## UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

## FORM 8-K

CURRENT REPORT Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 10, 2013

# **OPKO** Health, Inc.

(Exact Name of Registrant as Specified in Charter)

Delaware (State or Other Jurisdiction of Incorporation) 001-33528 (Commission File Number) 75-2402409 (IRS Employer Identification No.)

4400 Biscayne Blvd Miami, Florida 33137 (Address of Principal Executive Offices) (Zip Code)

Registrant's telephone number, including area code: (305) 575-4100

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

□ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

□ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

#### ITEM 7.01. Regulation FD Disclosure.

On September 10, 2013, the Company made a presentation to a group of investors. A copy of the Company's presentation slides is furnished as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference.

The information contained in Item 7.01 to this Current Report on Form 8-K and Exhibit 99.1 attached hereto shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing by the Company under the Act, unless expressly stated otherwise.

#### ITEM 8.01. Other Events.

On September 10, 2013, the Company filed a report with the Israeli Securities Authority ("ISA") and with the Tel-Aviv Stock Exchange ("TASE"). A copy of the English translation of the report is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

#### ITEM 9.01. Financial Statements and Exhibits

(d) Exhibits

Exhibit Number	Description
99.1	Investor Presentation.
99.2	Report filed on September 10, 2013 with the ISA and TASE.

#### SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

OPKO Health, Inc.

By /s/ Juan F. Rodriguez

Name: Juan F. Rodriguez Title: Senior Vice President, Chief Financial Officer

Date September 11, 2013



Corporate Presentation September 2013

# **Safe Harbor Statement**

This presentation contains forward-looking statements, including statements regarding the results of current clinical studies and pre-clinical experiments and the effectiveness of OPKO's and PROLOR's programs are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Investors are cautioned that forward-looking statements involve risks and uncertainties that may affect OPKO's and PROLOR's business and prospects, that OPKO and PROLOR may not succeed in developing any commercial products, and that ongoing studies may not show substantial activity; and other risks and uncertainties that may cause results to differ materially from those set forth in the forward-looking statements. A number of the matters discussed in this presentation that are not historical or current facts deal with potential future circumstances and developments. The discussion of such matters is qualified by the inherent risks and uncertainties surrounding future expectations generally and other factors that could cause actual results to differ materially from future results expressed or implied by such forward-looking statements. In addition to the risks described above, investors should consider the economic, competitive, governmental, technological and other factors discussed in OPKO's filings with the Securities and Exchange Commission.

# **OPKO – A High Growth Multi-National Biopharmaceutical and Diagnostics Company with a Diversified Pipeline**

Pharmaceuticals	<ul> <li>Late-stage pipeline of multi-billion dollar drugs in specialty indications</li> </ul>
Diagnostics	<ul> <li>Revolutionary diagnostic technology for physicians (primary care and specialists) that enhances their economics</li> </ul>
International Markets	<ul> <li>Emerging markets infrastructure to propel the sales of marketed and pipeline products</li> </ul>
Opportunistic Investments	<ul> <li>Clinically and commercially validated platform to create improved versions of top-selling biologics</li> </ul>
(1) Secondary Hyperparathyroidism	ОРКО 3

## **Highly Experienced Management Team**

Demonstrated Ability to Successfully Build and Manage Pharmaceutical Businesses

## Phillip Frost, M.D.

Chairman and CEO

- TEVA (Chairman), IVAX (Chairman and CEO)
- Key Pharmaceuticals (Chairman)

## Jane H. Hsiao, Ph.D.

Vice Chairman and Chief Technical Officer

• IVAX (Vice Chairman of Technical Affairs)

## Steven D. Rubin

Executive Vice President – Administration

IVAX (General Counsel)

## Juan F. Rodriguez

Senior Vice President and CFO

Kos Pharmaceuticals (Senior Vice President, Controller)

## Charles Bishop, Ph.D.

CEO – OPKO Renal Division

- Cytochroma Inc. (President and CEO)
- Bone Care International (President and CEO)

Avri Havron, Ph.D. CEO – PROLOR Biotech • Serono (VP R&D, Israel)

Shai Novik President – PROLOR Biotech • THCG (COO)



# Financial Highlights (June 2013, Pro-Forma)

Cash & Marketable Securities	\$193 mm
Total Assets	\$1.25 bn
Current Liabilities	62mm
3% Convertible Notes, Due 2023	\$188 mm
Other Long-Term Liabilities	\$81 mm
Total Shareholders Equity	\$924 mm
Shares Outstanding	400 mm
Warrants, Options, Convertible Debt	79 mm
Market Cap ~	\$3.3 bn
Total OPKO Share Purchases by Dr. Frost	\$240 mm
Average Daily Trading NYSE	2.4 mm shares
Employees	600



