares of PROLOR common stock at an exercise price of \$2.00 per share, upon completion of the Merger, such warrant will be converted into a warrant to

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purchase up to 996 shares of OPKO common stock (995.1 shares rounded up to the nearest whole share) at an exercise price of \$2.01 per share (\$2.009 rounded up to the nearest whole cent).

For a more complete discussion of what holders of PROLOR stock options and warrants will receive in connection with the Merger, see the section titled "The Merger Treatment of PROLOR Stock Options and Warrants" beginning on page 47.

### **What OPKO Stockholders Will Receive in the Merger**

OPKO stockholders will not receive any additional shares of OPKO common stock as a result of the Merger, and the rights associated with their shares of OPKO common stock will remain unchanged, except insofar as the relative voting power associated with such shares will be diluted as a result of the issuance of additional shares of OPKO common stock to PROLOR stockholders in connection with the Merger such that each share of OPKO common stock outstanding immediately prior to the completion of the Merger will represent a smaller percentage of the aggregate number of shares of OPKO common stock (and therefore a smaller percentage of the outstanding voting power and equity value) outstanding after the completion of the Merger than it did prior to completion of the Merger.

### **Treatment of OPKO Equity Awards**

Equity awards previously issued by OPKO will remain outstanding and will not be affected by the Merger.

### **Board of Directors and Executive Officers of OPKO After the Completion of the Merger**

The Merger will not have any effect on the composition of the Board of Directors and executive officers of OPKO, who shall remain the same following the completion of the Merger.

### **PROLOR Severance Arrangements**

PROLOR has entered into an employment agreement with Mr. Novik, PROLOR's President, that provides for severance benefits upon a qualifying termination of employment within twelve months of the Merger. Pursuant to the stock option agreements governing PROLOR's outstanding stock option awards, each PROLOR stock option that is not currently vested (including stock options held by PROLOR's named executive officers) will become fully vested and exercisable upon the consummation of the Merger; provided that Dr. Havron and Messrs. Novik and Fima have each executed waiver agreements with PROLOR whereby they have waived their right to acceleration of the vesting of the stock options that were granted to each of them in February 2013 upon the closing of the Merger. Except as provided in Mr. Novik's employment agreement, and the acceleration of unvested stock options, PROLOR's executive officers will not receive any additional compensation in connection with the closing of the Merger. Because the only compensation that any of PROLOR's executive officers may potentially receive in connection with the Merger is pursuant to existing contractual obligations, such compensation will be payable regardless of the outcome of this advisory vote, subject only to the conditions thereto contained in Mr. Novik's employment agreement.

In accordance with Section 14A of the Exchange Act, PROLOR is providing its stockholders with the opportunity to cast an advisory vote on the "golden parachute" compensation that PROLOR's named executive officers may potentially receive in connection with the Merger, as reported on the table included under the caption "Severance Arrangements with Executive Officers of PROLOR PROLOR's Named Executive Officer Golden Parachute Compensation" on page 102. PROLOR's Board of Directors unanimously recommends that you vote **FOR** the PROLOR Compensation Advisory Vote Proposal.

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For a more complete discussion of the potential severance payments payable to PROLOR executive officers upon a qualifying termination in connection with the Merger, see the section titled "Severance Arrangements with Executive Officers of PROLOR" beginning on page 102.

### **Recommendation of OPKO's Board of Directors and its Reasons for the Merger**

OPKO's Board of Directors (with Dr. Frost, Dr. Hsiao and Mr. Rubin, each of whom serves as a director of both PROLOR and OPKO, abstaining) approved and adopted the Merger Agreement and the transactions contemplated thereby, including the Merger, and therefore recommends that OPKO's stockholders vote **FOR** the OPKO Share Issuance Proposal. In reaching these decisions, the OPKO Board of Directors considered a number of factors. See the section titled "The Merger Recommendation of OPKO's Board of Directors and its Reasons for the Merger" beginning on page 53.

### **Recommendation of PROLOR's Board of Directors and its Reasons for the Merger**

PROLOR's Board of Directors (with Dr. Frost, Dr. Hsiao and Mr. Rubin, each of whom serves as a director of both PROLOR and OPKO, abstaining) approved and adopted the Merger Agreement and the transactions contemplated thereby, including the Merger. PROLOR's Board of Directors, based on the unanimous recommendation of a strategic alternatives committee thereof consisting solely of disinterested directors of PROLOR, or the Special Committee, determined that the Merger is fair to, and in the best interests of, PROLOR and its stockholders, and therefore recommends that PROLOR's stockholders vote **FOR** the PROLOR Merger Proposal. In reaching these decisions, the PROLOR Board of Directors considered a number of factors. See the section titled "The Merger Recommendation of PROLOR's Board of Directors and its Reasons for the Merger" beginning on page 56.

### **Opinion of Financial Advisor to OPKO's Board of Directors**

Barrington Research Associates, Inc., or Barrington, delivered its written opinion to OPKO's Board of Directors that, as of April 23, 2013, and based upon and subject to the factors, procedures, assumptions, qualifications and limitations set forth therein, the consideration to be paid by OPKO in the proposed transaction was fair, from a financial point of view, to OPKO.

The full text of Barrington's written opinion, dated April 23, 2013, is attached as Annex B to this joint proxy statement/prospectus and is incorporated herein by reference. Barrington's opinion sets forth, among other things, the assumptions made, procedures followed, matters considered, and qualifications and limitations on the review undertaken in connection with its opinion. **Barrington provided its opinion for the benefit of OPKO's Board of Directors (in its capacity as such) in connection with, and for the purposes of, its evaluation of the transactions contemplated by the Merger Agreement. Barrington's opinion addresses only the fairness to OPKO of the consideration to be paid by OPKO in the proposed transaction and does not address any other matter. The opinion does not constitute a recommendation to any stockholder as to how to vote or act with respect to the merger.**

For a more complete discussion of Barrington's opinion, see the section titled "The Merger Opinion of Financial Advisor to OPKO's Board of Directors" beginning on page 58. See also Annex B to this joint proxy statement/prospectus, which includes the full text of Barrington's opinion.

### **Opinion of Financial Advisor to the Special Committee of PROLOR's Board of Directors**

In connection with the Merger, the Special Committee received a written opinion, dated April 23, 2013, from Oppenheimer & Co., or Oppenheimer, the independent financial adviser to the Special Committee, as to the fairness, from a financial point of view and as of the date of such opinion, of the Exchange Ratio to the holders of



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PROLOR common stock (excluding OPKO, its subsidiaries and any of their respective affiliates). Holders of PROLOR common stock are encouraged to read Oppenheimer's opinion carefully in its entirety for a description of the assumptions made, procedures followed, matters considered and limitations on the review undertaken by Oppenheimer. **Oppenheimer's opinion was provided for the benefit of the Special Committee in connection with, and for the purpose of, its evaluation of the Exchange Ratio from a financial point of view and does not address any other aspect of the Merger. The opinion does not address the relative merits of the Merger as compared to other business strategies or transactions that might be available with respect to PROLOR or PROLOR's underlying business decision to effect the Merger. The opinion does not constitute a recommendation to any PROLOR stockholder as to how to vote or act with respect to the Merger.**

For a more complete discussion of Oppenheimer's opinion, see the section titled "The Merger - Opinion of Financial Advisor to the Special Committee of PROLOR's Board of Directors" beginning on page 64. See also Annex C to this joint proxy statement/prospectus, which includes the full text of Oppenheimer's opinion.

### **Interests of OPKO and PROLOR Directors and Executive Officers in the Merger**

You should be aware that certain directors and executive officers of OPKO and PROLOR have interests in the Merger that are different from, or in addition to, the interests of the stockholders of OPKO and PROLOR generally.

Interests of the PROLOR directors and executive officers include (i) the existing employment agreement with Mr. Novik, PROLOR's President, that provides for severance benefits upon a qualifying termination within 12 months following the completion of the Merger, (ii) the acceleration of the vesting of certain stock options held by PROLOR's executive officers and directors and (iii) the right to continued indemnification and insurance coverage for directors and executive officers of PROLOR after the Merger is completed pursuant to the terms of the Merger Agreement.

In addition, certain of PROLOR's directors, executive officers and stockholders are directors and stockholders of OPKO. Dr. Frost, the Chairman of the Board of Directors of PROLOR and the holder of approximately 1% of the outstanding shares of PROLOR common stock as of the date of this joint proxy statement/prospectus, is OPKO's Chairman and Chief Executive Officer and the holder of approximately 1% of the outstanding shares of OPKO common stock as of the date of this joint proxy statement/prospectus. Dr. Hsiao, a stockholder of PROLOR and a member of the Board of Directors of PROLOR, is OPKO's Vice Chairman of its Board of Directors and Chief Technical Officer and the holder of approximately 1% of the outstanding shares of OPKO common stock as of the date of this joint proxy statement/prospectus, and Mr. Rubin, a stockholder of PROLOR and a member of the Board of Directors of PROLOR, is OPKO's Executive Vice President Administration, a member of the Board of Directors of OPKO, and a less than 5% stockholder of OPKO and PROLOR. The foregoing directors recused themselves from all deliberations of the Board of Directors of each of OPKO and PROLOR relating to the Merger and abstained from the vote of the Board of Directors of each such company with respect to the approval and adoption of the Merger Agreement and the transactions contemplated thereby, including the Merger.

For a more complete discussion of the interests of the directors and executive officers of PROLOR and OPKO in the Merger, see the sections titled "The Merger - Interests of OPKO and PROLOR Directors and Executive Officers in the Merger" and "Severance Arrangements with Executive Officers of PROLOR" beginning on pages 73 and 102, respectively.

### **Anticipated Accounting Treatment of the Merger**

The Merger will be accounted for under the acquisition method of accounting in conformity with U.S. generally accepted accounting principles (which we refer to as GAAP), for accounting and financial reporting purposes.

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**Material United States Federal Income Tax Consequences of the Mergers**

OPKO and PROLOR intend for the Mergers to qualify as a reorganization within the meaning of Section 368(a) of the Code, and it is a condition to the completion of the Merger that OPKO and PROLOR each receive written opinions from their respective outside legal counsel, dated as of the closing date of the Merger, to the effect that the Merger will be treated as a reorganization within the meaning of Section 368(a) of the Code. We intend to take the position that the Merger and the PROLOR-LLC Merger are two parts of the same integrated transaction. Assuming the Mergers qualify as a reorganization, PROLOR stockholders will not recognize gain or loss for U.S. federal income tax purposes upon the exchange of their shares of PROLOR common stock for shares of OPKO common stock in connection with the Merger or upon the closing of the PROLOR-LLC Merger.

**Tax matters are very complicated, and the tax consequences of the Mergers to a particular stockholder will depend on such stockholder's circumstances. Accordingly, OPKO and PROLOR urge you to consult your tax advisor for a full understanding of the tax consequences of the Mergers to you, including the applicability and effect of U.S. federal, state, local and foreign income and other tax laws. For more information, see the section titled Material United States Federal Income Tax Consequences of the Mergers beginning on page 77.**

**No Appraisal Rights**

Neither OPKO stockholders nor PROLOR stockholders will be entitled to exercise any appraisal rights in connection with the Merger under Delaware law, Nevada law or otherwise.

**Regulatory Approvals**

Under the Hart-Scott Rodino Antitrust Improvements Act of 1976, as amended, or the HSR Act, and the rules and regulations promulgated thereunder, the Merger may not be completed until the required information and materials have been furnished to the Antitrust Division of the U.S. Department of Justice, or the Antitrust Division, and the U.S. Federal Trade Commission, or the FTC, and until certain waiting period requirements have expired or been earlier terminated. OPKO and PROLOR each filed notification and report forms under the HSR Act with the FTC and the Antitrust Division on June 12, 2013, and the waiting period applicable to the Merger was terminated on June 26, 2013. There are no further U.S. antitrust conditions to consummation of the Merger.

The period of time for completion of the Merger is subject to the grant by the Israel Securities Authority, in accordance with its authority under the Israeli Securities Law 5728-1968, to OPKO of an exemption from publishing a prospectus in Israel in respect to the conversion of PROLOR securities traded on the Tel Aviv Stock Exchange Ltd. into OPKO securities or a clearance. In the event that such exemption or clearance is withheld, the Merger is expected to be delayed for the period of time required for the preparation, approval and publication of a prospectus.

As a condition to the obligations of PROLOR to consummate the Merger, PROLOR is seeking a ruling from the ITA whereby the Merger will be treated as a tax-exempt transaction under Israeli law. Pursuant to the Merger Agreement, PROLOR may waive such condition and, absent an interim arrangement with the ITA, the consideration paid to PROLOR stockholders that are Israeli tax payors will be subject to Israeli tax. For a more complete discussion of the tax ruling, see Israeli Tax Treatment of the Merger beginning on page 80. For a more complete discussion of the anticipated effects of such tax ruling, if received, see Israeli Income Tax Treatment of the Merger beginning on page 80.

For a more complete discussion of the regulatory approvals relating to the Merger, see the section titled The Merger Regulatory Approvals Required for the Merger beginning on page 74.

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### **Conditions to the Completion of the Merger**

OPKO and PROLOR currently expect to complete the Merger in the second half of 2013. However, completion of the Merger will be possible only if all of the conditions to the completion of the Merger contained in the Merger Agreement, including the approval of the OPKO Share Issuance Proposal and the PROLOR Merger Proposal and receipt of the required regulatory approvals, have been satisfied or waived. Therefore, factors outside of either company's control could delay or prevent the completion of the Merger.

The obligations of OPKO and PROLOR to complete the Merger are each subject to the satisfaction of the following conditions. Pursuant to the Merger Agreement, other than the approval by the PROLOR stockholders of the PROLOR Merger Proposal, any of the following conditions may be waived by the parties if not satisfied on or prior to the closing date of the Merger:

approval by the PROLOR stockholders of the PROLOR Merger Proposal;

absence of any statute, rule, regulation, executive order, decree, ruling, temporary restraining order, preliminary or permanent injunction or other order issued by a court or other United States governmental authority of competent jurisdiction that has the effect of making the Merger or the other transactions contemplated by the Merger Agreement illegal or otherwise prohibiting consummation of the Merger or the other transactions contemplated thereby;

expiration or termination of the waiting period applicable to the consummation of the Merger under the HSR Act and the expiration or termination of any waiting period under, and the receipt of all consents, clearances, waivers, licenses, orders, registrations, approvals, permits and authorizations necessary or advisable under, applicable foreign antitrust laws;

receipt of certain governmental or regulatory consents, waivers, authorizations and approvals required in connection with the execution, delivery and performance of the Merger Agreement and the other transactions contemplated thereby;

approval of the OPKO common stock to be issued in the Merger for quotation or listing, as the case may be, on the NYSE (or any successor inter-dealer quotation system or stock exchange thereto) subject to official notice of issuance;

effectiveness under the Securities Act of the registration statement on Form S-4, of which this joint proxy statement/prospectus is a part, the absence of a stop order issued by the SEC suspending the effectiveness of such registration statement and the absence of a proceeding seeking a stop order or any similar proceeding with respect to this joint proxy statement/prospectus initiated or threatened by the SEC;

approval by the OPKO stockholders of the OPKO Share Issuance Proposal; and

clearance by the ISA or an exemption with respect to the delivery of prospectuses in connection with the offering of OPKO common stock offered by OPKO in Israel in connection with the Merger.

The obligations of OPKO and POM to complete the Merger are subject to the satisfaction or waiver of the following additional conditions:

accuracy in all respects as of the date of the Merger Agreement and as of the closing date of the Merger of a limited number of specified representations and warranties made by PROLOR in the Merger Agreement (except, with respect to certain representations and warranties, for inaccuracies that are de minimis in the aggregate);

accuracy in all material respects as of the date of the Merger Agreement and as of the closing date of a limited number of specified representations and warranties made by PROLOR in the Merger Agreement;

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accuracy in all respects as of the date of the Merger Agreement and as of the closing date of the balance of the representations and warranties made by PROLOR in the Merger Agreement, except for such breaches as have not had, and would not reasonably be expected to have, a material adverse effect on PROLOR;

compliance with and performance by PROLOR, in all material respects, of all agreements and covenants required to be performed or complied with by it under the Merger Agreement on or prior to the closing date of the Merger;

receipt of an opinion from Akerman Senterfitt, or Akerman, OPKO's outside legal counsel, that is reasonably acceptable to OPKO and dated as of the closing date of the Merger, to the effect that the Merger will be treated for U.S. federal income tax purposes as a reorganization within the meaning of Section 368(a) of the Code; provided that if Akerman does not render such opinion, this condition may be satisfied if DLA Piper LLP (US), or DLA Piper, renders such opinion;

the amendment of PROLOR's outstanding warrants to permit the modifications thereto required in connection with the Merger; and

the absence of any material restrictions pursuant to the ruling from the ITA required as a condition to PROLOR's obligation to complete the Merger on (1) any person that is a stockholder of OPKO as of immediately prior to or following the closing of the Merger or (2) the transfer of assets, business or operations of OPKO, any of its material subsidiaries or PROLOR, in each case pursuant to Section 103(k) to Israeli Income Tax Ordinance [New Version] 5721-1961, or the Ordinance.