# **Pharmaceuticals**



# Pharmaceuticals – Clinical Pipeline

	Products	Indication	Preclinical	Phase I	Phase II	Phase III	Milestone	Market Size
	Rayaldy™	SHPT (CKD Stage 3-4 Patients)				$\Rightarrow$	Phase III results expected H1 2014	\$12.0 BN
OPKO	Alpharen™	Hyperphosphatemia (CKD Stage 5 Patients)				$\rightarrow$	Phase III results expected H1 2017	\$1.2 BN
ö	Rolapitant	CINV (vomiting)	Outlicense	d to TESARO		$\rightarrow$	Phase III results expected H2 2013	\$1.5 BN
	CTA018	Moderate to severe SHPT (CKD Stage 5 Patients)			$\Rightarrow$			\$1.5 BN
	CTA018 (Topical)	Mild to moderate psoriasis			$\rightarrow$			\$0.5 BN

	Products	Indication	Preclinical	Phase I	Phase II	Phase III	Milestone	Market Size
ĸ	hGH-CTP	Growth Hormone Deficiency				$ \rightarrow $	Adult PIII – H2 2015 Ped PIII – H1 2018	\$3.5 BN
PROLOR	Factor VIIa - CTP	Hemophilia		$\Rightarrow$			Phase II – 2014	\$1.3 BN
R	Factor IX – CTP	Hemophilia						\$0.7 BN
	GLP1/Glucagon dual receptor agonist	Diabetes Type II and Obesity		⇒			Phase I – 2014	\$10.0 BN



# Pharmaceuticals – Pre-Clinical Pipeline

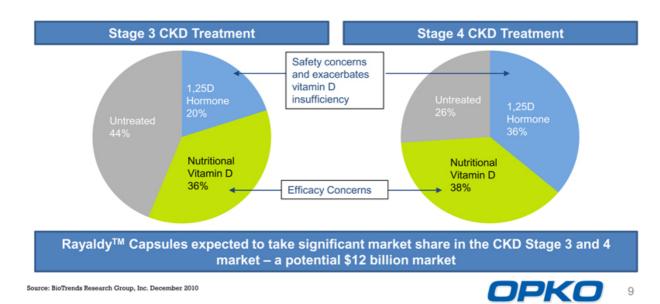
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Products	Indication	Preclinical	Phase I	Phase II	Phase III	Milestone	Market Size
SR-3306	Neurodegenerative diseases	$\implies$					NM
CTA091	Mild to moderate SHPT (CKD Stage 5 Patients) Psoriasis (oral or topical)	$\Rightarrow$					>\$2.0 BN
OPK-0018	Asthma and COPD	$\Rightarrow$					NM
AntagoNAT Platform	Cancer, CV, metabolic and genetic disorders	$\Rightarrow$					NM

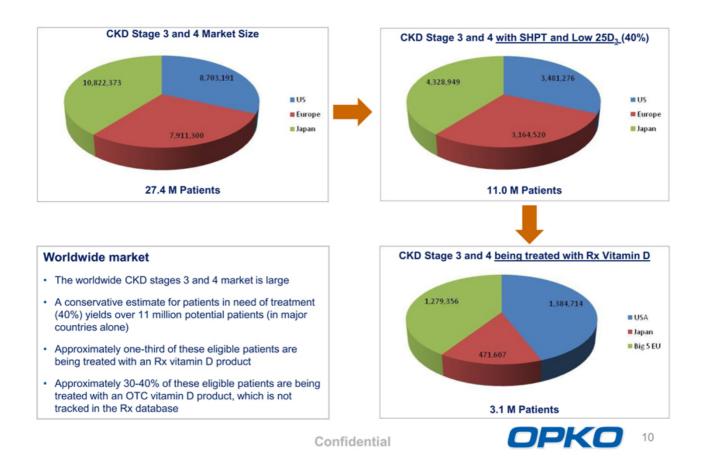


# Rayaldy<sup>™</sup> – Significant Commercial Opportunity

- · Low serum 25D and high plasma PTH are prevalent in CKD Stage 3-4 patients
  - 8.0 million CKD Stage 3-4 patients in the U.S.
- U.S. has 4.0 million patients with low serum 25D and high plasma PTH
- Existing treatments are not effective or have significant safety issues (increased serum or urine calcium, leading to accumulation in kidney and additional damage)
  - Rayaldy<sup>™</sup>'s efficacy and safety compare favorably to both nutritional vitamin D and hormones in patients with Stage 3 or 4 CKD and will drive untreated patients to initiate treatment