The obligations of PROLOR to complete the Merger are subject to the satisfaction or waiver of the following additional conditions:

accuracy in all respects as of the date of the Merger Agreement and as of the closing date of the Merger of a limited number of specified representations and warranties made by OPKO and POM in the Merger Agreement (except, with respect to certain representations and warranties, for inaccuracies that are de minimis in the aggregate);

accuracy in all material respects as of the date of the Merger Agreement and as of the closing date of a limited number of specified representations and warranties made by OPKO and POM in the Merger Agreement;

accuracy in all respects as of the date of the Merger Agreement and as of the closing date of the balance of the representations and warranties made by OPKO and POM in the Merger Agreement, except for such breaches as have not had, and would not reasonably be expected to have, a material adverse effect on OPKO and POM;

compliance with and performance by OPKO, in all material respects, of all agreements and covenants required to be performed or complied with by it under the Merger Agreement on or prior to the closing date of the Merger;

receipt of an opinion from DLA Piper, outside counsel to the Special Committee, that is reasonably acceptable to PROLOR and dated as of the closing date of the Merger, to the effect that the Merger will be treated for U.S. federal income tax purposes as a reorganization within the meaning of Section 368(a) of the Code; provided that if DLA Piper does not render such opinion, this condition may be satisfied if Akerman renders such opinion; and

receipt of a ruling from the ITA with respect to certain Israeli tax matters relating to the Merger. Pursuant to the Merger Agreement, PROLOR may waive such condition and, absent an interim arrangement with the ITA, the consideration paid to PROLOR stockholders that are Israeli tax payors will be subject to Israeli tax. For a more complete discussion of the tax ruling, see Israeli Tax Treatment of the Merger beginning on page 80.



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**Restrictions on Solicitation**

Pursuant to the Merger Agreement, during the period beginning on April 23, 2013 and continuing until 11:59 p.m. (New York City time) on June 2, 2013, PROLOR, its subsidiaries and their respective representatives (acting under the supervision of the Special Committee) were permitted to solicit, initiate, facilitate and encourage from any third party a competing proposal to acquire at least 15% of the assets of, equity interest in, or business of PROLOR and its subsidiaries taken as a whole, or a Company Acquisition Proposal, including by way of providing access to information pursuant to one or more confidentiality agreements meeting certain parameters specified in the Merger Agreement. In addition, during such go-shop period, PROLOR, its subsidiaries and their respective representatives (acting under the supervision of the Special Committee) were permitted to enter into or otherwise participate in discussions and negotiations with respect to a Company Acquisition Proposal. PROLOR solicited offers from 24 third parties during the go-shop period, but no such party requested access to information regarding PROLOR or made a Company Acquisition Proposal. Had any third party made a Company Acquisition Proposal on or prior to June 2, 2013 that PROLOR's Board of Directors and the Special Committee determined in good faith would reasonably be expected to result in a Superior Proposal (as defined below), PROLOR would have been permitted to continue discussions with the proponent of such proposal through June 22, 2013.

Pursuant to the Merger Agreement, on June 2, 2013, PROLOR was required to and did, and instructed its subsidiaries and representatives to, immediately cease all discussions and negotiations that may be ongoing with respect to a Company Acquisition Proposal. In addition, PROLOR agreed that, from June 2, 2013 through the Effective Time or the date of the termination of the Merger Agreement, it will not solicit competing acquisition proposals or, subject to certain exceptions, enter into discussions or negotiations concerning, or furnish nonpublic information in connection with, any Company Acquisition Proposal.

PROLOR further agreed that, subject to certain exceptions, its Board of Directors will not: (1) withdraw or propose to publicly withdraw or modify in a manner that is adverse to OPKO and POM its recommendation to PROLOR's stockholders that they vote in favor of the PROLOR Merger Proposal and (2) adopt, approve or recommend, or allow PROLOR to execute or enter into, any definitive agreement with respect to a Company Acquisition Proposal (other than a confidentiality agreement meeting certain parameters specified in the Merger Agreement), or (3) fail to recommend against acceptance of any tender offer or exchange offer with respect to a Company Acquisition Proposal. However, if after June 2, 2013 and prior to the time of any approval by PROLOR's stockholders of the PROLOR Merger Proposal, PROLOR receives a written Company Acquisition Proposal, then:

if, after consultation with PROLOR's outside legal advisors, including its outside counsel, the Special Committee determines in good faith that failure to do so would likely be inconsistent with the Special Committee's exercise of its fiduciary duties under applicable law, PROLOR's Board of Directors may withdraw or propose to publicly withdraw or modify in a manner that is adverse to OPKO and POM its recommendation to PROLOR's stockholders that they vote in favor of the PROLOR Merger Proposal; and

if, after consultation with PROLOR's outside financial and legal advisors, PROLOR's Board of Directors determines that such a Company Acquisition Proposal constitutes a Superior Proposal, PROLOR may execute or enter into any definitive agreement with respect to such Company Acquisition Proposal and/or approve, endorse or recommend a tender offer or exchange offer for shares of PROLOR common stock in connection with such Company Acquisition Proposal.

For purposes of the Merger Agreement, a Superior Proposal is a Company Acquisition Proposal that:

if consummated would result in a person or group owning, directly or indirectly,

- i 50% or more of all classes of outstanding equity securities of PROLOR or of the surviving entity in a merger involving PROLOR or the resulting direct or indirect parent of PROLOR or such surviving entity, or

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- i 50% or more (based on the fair market value thereof) of the assets of PROLOR and its subsidiaries (including capital stock of PROLOR's subsidiaries) taken as a whole, and

PROLOR's Board of Directors or the Special Committee determines in good faith (after consultation with its outside legal counsel and financial advisor) is superior, from a financial point of view, to the transactions contemplated by the Merger Agreement, taking into account all financial, legal, regulatory and other aspects of such proposal and of the Merger Agreement (including the relative risks of non-consummation and any changes to the terms of the Merger Agreement proposed by OPKO to PROLOR).

For further discussion of the prohibition on solicitation of acquisition proposals from third parties and on changes to the recommendation of PROLOR's Board of Directors with respect to the approval of the Merger, see the section titled "The Merger Agreement Restrictions on Solicitation" and "The Merger Agreement Recommendation of PROLOR's Board of Directors; Change of Recommendation" beginning on pages 92 and 93, respectively.

**Termination of the Merger Agreement**

Generally and except as specified below, the Merger Agreement may be terminated and the Merger may be abandoned at any time prior to the completion of the Merger, including after the required OPKO stockholder approval and/or PROLOR stockholder approval is obtained:

by mutual written consent of OPKO and PROLOR;

by either party, if:

- i the Merger has not been consummated on or before February 23, 2014, subject to extension for a period of 60 days under certain circumstances;
- i a court of competent jurisdiction or other governmental entity issues a final and non-appealable order, or has taken any other action having the effect of permanently restraining, enjoining or otherwise prohibiting or making illegal the transactions contemplated by the Merger Agreement; or
- i the required approval of the PROLOR Merger Proposal by the PROLOR stockholders has not been obtained at the PROLOR special meeting (or at any adjournment or postponement thereof);

by OPKO if:

- i PROLOR has breached or failed to perform in any respect any of its representations, warranties, covenants or agreements contained in the Merger Agreement, which breach or failure to perform (1) is not cured within thirty (30) days following receipt by PROLOR of written notice of such breach or failure to perform from OPKO (or, if earlier, February 23, 2014) and (2) would result in a failure of any condition to the obligations of OPKO and POM to consummate the Merger; provided, that such termination right shall not be available if OPKO or POM is in material breach of any of its representations, warranties, covenants or agreements under the Merger Agreement that would result in the failure of any conditions to the obligations of PROLOR to consummate the Merger; or
- i PROLOR's Board of Directors fails to recommend that PROLOR's stockholders approve the PROLOR Merger Proposal, PROLOR's Board of Directors fails to publicly reaffirm its recommendation that PROLOR's stockholders approve the PROLOR Merger Proposal in the absence of a publicly announced Company Acquisition Proposal within five business days



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after OPKO so requests in writing (provided that OPKO may only make one such request in any 30 day period), PROLOR enters into a written agreement in respect of a Company Acquisition Proposal or PROLOR, its Board of Directors or the Special Committee publicly announces its intention to do any of the foregoing;

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by PROLOR if:

- i OPKO or POM has breached or failed to perform in any respect any of its respective representations, warranties, covenants or agreements contained in the Merger Agreement, which breach or failure to perform (1) is not cured within thirty (30) days following receipt by OPKO of written notice of such breach or failure to perform from PROLOR (or, if earlier, February 23, 2014) and (2) would result in a failure of any condition to the obligations of PROLOR to consummate the Merger; provided that such termination right shall not be available if PROLOR is in material breach of any of its representations, warranties, covenants or agreements under the Merger Agreement that would result in the failure of any conditions to the obligations of OPKO or POM to consummate the Merger;
- i PROLOR's Board of Directors (1) withdraws (or modifies in a manner adverse to OPKO or POM) its recommendation that PROLOR's stockholders approve the PROLOR Merger Proposal or (2) adopts, approves or recommends, or proposes publicly to adopt, approve or recommend, any Company Acquisition Proposal;
- i PROLOR enters into a written agreement with respect to a Superior Proposal and concurrently with such termination pays to OPKO the applicable termination fee;
- i all conditions to the obligations of OPKO and POM to complete the Merger have been satisfied or waived and OPKO and POM fail to complete the closing within six business days thereof;
- i there is a termination of the employment of, or change in, the chief executive officer of OPKO as of the date of the Merger Agreement prior to the closing of the Merger;
- i OPKO's Board of Directors fails to recommend or changes its recommendation that OPKO's stockholders approve the OPKO Share Issuance Proposal; or
- i the required approval of the OPKO Share Issuance Proposal by the OPKO stockholders has not been obtained at the OPKO annual meeting (or at any adjournment or postponement thereof).