## **Worldwide Prevalence and Treatment of SHPT**



# Rayaldy<sup>™</sup> – Phase III and NDA Timelines

2012	2012				2013					2014						2016	6		
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
		Dose	ranging		SPA	TG N	louse Car	cinogenici	ity Study										
	SP	AC	L-3001 tr	ial				CL-30 Data	01										
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			CL-3	3002 trial					Data	•									
					↓ ▼														
				>	Open L	_abel Ext	tension					NDA	NDA Safety						
												Filing	Update			NDA Approval			
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#### **Product Indication:**

Management of SHPT in Patients with Stages 3 and 4 CKD and Vitamin D Insufficiency

### Primary Endpoint:

Maintenance of 30% reduction in iPTH levels

Secondary Endpoint: Maintenance of serum  $25D_3 \ge 30$  ng/mL

## Safety Endpoint:

Serum Ca and P, and urinary Ca



# Pharmaceuticals: PROLOR



# Lead Product – hGH-CTP BioBetter to Reduce Injection Frequency

- \$3.5 billion market
- Growing 5% annually
- Requires daily injections
- Growth hormone deficient children
- · Growth hormone deficient adults



# hGH Effect in GH Deficient Adults

## Proper hGH treatment results in:



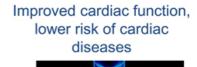
Increase in bone density



Decrease in fat mass



Increase in lean body mass



Improved overall physical performance





## hGH-CTP Phase II Positive Data

Analysis and Conclusions

- A single weekly injection of hGH-CTP can replace 7 daily injections of commercially available GH
  - Identified kick-start dosing for Phase III trial
  - Post-Phase II hGH-CTP Pilot Study Supports two hGH-CTP Injections Per Month
- · Very Good safety and tolerability profile
- Only 50-65% of the cumulative daily GH dosing was required to maintain the majority of the patients within the normal range of IGF-1
- · Estimated COG 50-75% of commercially available GH



## hGH-CTP Phase II and III

- · Pediatric GHD Phase II trial (ongoing)
  - 40-50 patients
  - 4 cohorts; 3 receiving once weekly hGH-CTP at different doses, one control daily commercial
  - 12 months efficacy and safety
  - Key outcome: Height velocity
- Adult Pivotal Phase III trial (initiated June 2013)
  - 189 patients, estimated \$20 million study
  - 6 months efficacy and 6 months safety
  - Key outcome: Improvement in truncal fat
  - Confirmed by FDA as pivotal, planned for BLA submission in 2015
- · Received U.S. orphan drug status for children and adults
- · First ever to receive E.U. orphan drug status for children and adults



## hGH-CTP Competitive Advantages

- Needle size 31G
  - No additional drug product viscosity that is typically associated with long-acting formulations
- Highly concentrated formulation
  - No need for 2 injections sites, once per week
- · Superb clinical, safety and immunogenicity profile
- Low COGS
  - 50-75% of commercial products
- · Robust manufacturing process
- · Orphan drug designation in the U.S., Europe



# **Anticipated Milestones**

## **Clinical Priorities**

Event	Timing
hGH-CTP: Phase II pediatric study	Ongoing
hGH-CTP: Phase III adult pivotal study	Ongoing
Planned marketing approval 2016	

## **Preclinical Priorities**

Event	Timing
MOD-6030: Further diabetes studies and process, analytical and pharmaceutical development to IND submission level	H1 2014
Factor-VIIa-CTP: process, analytical, and pharmaceutical development to IND submission level	H2 2013



# **Diagnostics**



## **Diagnostics – Our Vision**

Low Cost / Highly Quantitative Point-of-Care System

- Easy-to-use
- Inexpensive
- Significant economic benefit to physicians through in-sourcing of basic panels
- Urology, Ob/Gyn, HIV, Hepatitis B, Vitamin D

Innovative Technology to Discover New Diagnostics

- Alzheimer's Disease
- Pancreatic Cancer
- Lung Cancer
- Multiple Sclerosis
- Type-I Diabetes

## CLIA Lab

- Commercial platform for U.S. launch of novel OPKO tests including novel 4KScore<sup>™</sup> diagnostic
- Established CLIA lab with urologic pathology focus, based in Nashville
- About 15+ person national sales force focused on urology



# **Point-of-Care Diagnostics – Claros-1 System**

#### · Lab test results in minutes

- Accurate Quantitative, laboratory quality immunoassays
- o Multiplex Up to 10 separate tests simultaneously on a single finger stick
- Inexpensive Inexpensive analyzer appropriate for physician budget, tests profitable for any user
- o Convenient Only a finger-stick is required from the patient, and no training for the user

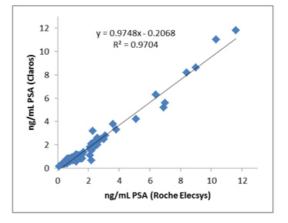




## Claros-1 – Laboratory Quality Assay Performance (Total PSA)

Total PSA will be the first Point-of-Care Assay run on the Claros-1 System

- Dynamic Range of Assay
  - Demonstrated 15pg/mL to 100ng/mL
- Clinical Results
  - o Finger-stick samples acquired in clinical setting by untrained users
  - o Compared to serum samples run in laboratory (Roche Elecsys)
  - N = 100 kits, multiple batches
  - R<sup>2</sup> = 0.97, slope 0.97





# Initial Point-of-Care Claros-1 Product Offerings

Men's Health

- Total-PSA, free-PSA
- Testosterone

### **Market Opportunity**

- WW market: 70 million PSA tests annually
- US Market sizes
  - PSA: \$1 billion (35M tests/year)
  - Testosterone: \$160 million (4M tests/year)

## General and Specialty Practice

Vitamin D Point-of-Care Tests

### Market Opportunity

- WW market: 100 million tests annually (70 million U.S.)
- WW market size: about \$5 billion

#### Projected Launch

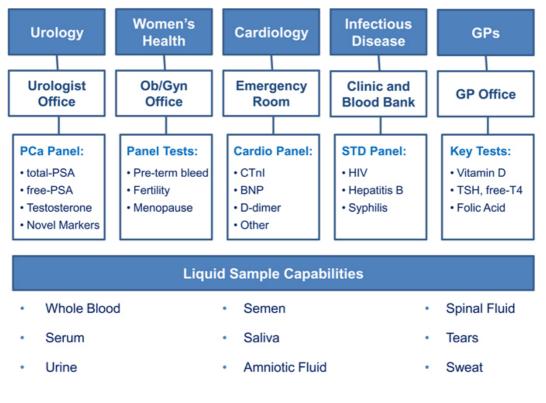
- POC platform
  - EU CE Mark cleared
  - EU Launch Q4 2013
  - US FDA expected 2014

### **Projected Launch**

- POC platform
  - EU by Q1 2014
  - o U.S. by Q4 2014



## **Claros-1 Product Roadmap**





## Next Generation Prostate Cancer Testing – 4KScore™

The 4KScore<sup>™</sup> address a <u>critical unmet need</u> in Prostate Cancer care:

- · Current screening (based on PSA) leads to over-biopsy and over-treatment
  - PSA lacks predictive accuracy in the "grey zone" (3-10ng/mL) due to false positives (up to 75%)<sup>(1)</sup>
  - >1 million annual biopsies in the US, 750,000 are negative<sup>(2)</sup>
  - 4.2% of biopsies result in a complication that require an inpatient admission<sup>(3)</sup>
- 4Kscore<sup>™</sup> provides prostate cancer risk assessment based four blood based biomarkers:
  - Total PSA (tPSA)
  - Free PSA (fPSA)
  - Intact PSA (iPSA) the subset of free PSA with a preserved bond at Lys145-Lys146
  - Human kallikrein 2 (hK-2) also known as kallikrein-related peptidase 2
- · Validated across multiple patient cohorts predict cancer before biopsy
  - Retrospective tests in over 10,000 patients
  - Shows >80% accuracy in predicting prostate cancer
  - Can eliminate 50% of prostate biopsies

### OPKO 4KScore<sup>™</sup> strategy

- Laboratory Developed Test in the US with a planned Q4 2013 introduction
  - \$300 million market size as a new lab test before the first biopsy
- FDA-cleared point-of-care test on the Claros-1 System in 4-5 years
   Will compete as an alternative to total PSA alone in the US \$1B PSA market

Gilligan 2009
 Loeb et al. 2001
 Chou et al. 2011



## **Near-term Milestones** 2013 2014 2017 2015 2016 Q1 Q2 Q3 Q4 4KScore™ – US LDT Vitamin D Point-of-Care Expected Launch Total PSA Test – Launch in US Rayaldy™ – Phase III Results Rayaldy™ – 505(b)(2) NDA Filing Rayaldy<sup>™</sup> – NDA Approval Rayaldy<sup>™</sup> – Phase III Trials Alpharen<sup>™</sup> – FDA and EU Meetings Alpharen™ – Safety Trial Initiation Alpharen™ – Phase III Results Alpharen<sup>™</sup> – DDI Studies Citicoline – Launch in Spain Rolapitant – Phase III Results Factor VIIa – Begin Phase II Trials hGH-CTP – Adult Phase III (1)