For further discussion of termination of the Merger Agreement, see the section titled "The Merger Agreement - Termination of the Merger Agreement" beginning on page 98.

**Termination Fees and Expenses**

Generally, all fees and expenses incurred in connection with the Merger will be paid by the party incurring such expenses. However, OPKO and PROLOR will share equally all out-of-pocket fees and expenses, other than accountants' and attorneys' fees, incurred in connection with (i) the filing, printing and mailing of the registration statement on Form S-4 and this joint proxy statement/prospectus and any amendments or supplements thereto and (ii) the filing by the parties of any notice or other document under the HSR Act (so long as the acquisition valuation under the HSR Act is between \$141,100,000 and \$709,100,000) or applicable foreign antitrust laws.

A termination fee of \$9,600,000 may be payable by PROLOR to OPKO or OPKO to PROLOR upon the termination of the Merger Agreement under certain circumstances and a termination fee of \$14,400,000 may be payable by PROLOR to OPKO upon the termination of the Merger Agreement under certain circumstances.

For a more complete discussion of termination fees and expenses, see the section titled "The Merger Agreement - Termination Fees and Expenses" beginning on page 99.



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### **Rights of PROLOR Stockholders Will Change as a Result of the Merger**

Due to differences between the governing documents of OPKO and PROLOR, PROLOR stockholders receiving OPKO common stock in connection with the Merger will have different rights once they become OPKO stockholders. The material differences are described in detail under the section titled "Comparison of Rights of Holders of OPKO Common Stock and PROLOR Common Stock" beginning on page 157.

### **Risk Factors**

In evaluating the Merger Agreement and the Merger, you should consider certain risks discussed in the section titled "Risk Factors" beginning on page 36.

### **Matters to Be Considered at the OPKO Annual Meeting and PROLOR Special Meeting**

#### *OPKO annual meeting*

*Date, Time and Place.* The OPKO annual meeting will be held on August 28, 2013, at 10:00 a.m., local time, at OPKO's headquarters located at 4400 Biscayne Boulevard, Miami FL 33137.

*Matters to be Considered at the OPKO annual meeting.* At the OPKO annual meeting, and any adjournments or postponements thereof, OPKO stockholders will be asked to:

elect as directors the ten nominees named in this joint proxy statement/prospectus for a term of office expiring at the 2014 annual meeting of stockholders and until their respective successors are duly elected and qualified;

approve the OPKO Plan Amendment Proposal;

approve the OPKO Authorized Share Increase Proposal;

approve the OPKO Share Issuance Proposal;

approve the OPKO Adjournment Proposal; and

conduct any other business as may properly come before the OPKO annual meeting or any adjournment or postponement thereof.

*Record Date.* The OPKO Board of Directors has fixed the close of business on July 22, 2013 as the record date for determination of OPKO stockholders entitled to notice of and to vote at the OPKO annual meeting and any adjournment thereof.

#### *Required Vote.*

If a quorum is present, the following votes will be required for the approval of the proposals to be voted on at the OPKO annual meeting:

*Election of Directors.* A nominee for director will be elected to OPKO's Board of Directors if the votes cast in favor of such nominee by the holders of shares of OPKO common stock present in person or represented by proxy and entitled to vote at the OPKO annual meeting exceed the votes cast against such nominee.

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*OPKO Plan Amendment Proposal.* The OPKO Plan Amendment Proposal will be approved if the votes cast in favor of such proposal by the holders of shares of OPKO common stock present in person or represented by proxy and entitled to vote at the OPKO annual meeting exceed the votes cast against such proposal; provided that, pursuant to the NYSE's shareholder approval policy, the total votes cast on the proposal must represent over 50% of all securities entitled to vote on the proposal.

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*OPKO Authorized Share Increase Proposal.* The OPKO Authorized Share Increase Proposal will be approved if the holders of a majority of the shares of OPKO common stock outstanding and entitled to vote at the OPKO annual meeting vote in favor of the proposal.

*OPKO Share Issuance Proposal.* The OPKO Share Issuance Proposal will be approved if the votes cast in favor of such proposal by the holders of shares of OPKO common stock present in person or represented by proxy and entitled to vote at the OPKO annual meeting exceed the votes cast against such proposal; provided that, pursuant to the NYSE's shareholder approval policy, the total votes cast on the proposal must represent over 50% of all securities entitled to vote on the proposal.

*OPKO Adjournment Proposal.* The OPKO Adjournment Proposal will be approved if the votes cast in favor of such proposal by the holders of shares of OPKO common stock present in person or represented by proxy and entitled to vote at the OPKO annual meeting exceed the votes cast against such proposal.

*Shares Outstanding and Entitled to Vote.* As of the close of business on the record date for the OPKO annual meeting, there were issued and outstanding \_\_\_\_\_ shares of OPKO common stock.

For additional information about the OPKO annual meeting, see the section titled "The 2013 Annual Meeting of OPKO Stockholders" beginning on page 133.

***PROLOR Special Meeting***

*Date, Time and Place.* The PROLOR special meeting will be held on August 28, 2013, at 10:00 a.m., local time, at PROLOR's headquarters located at 7 Golda Meir Street, Weizmann Science Park, Nes-Ziona, Israel L3 74140.

*Matters to be Considered at the PROLOR Special Meeting.* At the PROLOR special meeting, and any adjournments or postponements thereof, PROLOR stockholders will be asked to:

approve the PROLOR Merger Proposal;

approve, on an advisory basis, the PROLOR Compensation Advisory Vote Proposal;

approve the PROLOR Adjournment Proposal; and

conduct any other business as may properly come before the PROLOR special meeting or any adjournment or postponement thereof.

*Record Date.* The PROLOR Board of Directors has fixed the close of business on July 22, 2013 as the record date for determination of PROLOR stockholders entitled to notice of and to vote at the PROLOR special meeting and any adjournment thereof.

*Required Vote.* If a quorum is present, the following votes will be required for the approval of the proposals to be voted on at the PROLOR special meeting:

*PROLOR Merger Proposal.* The PROLOR Merger Proposal will be approved if the holders of a majority of the shares of PROLOR common stock outstanding and entitled to vote at the PROLOR special meeting vote in favor of the proposal.

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*PROLOR Compensation Advisory Vote Proposal.* The PROLOR Compensation Advisory Vote Proposal will be approved if the holders of a majority of the shares of PROLOR common stock present in person or represented by proxy and entitled to vote at the PROLOR special meeting vote in favor of the proposal. The PROLOR Compensation Advisory Vote Proposal is advisory in nature and will not be binding on PROLOR or PROLOR's Board of Directors and will not impact whether or not the Merger is completed or the compensation is paid.

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*PROLOR Adjournment Proposal.* The PROLOR Adjournment Proposal will be approved if the holders of a majority of the shares of PROLOR common stock present in person or represented by proxy and entitled to vote at the PROLOR special meeting vote in favor of the proposal.

*Shares Outstanding and Entitled to Vote.* As of the close of business on the record date, there were issued and outstanding \_\_\_\_\_ shares of PROLOR common stock.

For additional information about the PROLOR special meeting, see the section titled *The Special Meeting of PROLOR Stockholders* beginning on page 151.

**Legal Proceedings Related to the Merger**

Six putative class action lawsuits have been filed in connection with the Merger: (1) Peter Turkell v. PROLOR Biotech, Inc., et al. (Case No. A-13-680860-B), filed April 29, 2013 in the Eighth Judicial District Court in and for Clark County, Nevada; (2) Floyd A. Fried v. PROLOR Biotech, Inc., et al., (Case No. A-13-681060), filed May 1, 2013 in the Eighth Judicial District Court in and for Clark County, Nevada; (3) Marc Henzel v. PROLOR Biotech, Inc., et al. (Case No. A-13-681020-C), filed May 1, 2013, in the Eighth Judicial District Court in and for Clark County, Nevada; (4) Bradford W. Baer, et al., v. PROLOR Biotech, Inc. et al. (Case No. A-13-681218-B, filed May 3, 2013 in the Eighth Judicial District Court in and for Clark County, Nevada; (5) James Hegarty v. PROLOR Biotech, Inc., et al (Case No. A-13-681250-C), filed May 6, 2013 in the Eighth Judicial District Court in and for Clark County, Nevada; and (6) Jorge L. Salas, et al. v. PROLOR Biotech, Inc., et al. (Case No. A-13-681279-C), filed May 6, 2013 in the Eighth Judicial District Court in and for Clark County, Nevada.

All six suits name PROLOR, the members of PROLOR's Board of Directors and OPKO as defendants and the Fried and Salas suits also name POM as a defendant. All six lawsuits are brought by purported holders of PROLOR's common stock, both individually and on behalf of a putative class of PROLOR's stockholders, alleging that PROLOR's Board of Directors breached its fiduciary duties in connection with the proposed Merger by purportedly failing to maximize stockholder value, and that PROLOR and OPKO aided and abetted the alleged breaches and the Fried and Salas suits also allege that POM aided and abetted the alleged breaches. All six lawsuits seek equitable relief, including, among other things, to enjoin consummation of the Merger, rescission of the Merger Agreement and (in all of the suits other than the Turkell suit) an award of all costs, including reasonable attorneys' fees. Certain of the complaints additionally seek compensatory and/or rescissory damages, and/or imposition of a constructive trust for any benefits improperly received by the defendants.

Each of PROLOR, OPKO and POM believes that the claims made in these lawsuits are without merit and intends to defend such claims vigorously; however, there can be no assurance that any of the companies will prevail in its defense of any of these lawsuits to which it is a party. Due to the preliminary nature of all six suits, none of PROLOR, OPKO or POM is able at this time to estimate their outcome.



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**SELECTED HISTORICAL CONSOLIDATED FINANCIAL DATA OF OPKO**

The following table shows selected historical consolidated financial data for OPKO for the periods indicated. The selected financial data as of December 31, 2012, 2011, 2010, 2009, and 2008 and for each of the five years then ended were derived from the audited historical consolidated financial statements and related footnotes of OPKO. The selected historical financial data for the three month periods ended March 31, 2013 and 2012 were derived from the unaudited condensed consolidated financial statements of OPKO. Detailed historical financial information included in the audited consolidated balance sheets as of December 31, 2012 and 2011, and the consolidated statements of operations, comprehensive loss, shareholders' equity, cash flows and related notes for each of the years in the three-year period ended December 31, 2012, are included in OPKO's Annual Report on Form 10-K for the fiscal year ended December 31, 2012 and incorporated by reference in this joint proxy statement/prospectus.

You should read the following selected historical consolidated financial data together with OPKO's historical consolidated financial statements, including the related notes, and the other information contained or incorporated by reference in this joint proxy statement/prospectus. See [Where You Can Find Additional Information](#). The selected consolidated balance sheet data as of December 31, 2010, 2009 and 2008 and the selected consolidated financial and operating data for the years ended December 31, 2009 and 2008 have been derived from OPKO's audited consolidated financial statements and related notes for such years, which have not been incorporated by reference into this joint proxy statement/prospectus.

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(In thousands, except share and per share data)	For the three months ended March 31,			For the years ended December 31,			
	2013	2012	2012	2011	2010	2009	2008
Statement of operations data:							
Revenues	\$ 31,376	\$ 8,777	\$ 47,044	\$ 27,979	\$ 28,494	\$ 4,418	\$
Costs and expenses:							
Cost of revenues	11,757	4,987	27,878	17,243	13,495	2,876	
Selling, general and administrative	12,424	4,671	27,795	19,169	18,133	10,372	9,644
Research and development	9,910	4,831	19,520	11,352	5,949	10,836	19,960
Other operating expenses	4,058	3,135	9,120	3,404	2,053	2,481	1,398
Total costs and expenses	38,149	17,624	84,313	51,168	39,630	26,565	31,002
Operating loss from continuing operations	(6,773)	(8,847)	(37,269)	(23,189)	(11,136)	(22,147)	(31,002)
Fair value changes of derivative instruments, net	(23,549)	1,117	1,340				
Other income and (expense), net	(507)	(143)	(1,284)	(1,044)	(844)	(1,916)	(1,311)
Loss from continuing operations before income taxes and investment losses	(30,829)	(7,873)	(37,213)	(24,233)	(11,980)	(24,063)	(32,313)
Income tax (provision) benefit	(43)	(215)	9,626	19,358	18	25	
Loss from continuing operations before investment losses and net loss attributable to non-controlling interests	(30,872)	(8,088)	(27,587)	(4,875)	(11,962)	(24,038)	(32,313)
Loss from investments in investees	(3,890)	(523)	(2,062)	(1,589)	(714)	(353)	
Loss from continuing operations and net loss attributable to non-controlling interests	(34,762)	(8,611)	(29,649)	(6,464)	(12,676)	(24,391)	(32,313)
Income (loss) from discontinued operations, net of tax			109	5,181	(6,250)	(5,722)	(7,521)
Net loss and net loss attributable to non-controlling interests	(34,762)	(8,611)	(29,540)	(1,283)	(18,926)	(30,113)	(39,834)
Less: Net loss attributable to non-controlling interests	(547)		(492)				
Net loss attributable to common shareholders	(34,215)	(8,611)	(29,048)	(1,283)	(18,926)	(30,113)	(39,834)
Preferred stock dividend	(420)	(560)	(2,240)	(2,379)	(2,624)	(4,718)	(217)
Net loss attributable to common shareholders after preferred stock dividend	\$ (34,635)	\$ (9,171)	\$ (31,288)	\$ (3,662)	\$ (21,550)	\$ (34,831)	\$ (40,051)
(Loss) income per share, basic and diluted:							
Loss from continuing operations	\$ (0.11)	\$ (0.03)	\$ (0.11)	\$ (0.03)	\$ (0.06)	\$ (0.12)	\$ (0.17)
Income (loss) from discontinued operations	\$	\$	\$ 0.00	\$ 0.02	\$ (0.02)	\$ (0.03)	\$ (0.04)
Net loss per share	\$ (0.11)	\$ (0.03)	\$ (0.11)	\$ (0.01)	\$ (0.08)	\$ (0.15)	\$ (0.21)
Weighted average number of common shares outstanding basic and diluted							
Balance sheet data:	312,932,561	297,543,066	295,750,077	280,673,122	255,095,586	233,191,617	187,713,041

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Total assets	\$ 653,935	\$ 231,570	\$ 289,830	\$ 229,489	\$ 77,846	\$ 87,430	\$ 21,764
Working capital	\$ 179,459	\$ 69,706	\$ 26,275	\$ 80,804	\$ 29,793	\$ 50,795	\$ 5,754
Long-term liabilities	\$ 275,933	\$ 22,499	\$ 34,168	\$ 25,443	\$ 7,908	\$ 11,932	\$ 11,867
Series D Preferred Stock	\$	\$ 24,386	\$ 24,386	\$ 24,386	\$ 26,128	\$ 26,128	\$
Shareholders' equity	\$ 320,817	\$ 154,980	\$ 179,386	\$ 160,882	\$ 23,052	\$ 31,599	\$ 359
Total equity	\$ 319,778	\$ 154,980	\$ 178,894	\$ 160,882	\$ 23,052	\$ 31,599	\$ 359

**Table of Contents****SELECTED HISTORICAL CONSOLIDATED FINANCIAL DATA OF PROLOR**

The following table shows selected historical financial data for PROLOR for the periods indicated. The selected financial data as of December 31, 2012, 2011, 2010, 2009, and 2008 and for each of the five years then ended were derived from the audited historical consolidated financial statements and related footnotes of PROLOR. The selected historical financial data for the three month periods ended March 31, 2013 and 2012 were derived from the unaudited condensed consolidated financial statements of PROLOR. Detailed historical financial information included in the audited consolidated balance sheets as of December 31, 2012 and 2011, and the consolidated statements of operations, comprehensive loss, shareholders' equity, cash flows and related notes for each of the years in the three-year period ended December 31, 2012 are included in PROLOR's Annual Report on Form 10-K for the fiscal year ended December 31, 2012 and incorporated by reference in this joint proxy statement/prospectus.

You should read the following selected financial data together with PROLOR's historical consolidated financial statements, including the related notes, and the other information contained or incorporated by reference in this joint proxy statement/prospectus. See "Where You Can Find Additional Information." The selected consolidated balance sheet data as December 31, 2010, 2009 and 2008 and the selected consolidated financial and operating data for the years ended December 31, 2009 and 2008 have been derived from PROLOR's audited consolidated financial statements and related notes for such years, which have not been incorporated by reference into this joint proxy statement/prospectus.