- Diagnostics - Pharmaceuticals

(1) Pediatric Phase III expected H1 2018



# International Markets



# **OPKO Latin America**

- OPKO Mexico Pharmacos Exakta S.A. de C.V.
  - 25 products across a range of therapeutic indications
  - Primarily branded ophthalmics, with expanding proprietary focus
  - 12 sales and marketing personnel
  - 2 commercial operations
- OPKO do Brazil Comercio de Produtos Farmaceuticos Ltda.
  - Acquired February 2013
  - ANVISA licensed pharmaceutical company in most important growth market in South America
- · OPKO Chile S.A.
  - Rapidly growing sales from >100 products
  - Acquired ALS Distribution Limited, the exclusive product distributor of Arama Laboratories, in April 2012
  - 20 sales and marketing personnel
  - 7 commercial operations

Source: Business Monitor International Note: CAGRs calculated in USD





# **OPKO European Union**

## Farmadiet Group

- · Established 20-year presence within EU
  - Based in Barcelona, Spain
- · Fully integrated specialty pharmaceutical entity
  - 42-person sales force
  - Production/research facility in Banyoles, Spain
- · Broad pharmaceutical, nutritional and veterinary products lineup
  - Medical prescription: 25 Products
  - OTC nutritional: 90 Products
  - Veterinary: 50 Products
- · Access to promising products in development:
  - Citicoline (supports memory function) is a ~\$100 million product market in Spain
  - Projected launch in Spanish market Q4 2013
  - o 25-Hydroxyvitamin D for animal use
  - o Novel raw material for intra-articular injection (patent pending)
  - Novel raw material based on plasma protein concentrate (patent pending)

Source: Business Monitor International Note: CAGRs calculated in USD

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Pharma Market: **\$23.3 billion** 2012 – 2017 CAGR: **(6.9%)** 

# Strategic Investments



# **Strategic Investments**

## Proprietary Technologies with Significant Upside Potential

- CoCrystal Discovery, Inc. (~16% equity interest<sup>(1)</sup>)
  - Founded by Nobel Laureate, Roger Kornberg, Ph.D.
  - New approach to develop broad spectrum anti-viral drugs
  - Development program with Teva for Hepatitis C drug
- RXi, Inc. (~21% equity interest<sup>(1)</sup>)
  - o RNA interference platform that down-regulates abnormal gene expression
  - o RXI-109 in development to reduce or inhibit scar formation in the skin following surgery
- Sorrento Therapeutics (~20% equity interest<sup>(1)</sup>)
  - o New technology to produce human monoclonal antibodies libraries that are more complete
- Fabrus, LLC (~13% equity interest<sup>(1)</sup>)
  - o Next gen technology to identify therapeutic antibody targets
- · Pharmsynthez, Inc. (~10% equity interest)
  - o Manufactures and sells branded pharmaceutical products, primarily in Russia and Baltic countries
  - o Develop and commercialize OPKO products in Eastern Europe
- Tesaro, Inc. (~1% equity interest<sup>(1)</sup>)
  - o Oncology-focused biopharmaceutical company founded by former executives of MGI Pharma
- Neovasc, Inc. (~ 4% equity interest<sup>(1)</sup>)
  - Developing innovative vascular devices
  - ChromaDex, Inc. (~1% equity interest<sup>(1)</sup>)
    - o Dietary supplement BlueScience and antioxidant pterostilbene pTeroPure
    - OPKO distribution rights in Latin America
    - (1) As of March 31, 2013



September 10, 2013

Israel Securities Authority 22 Kanfei Nesharim st. Jerusalem 95464 Tel Aviv Stock Exchange Ltd. 54 Ahad Ha'Am st. <u>Tel Aviv 65202</u>

#### **<u>RE: ISSUANCE OF SECURITIES IN THE COMPANY TO HOLDERS OF</u>** <u>SECURITIES IN PROLOR BIOTECH, INC. (hereinafter: "PROLOR")</u>

Further to OPKO Health, Inc.'s (the "Company") immediate reports dated August 29 and September 1, 2013 (Ref: 2013-02-132720 and 2013-02-133389 respectively), the actual allocation of OPKO common stock to PROLOR shareholders in exchange for their PROLOR common stock shall be carried out after the completion of the process which is in progress, inter alia, *vis-a-vis* the U.S. clearing system (DTC) and the Company's U.S. Transfer Agent.

Attached hereto to this immediate report and marked as <u>Appendix A</u>, are the relevant portions of the tax pre-ruling, received from the Israeli tax authority in connection with the merger of PROLOR with the Company, in relation to the public shareholders who held PROLOR common stock prior to the merger, and are not controlling shareholders of PROLOR (hereinafter the "Approval" and "PROLOR Public Shareholders", respectively).

It should be noted that the actions required by PROLOR Public Shareholders to be carried out in order to enable the allocation to them of the Company's common stock in exchange for PROLOR common stock, are specified in the Approval. Within the next few days, documentation in accordance with the Approval, which contains precise instructions regarding the procedures for the share exchange, are expected to be dispatched to the Company's shareholders.

OPKO Health Inc.

## TRANSLATION FROM HEBREW

## Israel Tax Authority Senior Director For Professional Affairs

Mergers and Divisions Department August 29, 2013

Gornitzky & Co. - Attorneys 45 Rothschild St. <u>Tel Aviv</u>

Dear Sirs,

#### Re: <u>Swapping Prolor Shares and Rights with Opko Shares and Rights</u> (Reference: your letter dated July 9, 2013)

#### 1. The facts, as provided to us by you:

- 1.1. Prolor Biotech Inc. (the "Company" or "Prolor") is a public company incorporated under the laws of the State of Nevada, USA. Prolor was incorporated on August 21, 2003 and as from before the end of the first quarter of 2007 its shares are traded in USA "over the counter". On March 29, 2010 its shares were registered for trading on the New York Stock Exchange (NYSE Amex) under the symbol "PBTH" (the "USA Stock Exchange"), and commencing from May 2010 Prolor's shares were also listed for trading on the Tel Aviv Stock Exchange Ltd. (the "Tel Aviv Stock Exchange"). Prolor owns all rights (indirectly) in Prolor Biotech Ltd., P.C. 513105205, a private Israeli company engaged in research and development in the field of proteins ("Prolor Israel").
- 1.2. As of April 25, 2013, Prolor's issued and outstanding share capital, consists of 63,680,118 shares par value of \$0.00001, while the major shareholder of Prolor (and the only one who has control as defined in Section 3(i) of the Income Tax Ordinance (New Version), 5721-1961 (the **"Ordinance"**)) is Dr. Phillip Frost, a U.S. resident who holds through Frost Gamma Investment Trust, in which Dr. Phillip Frost is the sole beneficiary (hereinafter: **"Frost"** and **"Frost Trust"** respectively), and through a nonprofit company which he fully controls (100%) (the "Frost Company"), 12,669,121 shares of Prolor constituting approximately 20% of the issued capital of Prolor and 622,000 options.

The remaining rights in Prolor are held as follows:

1.2.4 The remaining 49,107,169 shares are held by shareholders from the public all of whom are not controlling shareholders as defined in Section 3(i) of the Ordinance and purchased their shares after the Company registered its shares for trading on the Tel Aviv Stock Exchange "over the counter", before the end of the first quarter of 2007. These shareholders are Israeli residents and/or foreign residents who hold their shares directly through the Paying Trustee as defined below or through Israeli or foreign members of the Tel Aviv Stock Exchange. Such shareholders shall be referred herein as the "**Public Shareholders**".

- 1.3. All the rights holders specified in Section 1.2 above shall be hereinafter referred to collectively as the "Prolor Rights Holders".
- 1.5. Scrutiny of the share trading data of Prolor's share (as published on the Tel Aviv Stock Exchange's website), shows that the total trading volume of Prolor's shares (both on the Tel Aviv Stock Exchange and on NYSE Amex) after deduction of interested party transactions over a period of two years, from June 1, 2011 until June 1, 2013, is approximately 71,725,543 shares, so that the average daily trading volume of Prolor's shares on the Tel Aviv Stock Exchange over such two year period is approximately 144,608 shares per day. Given the number of Prolor shares not held by Prolor itself (the "Traded Shares"), then on average, the total number of shares traded on the Tel Aviv Stock Exchange is sold approximately every 440 days.
- 1.6. Opko is a public company, resident of the USA, incorporated in 1991. Its securities are traded on the New York Stock Exchange (NYSE) under the symbol "OPK".
- 1.7. Opko is a bio-pharma company, engaged in finding solutions for diagnosis, treatment and prevention of various medical conditions, including tests of molecular diagnostic, POCT (point of care testing), medications and vaccines. OPKO is mainly active in the U.S. with its related entities operating in Europe, South America, Canada and Israel.
- 1.8. Opko's issued and outstanding share capital, to date, consists of 336,737,265 shares par value of \$0.01, while the major shareholder of Opko is the Frost Trust. In addition, Frost is the CEO and the chairman of the board of Opko. As of April 22, 2012, the Frost Trust owns directly and indirectly through Frost Group LLC which it controls, an amount of about 41.7% of Opko's issued and outstanding share capital. The remainder of shareholders are members of the public.