(In thousands, except share and per share data)	For the three months ended March 31,		For the years ended December 31,				
	2013	2012	2012	2011	2010	2009	2008
Statement of operations data:							
Revenues	\$	\$	\$	\$	\$	\$	\$
Cost and expenses:							
Cost of revenues							
Selling, general and administrative	1,531	790	3,356	3,226	2,362	1,902	2,410
Research and development	3,198	4,304	15,033	11,621	5,315	5,555	4,781
Total costs and expenses	4,729	5,094	18,389	14,847	7,677	7,457	7,191
Operating loss	(4,729)	(5,094)	(18,389)	(14,847)	(7,677)	(7,457)	(7,191)
Other income and (expense), net	(16)	95	118	(216)	118	(28)	157
Loss from operations before income taxes	(4,745)	(4,999)	(18,271)	(15,063)	(7,559)	(7,485)	(7,034)
Income tax (provision) benefit							
Net loss	\$ (4,745)	\$ (4,999)	\$ (18,271)	\$ (15,063)	\$ (7,559)	\$ (7,485)	\$ (7,034)
Loss per share, basic and diluted	\$ (0.07)	\$ (0.09)	\$ (0.30)	\$ (0.29)	\$ (0.19)	\$ (0.21)	\$ (0.20)
Weighted average number of common shares outstanding basic and diluted							
	63,420,545	54,730,050	60,244,754	51,960,929	40,030,008	35,549,083	35,530,378
Balance sheet data:							
Total assets	\$ 31,723	\$ 10,805	\$ 35,917	\$ 15,025	\$ 27,205	\$ 4,109	\$ 8,355
Working capital	\$ 28,471	\$ 7,446	\$ 32,110	\$ 11,610	\$ 24,669	\$ 2,859	\$ 7,573
Long-term liabilities	\$ 459	\$ 334	\$ 381	\$ 285	\$ 221	\$ 140	\$ 91
Shareholders' equity	\$ 29,454	\$ 8,400	\$ 33,200	\$ 12,521	\$ 24,995	\$ 3,129	\$ 7,868

**Table of Contents****SELECTED UNAUDITED PRO FORMA CONDENSED COMBINED FINANCIAL DATA**

The following Selected Unaudited Pro Forma Condensed Combined Financial Data is based on the historical financial data of OPKO and PROLOR, and has been prepared to illustrate the effects of the Merger. In addition, the Selected Unaudited Pro Forma Condensed Combined Statements of Operations from Continuing Operations Data include pro forma adjustments to reflect OPKO's acquisition of certain net assets of Cytochroma Canada Inc., or Cytochroma. The Selected Unaudited Pro Forma Condensed Combined Financial Data does not give effect to any anticipated synergies, operating efficiencies or costs savings that may be associated with the Merger. The Selected Unaudited Pro Forma Condensed Combined Financial Data also does not include any integration costs the companies may incur related to the Merger as part of combining the operations of the companies. The Selected Unaudited Pro Forma Condensed Combined Statements of Income Operations from Continuing Operations Data below is presented as if the Merger were completed on January 1, 2012, and the Selected Unaudited Pro Forma Condensed Combined Balance Sheet Data below is presented as if the Merger were completed on March 31, 2013. The unaudited pro forma financial data included in this joint proxy statement/prospectus is based on the historical financial statements of OPKO and PROLOR, and on publicly available information and certain assumptions that we believe are reasonable, which are described in the notes to the Unaudited Pro Forma Condensed Combined Consolidated Financial Statements included in this joint proxy statement/prospectus. This data should be read in conjunction with OPKO's and PROLOR's historical consolidated financial statements, including the related notes, and the other information contained or incorporated by reference in this joint proxy statement/prospectus. OPKO has not performed a detailed valuation analysis necessary to determine the fair market values of PROLOR's assets to be acquired and liabilities to be assumed. Accordingly, the pro forma financial statements include only a preliminary allocation of the purchase price, which will be finalized after closing. The preliminary purchase price allocation is primarily based on the carrying value of PROLOR's assets and liabilities. See also the Unaudited Pro Forma Condensed Combined Consolidated Financial Statements and notes thereto beginning on page 166.

	<b>For the three months ended March 31, 2013</b>	<b>For the Year Ended December 31, 2012</b>
	<b>(In thousands, except share and per share data)</b>	
<b>RESULTS OF CONTINUING OPERATIONS:</b>		
Total revenue	\$ 31,376	\$ 53,595
Operating loss	(13,352)	(62,479)
Loss from continuing operations before estimated nonrecurring charges related to the transaction attributable to the combined company	(41,252)	(56,521)
Loss from continuing operations before estimated nonrecurring charges related to the transaction per common share attributable to the combined company	\$ (0.11)	\$ (0.15)
Loss per common share, basic and diluted	\$ (0.11)	\$ (0.15)
Weighted average shares outstanding, basic and diluted:	398,888,845	388,089,437

	<b>As of March 31, 2013</b>
	<b>(In thousands)</b>
<b>BALANCE SHEET DATA:</b>	
Current assets	\$ 267,964
Current liabilities	60,035
Total assets	1,163,989
Total long-term liabilities	276,392
Total liabilities	336,427
Total shareholders' equity	\$ 828,601

**Table of Contents****COMPARATIVE HISTORICAL AND UNAUDITED PRO FORMA PER SHARE DATA**

The following table sets forth certain selected per share data for each of OPKO and PROLOR separately on a historical basis as of and for the three months ended March 31, 2013 and as of and for the year ended December 31, 2012. It also includes unaudited pro forma combined per share data for OPKO, which combines the data of OPKO and PROLOR on a pro forma basis giving effect to the Merger. This data does not give effect to any anticipated synergies, operating efficiencies or costs savings that may be associated with the Merger. This data also does not include any integration costs the companies may incur related to the Merger as part of combining the operations of the companies. This data should be read in conjunction with OPKO's and PROLOR's historical consolidated financial statements and accompanying notes in their respective Annual Reports for the year ended December 31, 2012 and Quarterly Reports for the quarter ended March 31, 2013, which are incorporated by reference into this joint proxy statement/prospectus.

	As of and for the three months ended March 31, 2013	As of and for the year ended December 31, 2012
<b>OPKO Historical Per Share Data:</b>		
Loss from continuing operations per share, basic and diluted	\$ (0.11)	\$ (0.11)
Cash dividends per share		
Book value per diluted share	1.02	0.61
<b>OPKO Unaudited Pro Forma Combined Per Share Data:</b>		
Loss from continuing operations per share, basic and diluted	\$ (0.11)	\$ (0.15)
Cash dividends per share		
Book value per diluted share	2.14	1.77
<b>Prolor Historical Per Share Data:</b>		
Loss from continuing operations per share, basic and diluted	\$ (0.07)	\$ (0.30)
Cash dividends per share		
Book value per diluted share	0.46	0.55

**Table of Contents****COMPARATIVE MARKET PRICE DATA AND DIVIDEND INFORMATION****Stock Prices**

The table below sets forth, for the periods indicated, the high and low sales prices per share of OPKO common stock, which trades on the NYSE under the symbol OPK, and PROLOR common stock, which trades on the NYSE MKT under the symbol PBTH.

Fiscal Year Ended	OPKO Price Range of Common Stock		PROLOR Price Range of Common Stock	
	High	Low	High	Low
<b>December 31, 2011:</b>				
First Quarter	\$ 5.03	\$ 3.43	\$ 6.75	\$ 4.55
Second Quarter	4.12	3.15	6.40	4.06
Third Quarter	4.74	3.49	6.50	3.95
Fourth Quarter	5.85	4.00	5.14	3.11
<b>December 31, 2012:</b>				
First Quarter	\$ 5.53	\$ 4.63	\$ 6.69	\$ 4.36
Second Quarter	5.05	4.22	6.07	4.64
Third Quarter	4.80	4.00	5.32	4.66
Fourth Quarter	4.84	4.10	5.36	4.25
<b>December 31, 2013:</b>				
First Quarter	\$ 7.83	\$ 4.83	\$ 5.32	\$ 4.54
Second Quarter (through )				

**Dividends**

OPKO has never paid cash dividends on its common stock and does not anticipate paying cash dividends in fiscal year 2013. OPKO currently intends to retain earnings, if any, for use in its business. Prior to March 8, 2013, OPKO had shares of Series D Preferred Stock outstanding that had preferential dividend rights over any dividend payments to holders of OPKO common stock. On March 1, 2013, OPKO's Board of Directors declared a cash dividend to all holders of its Series D Preferred Stock as of March 8, 2013. The total cash dividend was approximately \$3.0 million. In addition, on March 1, 2013, OPKO's Board of Directors also exercised its option to convert all 1,129,032 shares of OPKO's outstanding Series D Preferred Stock into 11,290,320 shares of OPKO common stock, effective on March 8, 2013. Following the conversion, there are no outstanding shares of OPKO Series D Preferred Stock.

PROLOR has never paid cash dividends on its common stock. PROLOR currently intends to retain earnings, if any, for use in its business and does not anticipate paying any cash dividends in the foreseeable future.

**Table of Contents****Comparative Per Share Market Value Data**

The following table presents the closing per share price of OPKO common stock and PROLOR common stock as reported on the NYSE and the NYSE MKT, respectively, on each of April 23, 2013, the last trading day before OPKO and PROLOR announced that they had entered into the Merger Agreement, and \_\_\_\_\_, 2013, the latest practicable date before the printing of this joint proxy statement/prospectus. The table also includes the equivalent closing per share price of PROLOR common stock on those dates. These equivalent closing per share prices reflect the fluctuating value of the OPKO common stock that PROLOR stockholders would receive in exchange for each share of PROLOR common stock if the Merger had been completed on either of these dates, applying the Exchange Ratio of 0.9951 shares of OPKO common stock for each share of PROLOR common stock.

	<b>OPKO Common Stock</b>	<b>PROLOR Common Stock</b>	<b>Equivalent PROLOR Price Per Share</b>
April 23, 2013	\$ 7.06	\$ 5.83	\$ 7.03
_____, 2013	\$	\$	\$

The above table shows only historical comparisons. These comparisons may not provide meaningful information to PROLOR stockholders in determining whether to approve the PROLOR Merger Proposal. PROLOR stockholders are urged to obtain current market quotations for OPKO common stock and PROLOR common stock and to review carefully the other information contained in this joint proxy statement/prospectus or incorporated by reference into this joint proxy statement/prospectus. Historical stock prices are not indicative of future stock prices.



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**CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS**

This joint proxy statement/prospectus and the other documents incorporated by reference into this proxy statement/prospectus contain or may contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements can be identified by the fact that they do not relate strictly to historical or current facts. Statements that include words such as may, will, project, might, expect, believe, anticipate, intend, could, would, estimate, continue, or pursue or the negative of these words or other words or phrases of similar meaning may identify forward-looking statements. These forward-looking statements are found at various places throughout this joint proxy statement/prospectus and the other documents incorporated by reference and relate to a variety of matters, including: (1) the timing and anticipated completion of the proposed Merger, (2) the benefits and synergies expected to result from the proposed Merger and (3) other statements that are not purely statements of historical fact. These forward-looking statements are made on the basis of the current beliefs, expectations and assumptions of the management of OPKO and PROLOR, are not guarantees of performance and are subject to significant risks and uncertainty. These forward-looking statements should, therefore, be considered in light of various important factors, including those set forth in this joint proxy statement/prospectus and those that are incorporated by reference into this joint proxy statement/prospectus. In addition to the risk factors identified elsewhere, important factors that could cause actual results to differ materially from those described in forward-looking statements contained herein include:

the effect of changes in the price of either OPKO's or PROLOR's common stock prior to the completion of the Merger on the consideration to be received by PROLOR's stockholders;

the effect of changes in the number of shares of outstanding common stock of either OPKO or PROLOR prior to the completion of the Merger;

the potential adverse effects of the announcement and pendency of the Merger on OPKO's or PROLOR's stock price, business, financial condition, results of operations, reputation and business prospects;

restrictions on the business activities of OPKO and PROLOR while the Merger Agreement is in effect;

the potential adverse effects of the failure to complete the Merger on OPKO's and PROLOR's respective businesses, financial condition, results of operations or stock prices;

the effect of provisions in the Merger Agreement that could discourage or make it difficult for a third party to acquire PROLOR prior to the completion of the Merger;

litigation or adverse judgments relating to the proposed Merger;

the ability and timing of the parties to obtain required governmental approvals necessary to satisfy the conditions to the completion of the Merger;

tax matters relating to the proposed treatment of the Merger as a reorganization within the meaning of Section 368(a) of the Code, and the recognition by the Internal Revenue Service, or the IRS, of such treatment;

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the Israeli tax consequences to PROLOR stockholders who are Israeli tax payors if PROLOR is not successful in obtaining the requested tax ruling from the ITA, or if such ruling is issued after the Effective Date of the Merger;

risks relating to the successful integration of OPKO's and PROLOR's respective businesses and to realize the intended benefits of the Merger;

risks relating to the ability of the combined company to effectively manage its expanded operations following the Merger;

the expectation that the combined company will incur losses for the foreseeable future and will not become profitable in the near future;

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the dilutive effect on OPKO's current stockholders of the issuance of shares of OPKO common stock to PROLOR's stockholders in connection with the Merger;

the risks related to loss of personnel in connection with or as a result of the Merger or the announcement of the Merger;

risks relating to the ability of the combined company to maintain OPKO's and PROLOR's preexisting business relationships and to establish new business relationships after the Merger is completed;

expenses relating to the Merger;

risks relating to the ability of the combined company to achieve the results described in the unaudited pro forma financial statements presented in this joint proxy statement/prospectus and the financial forecasts prepared by OPKO and PROLOR in connection with discussions concerning the Merger;

the effect of the completion of the Merger on the combined company's stock price;

the risk of a decline in the market price of OPKO common stock if PROLOR stockholders sell the shares of OPKO common stock received in the Merger;

risks relating to the ability of the combined company to utilize OPKO's and PROLOR's net operating loss carryforwards after the Merger is completed;

differences in the rights associated with the OPKO common stock to be received by PROLOR stockholders in exchange for their shares of PROLOR common stock and the rights associated with the PROLOR common stock;

the effects of charges to earnings that may result from the accounting treatment of the Merger; and

risks relating to the substantial indebtedness of the combined company following the completion of the Merger.

Additional factors that could cause actual results to differ materially from those described in the forward-looking statements are set forth in Part I Item 1A Risk Factors of OPKO's Annual Report on Form 10-K for the year ended December 31, 2012, as filed with the SEC on March 18, 2013, Part I Item 1A Risk Factors of PROLOR's Annual Report on Form 10-K for the year ended December 31, 2012, as filed with the SEC on March 15, 2013, and in subsequent reports on Forms 10-Q and 8-K and other filings made with the SEC by each of OPKO and PROLOR.

You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this joint proxy statement/prospectus or, in the case of documents incorporated by reference, as of the date of those documents. Neither OPKO nor PROLOR undertakes any obligation to publicly update or release any revisions to these forward-looking statements, whether as a result of new information, future events or otherwise, after the date of this joint proxy statement/prospectus or to reflect the occurrence of unanticipated events, except as required by law.

**Table of Contents****RISK FACTORS**

*In addition to the other information included and incorporated by reference into this joint proxy statement/prospectus, including the matters addressed in the section titled "Cautionary Statement Regarding Forward-Looking Statements" beginning on page 34, you should carefully consider the following risk factors before deciding how to vote your shares of OPKO common stock at the OPKO annual meeting and/or your shares of PROLOR common stock at the PROLOR special meeting. These factors should be considered in conjunction with the other information included by OPKO and PROLOR in this joint proxy statement/prospectus. If any of the risks described below or in the documents incorporated by reference into this joint proxy statement/prospectus actually materializes, the businesses, financial condition, results of operations, prospects or stock prices of OPKO, PROLOR and/or the combined company could be materially and adversely affected. See the section titled "Where You Can Find Additional Information" beginning on page 176.*

**Risks Related to the Merger**

***Because the Exchange Ratio is fixed and will not be adjusted in the event of changes in the price of either OPKO's or PROLOR's common stock, the market value of the shares of OPKO common stock to be received by the PROLOR stockholders in connection with the Merger is subject to change prior to the completion of the Merger.***

The Exchange Ratio is fixed such that each share of PROLOR common stock will be converted into the right to receive 0.9951 of a share of OPKO common stock in connection with the Merger. No adjustments to this Exchange Ratio will be made pursuant to the Merger Agreement based on changes in the price of either the OPKO common stock or the PROLOR common stock prior to the completion of the Merger. Changes in stock prices may result from a variety of factors, including, among others, general market and economic conditions, changes in OPKO's or PROLOR's respective businesses, operations and prospects, market assessment of the likelihood that the Merger will be completed as anticipated or at all and regulatory considerations. Many of these factors are beyond OPKO's or PROLOR's control.