1.9. Prolor and Opko shall be collectively referred to hereinafter as the "Companies".

#### The Roadmap for the Structural Change:

- 1.10. Opko intends to acquire all of the rights in the Company by way of a share swap. According to the transaction, Opko (the "Acquiring Company") will acquire all the rights in Prolor (the "Transferred Company") held by Prolor Rights Holders, in exchange for rights issued to them in the Acquiring Company and without any further consideration (hereinafter: the "Share Swap Transaction" or the "Share Swap"), all as set forth below:
  - 1.10.1 Prolor shareholders (including the RS Shareholders and the option holders who chose to exercise the options held by them prior to the date of the merger) will receive in exchange for their Prolor shares, Opko shares (at a conversion ratio of 1: 0.9951) (the "Conversion Ratio").
  - 1.10.4 The actual Share Swap will be carried out by an Exchange Agent American Stock Trust & Transfer Company (the "**Paying Trustee**" and together with the "**102 Trustee**" will be referred as the "**Tax Trustee**"). On the date of the Closing, Opko will make available to the Paying Trustee the shares which will be issued to the shareholders of Prolor,
  - 1.10.5 After the Closing, the Paying Trustee shall send a notice to all shareholders of Prolor, according to which the shareholders will be requested to deliver to the Paying Trustee the Prolor shares owned by them as well as any other document which may be required for the performance of the Share Swap (the "**Documents**").

- 1.11. Prolor intends to request that among the Documents, the shareholders will provide a statement with respect to their residency for tax purposes, whether they are individuals or corporate entities, and a document from the entity through which their shares were held indicating the date and price at which they purchased the shares (the **"Statements"**). Note that as part of the Documents, the parties intend to request that Prolor shareholders designate a bank account to which they wish to transfer the Opko shares.
- 1.12. Upon receipt of the aforementioned Documents and Statements, the Paying Trustee will transfer to Prolor's shareholders the Opko shares to which they are entitled pursuant to the Merger Agreement, all subject to the taxation arrangement contained in this tax ruling.
- 1.13. According to the Merger Agreement, one year after the date of the Share Swap, the Paying Trustee will transfer to Opko the shares in respect of which it has not yet received such Documents and Statements (the "Remaining Shares").

#### 2. The Request:

- 2.1. The Acquiring Company is requesting an exemption from withholding tax at source upon transfer of the consideration in the Share Swap Transaction to the Paying Trustee or the 102 Trustee, as applicable.
- 2.4. To determine the arrangement of withholding tax at source by the Paying Trustee in respect to the consideration transferred to Public Shareholders, as a result of the execution of the Share Swap Transaction.
- 2.5. To confirm that for the interested public holding its shares in an Israeli financial institution and taxable in Israel under the Share Swap Transaction, the share transfer to the Acquiring Company will be considered as a sale not at the time of the swap with respect to part E of the Ordinance, but at the actual time of sale of the shares that are issued in the Share Swap, subject to compliance with the provisions of this tax ruling.

#### 3. The Tax Ruling and its Conditions

- 3.1. Any term in this tax ruling shall have the meaning and definition provided in part B of the Ordinance, unless specifically stated otherwise.
- 3.2. I hereby confirm that the date of the Share Swap shall be the date of the actual Share Swap (the "Swap Date").

#### Regarding the Exemption from Withholding Tax at Source in the Transfer to the Tax Trustee and the Liability of the Trustees

3.3. I hereby confirm that the Acquiring Company will be exempt from withholding tax at source due to the transfer of the full amount of consideration in the Share Swap Transaction to the Tax Trustee, as applicable, subject to compliance with the provisions of this tax ruling. It is emphasized that the exemption from withholding tax at source is subject to full transfer of the consideration to the trustees.

#### Arrangement of Tax Withholding at Source regarding Public Shareholders

- 3.22. It shall be noted that the tax withholding at source for Public Shareholders on the date of the transfer of the issued shares by the Tax Trustee to the shareholders, shall be in accordance with the provisions of the Ordinance and the rates specified in the Income Tax Regulations (Deduction from consideration, payment or capital gain from securities sale, from the sale of a trust fund unit or from a future transaction), 5763—2002 (the **"Regulations for Deduction from Capital Gains"**), and subject to the provisions of this tax ruling.
- 3.23. It is agreed that only for the purposes of withholding tax at source by the Tax Trustee, the provisions of Section 104h of the Ordinance shall be considered as applied to the swapped shares and the consideration from the sale of the Company shares will be calculated according to the exchange rate of the Company share on the date of the transfer of shares from the Tax Trustee to the Public Shareholder or to Opko as stated in Section 1.13 above, as applicable.
- 3.24. The transfer of consideration for the shares of the Public Shareholders to the Paying Trustee will be exempt from withholding tax at source. Withholding tax at source shall be in accordance with this tax ruling, at the date of transfer of the consideration by the Paying Trustee, directly or indirectly, to the Public Shareholders of the Company or to Opko. Note that the transfer of that part of the consideration attributable to Public Shareholders, whose shares are listed and traded on the Tel Aviv Stock Exchange from the Paying Trustee to members of the Tel Aviv Stock Exchange and/or to Israeli financial institution, will be exempt from withholding tax at source. The Regulations for the Deduction from Capital Gains and the provisions of Section 3.26 below shall apply to such Israeli financial institution.