As a result of any such changes in stock prices, the market value of the shares of OPKO common stock that a PROLOR stockholder will receive at the time that the Merger is completed could vary significantly from the value of such shares on the date of this joint proxy statement/prospectus, the date of the OPKO annual meeting, the date of the PROLOR special meeting or the date on which such PROLOR stockholder actually receives its shares of OPKO common stock. For example, based on the range of closing prices of OPKO common stock during the period from April 23, 2013, the last trading day before OPKO and PROLOR announced that they had entered into the Merger Agreement, through \_\_\_\_\_, 2013, the latest practicable date before the printing of this joint proxy statement/prospectus, the Exchange Ratio represented a market value ranging from a low of \$ \_\_\_\_\_ to a high of \$ \_\_\_\_\_ for each share of PROLOR common stock. Accordingly, at the time of the OPKO annual meeting or the PROLOR special meeting, as the case may be, neither the OPKO stockholders nor the PROLOR stockholders, as the case may be, will know or be able to calculate the exact market value of the consideration the PROLOR stockholders will receive upon completion of the Merger.

***Changes in the number of shares of outstanding common stock of either OPKO or PROLOR prior to the completion of the Merger would result in a corresponding change to the relative ownership percentages of the current OPKO stockholders and the current PROLOR stockholders in the combined company.***

Based on the number of shares of OPKO common stock and PROLOR common stock outstanding as of \_\_\_\_\_, 2013, the latest practicable date before the printing of this joint proxy statement/prospectus, if the Merger had been completed on such date, the holders of PROLOR common stock would have been entitled to receive shares of OPKO common stock representing approximately \_\_\_\_\_% of all shares of OPKO common stock outstanding immediately following the completion of the Merger. OPKO stockholders would have continued to own their existing shares, which would not have been affected by the Merger, and such shares would have represented approximately \_\_\_\_\_% of all shares of OPKO common stock outstanding immediately following the completion of the Merger. However, because the Exchange Ratio is fixed, to the extent that the number of shares of outstanding

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OPKO common stock or PROLOR common stock changes prior to the completion of the Merger, whether due to any new issuance of shares of OPKO common stock or PROLOR common stock, any exercise of any outstanding options or warrants to purchase shares of OPKO common stock or PROLOR common stock, or otherwise, there will automatically occur a corresponding change in the relative ownership percentages of the combined company by the current OPKO stockholders and the current PROLOR stockholders.

***The announcement and pendency of the Merger could have an adverse effect on OPKO's and/or PROLOR's stock price, business, financial condition, results of operations, reputation and business prospects.***

The parties' efforts to complete the Merger could cause substantial disruptions in OPKO's and/or PROLOR's respective businesses, which could have an adverse effect on their respective financial results. Among other things, uncertainty as to whether the Merger will be completed may affect the ability of OPKO and/or PROLOR to recruit prospective employees or to retain and motivate existing employees. Employee retention may be particularly challenging while the Merger is pending because employees may experience uncertainty about their future roles with the combined company.

Uncertainty as to the future could adversely affect OPKO's or PROLOR's respective businesses, reputation and relationships with potential customers. For example, vendors and others that deal with OPKO or PROLOR could defer decisions concerning working with such company, or seek to change existing business relationships with such company. Further, a substantial amount of the attention of management and employees of OPKO and PROLOR is being directed toward the completion of the Merger and thus is being diverted from such company's day-to-day operations because matters related to the Merger (including integration planning) require substantial commitments of time and resources.

***While the Merger Agreement is in effect, OPKO and PROLOR are subject to restrictions on their business activities.***

While the Merger Agreement is in effect, each of OPKO and PROLOR is subject to restrictions on its business activities and must generally operate its business in the ordinary course consistent with past practice (subject to certain exceptions). These restrictions could prevent each of OPKO and PROLOR from pursuing attractive business opportunities (if any) that arise prior to the completion of the Merger and are generally outside the ordinary course of its business, and otherwise have a material adverse effect on its future results of operations or financial condition.

***Failure to complete the Merger could negatively impact OPKO's and PROLOR's respective businesses, financial condition, results of operations or stock prices.***

Completion of the Merger is conditioned upon PROLOR and OPKO satisfying certain closing conditions as set forth in the Merger Agreement, including: (i) the approval of the OPKO Share Issuance Proposal by the OPKO stockholders; (ii) the approval of the PROLOR Merger Proposal by the PROLOR stockholders; (iii) the termination or expiration of the waiting period and any extension applicable to the Merger under the HSR Act; (iv) receipt of the required approvals/clearances from the Israeli Securities Authority and the Israeli Income Tax Commission; (v) the absence of any temporary restraining order, preliminary or permanent injunction or other order by a court or other governmental entity having the effect of making illegal or otherwise prohibiting the consummation of the Merger; and (vi) the approval for listing on the NYSE of the shares of OPKO common stock issuable in connection with the Merger. The required conditions to closing may not be satisfied in a timely manner, if at all, or, if permissible, waived. If the Merger is not consummated for these or any other reasons, the ongoing business of PROLOR and OPKO may be adversely affected and will be subject to a number of risks including:

The risk that the pursuit of the Merger could lead to PROLOR's and OPKO's failure to pursue other beneficial opportunities as a result of the focus of PROLOR's and OPKO's management on the Merger;

Under the Merger Agreement, each of OPKO and PROLOR is subject to certain restrictions on the conduct of its business prior to completing the Merger, which restrictions could adversely affect its ability to realize certain of its respective business strategies;

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The market price of PROLOR's and OPKO's common stock may decline to the extent that the current market price reflects a market assumption that the Merger will be completed;

PROLOR and OPKO may experience negative reactions to the termination of the Merger from suppliers, strategic partners, vendors, investors or analysts;

Neither OPKO nor PROLOR would realize any of the anticipated benefits of having completed the Merger;

PROLOR may be required to pay a termination fee of \$14,400,000 or \$9,600,000 to OPKO if the Merger Agreement is terminated under certain circumstances;

OPKO may be required to pay a termination fee of \$9,600,000 to PROLOR if the Merger Agreement is terminated under certain circumstances; and

The expenses of each of PROLOR and OPKO incurred related to the Merger, such as legal and accounting fees, must be paid even if the Merger is not completed and may not, except in certain circumstances, be recovered from the other party.

In addition, any delay in the consummation of the Merger, or any uncertainty about the consummation of the Merger, may adversely affect either or both companies' respective future businesses, growth, revenue and results of operations.

***The Merger Agreement contains provisions that could discourage or make it difficult for a third party to acquire PROLOR prior to the completion of the Merger.***

The Merger Agreement contains provisions that make it difficult for PROLOR to entertain a third-party proposal for an acquisition of PROLOR. These provisions include the general prohibition on PROLOR's soliciting or engaging in discussions or negotiations regarding any alternative acquisition proposal after the completion of the go-shop period, and the requirement that PROLOR pay a termination fee of \$14,400,000 or \$9,600,000 (as applicable) to OPKO if the Merger Agreement is terminated in specified circumstances. See the sections titled "The Merger Agreement - Restrictions on Solicitation," "The Merger Agreement - Recommendation of PROLOR's Board of Directors; Change of Recommendation" and "The Merger Agreement - Termination Fees and Expenses" beginning on pages 92, 93 and 99, respectively. These provisions might discourage an otherwise-interested third party from considering or proposing an acquisition of PROLOR, even one that may be deemed of greater value to PROLOR's stockholders than the Merger. Furthermore, even if a third party elects to propose an acquisition, the termination fee may result in that third party's offering of a lower value to PROLOR's stockholders than such third party might otherwise have offered.

***Several lawsuits have been filed against PROLOR, the members of PROLOR's Board of Directors, OPKO and POM challenging the Merger, and an adverse judgment in any such lawsuit may prevent the Merger from becoming effective or from becoming effective within the expected timeframe.***

Six putative class action lawsuits have been filed in connection with the Merger: (1) Peter Turkell v. PROLOR Biotech, Inc., et al. (Case No. A-13-680860-B), filed April 29, 2013 in the Eighth Judicial District Court in and for Clark County, Nevada; (2) Floyd A. Fried v. PROLOR Biotech, Inc., et al., (Case No. A-13-681060), filed May 1, 2013 in the Eighth Judicial District Court in and for Clark County, Nevada; (3) Marc Henzel v. PROLOR Biotech, Inc., et al. (Case No. A-13-681020-C), filed May 1, 2013, in the Eighth Judicial District Court in and for Clark County, Nevada; (4) Bradford W. Baer, et al., v. PROLOR Biotech, Inc. et al. (Case No. A-13-681218-B, filed May 3, 2013 in the Eighth Judicial District Court in and for Clark County, Nevada; (5) James Hegarty v. PROLOR Biotech, Inc., et al (Case No. A-13-681250-C), filed May 6, 2013 in the Eighth Judicial District Court in and for Clark County, Nevada; and (6) Jorge L. Salas, et al. v. PROLOR Biotech, Inc., et al. (Case No. A-13-681279-C), fil