- 3.25. Withholding of tax at source on the date of the payment of the consideration shall be as follows:
  - 3.25.1 The consideration paid for the shares listed on the Stock Exchange in the USA in the name of stock exchange members in Israel and/or Israeli financial institutions (the "Israeli Financial Institutions") will be exempt from withholding tax at source. Accordingly, the Paying Trustee shall transfer the said consideration in full to foreign brokers for Tel Aviv Stock Exchange members, together with a notice stating that the consideration is gross, and withholding tax was not deducted from it at source. This section shall also apply with respect to a shareholder requesting that the shares transferred to him by the Paying Trustee shall be deposited to an account in an Israeli Financial Institution. Identification will be carried out by a statement that shall be transferred by Israeli Financial Institutions to foreign brokers, and shall state that the Israeli Financial Institution is holding the shares of the Company for the shareholders of the Company. Israeli Financial Institutions will be responsible for withholding tax at source in accordance with the Ordinance, the rates specified in the Regulations of Deduction from Capital Gain and the provisions of Section 3.26 below. It is clarified that the Tax Trustee will also be exempted from withholding tax at source in respect of shares held by Israeli Financial Institutions (through foreign brokers), and which are held through the DTC (Deposit and Trust Company) the American depository company, in the name of the foreign brokers. Israeli Financial Institutions will be responsible for withholding tax at source in accordance with the Ordinance and rates specified in the Regulations for Deduction from Capital Gains.
  - 3.25.2 The consideration paid for the shares listed on the Stock Exchange in the USA in the name of the shareholders and/or foreign brokers will be exempt from withholding tax at source and the Paying Trustee shall transfer the said part of the consideration in full to the shareholders and/or foreign financial institution with a notice stating that the consideration is gross, and tax at source was not deducted from it, provided that at least one of the following conditions is met regarding <u>each of the shares of the Company</u> held by Public Shareholder or with respect to part of the shares of the Company held by him in which case the exemption from withholding tax at source shall apply to the part of shares as to which the notice was delivered:

- 3.25.3 From the consideration paid to the remaining shareholders who do not meet the conditions specified in Section 3.25.1 above or Section 3.25.2 above, tax at source will be withheld by the Tax Trustee from the consideration in U.S. dollars at the rate specified in the regulations governing withholding at source, unless a certificate by the Israel Tax Authority is issued determining another tax deduction rate or an exemption from withholding tax at source. Thus, to the extent that a certificate ordering exemption from withholding tax at source is not be issued, the Tax Trustee shall transfer the part of such consideration net of tax to foreign financial institutions or to the shareholders, as applicable, with a notice stating that the consideration is net, after deduction of tax at source.
- 3.26. It is agreed, that notwithstanding the provisions of Sections 3.24 and 3.25.1 above, for Public Shareholders holding their shares through an Israeli Financial Institution or wishing to transfer the shares from the Paying Trustee directly to an Israeli Financial Institution (the **"Interested Public"**), the Share Swap in the Share Swap Transaction shall not be deemed, at the time of swap, as a sale for the purposes of part E of the Ordinance and the provisions of Section 104h of the Ordinance shall apply mutatis mutandis as described below:

- 3.26.1 It is agreed, taking into account your declaration as specified in Section 1.5, the Interested Public shall be considered as those who sold their issued shares prior to the "date of end of the deferral period" as defined in Section 104h of the Ordinance. Therefore, the day of sale will be considered for the purposes of Section 104h of the Ordinance as the day when the issued shares were actually sold, and for this purpose provisions relating to the "date of the end of the deferral period" shall not apply after 24 months or 48 months from the date of the Share Swap, as applicable.
- 3.26.2 In accordance with Section 3.26.1 above, the imposition of tax held by the Interested Public, the calculation of profit or loss and calculation of tax derived thereof, held by the Interested Public, will be exercised only at the time of the initial sale of issued shares. Note that if an Interested Public shareholder requests an Israeli Financial Institution to consider the Share Swap as a taxable event, the consideration for the sale of shares of the Company will be calculated by the Israeli Financial Institution for purposes of withholding tax at source in accordance with the average closing exchange rates of share of the Company, during the three trading days preceding the date of the Closing.
- 3.26.3 Withholding tax at source on the initial sale of the issued shares shall be conducted in accordance with the Regulations for Deduction from Capital Gains by the Israeli Financial Institution.
- 3.26.4 For the calculation of profit gained by the Interested Public by the first sale of the issued shares, the original price of issued shares will be considered as the original price of the swapped transferred shares. The day of acquisition of issued shares shall be the day of acquisition of the swapped transferred shares.