Opko Health, Inc.
Form 10-K
February 27, 2015
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2014.

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to .

Commission file number 001-33528

OPKO Health, Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	75-2402409
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
4400 Biscayne Blvd., Miami, FL 33137	
(Address of Principal Executive Offices) (Zip Code)	

(Registrant's Telephone Number, Including Area Code):
(305) 575-4100

Securities registered pursuant to section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $.01 par value per share	New York Stock Exchange

Securities registered pursuant to section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ý No ¨
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No ý
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No ¨

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Indicate by check mark whether the Registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ý No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ý

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.

(in Rule 12b-2 of the Exchange Act) (Check one):

Large accelerated filer ý	Accelerated filer o
Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No ý

The aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the price at which the common equity was last sold, as of the last business day of the registrant's most recently completed second fiscal quarter was: $2,114,172,075.

As of February 20, 2015, the registrant had 451,627,482 shares of Common Stock outstanding.

Documents Incorporated by Reference

Portions of the registrant's definitive proxy statement for its 2015 Annual Meeting of Stockholders are incorporated by reference in Items 10, 11, 12, 13, and 14 of Part III of this Annual Report on Form 10-K.

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains "forward-looking statements," as that term is defined under the Private Securities Litigation Reform Act of 1995 ("PSLRA"), Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements include statements about our expectations, beliefs or intentions regarding our product development efforts, business, financial condition, results of operations, strategies or prospects. You can identify forward-looking statements by the fact that these statements do not relate strictly to historical or current matters. Rather, forward-looking statements relate to anticipated or expected events, activities, trends or results as of the date they are made. Because forward-looking statements relate to matters that have not yet occurred, these statements are inherently subject to risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements. These factors include those described below and in "Item 1A-Risk Factors" of this Annual Report on Form 10-K. We do not undertake an obligation to update forward-looking statements. We intend that all forward-looking statements be subject to the safe-harbor provisions of the PSLRA. These forward-looking statements are only predictions and reflect our views as of the date they are made with respect to future events and financial performance.

Risks and uncertainties, the occurrence of which could adversely affect our business, include the following:

- We have a history of operating losses and we do not expect to become profitable in the near future.
- Our technologies are in an early stage of development and are unproven.
- Our business is substantially dependent on our ability to develop, launch and generate revenue from our pharmaceutical and diagnostic programs.
- Our research and development activities, or that of our investees, may not result in commercially viable products.
- The timing and expenditures associated with the build-up of pre-launch inventory and capacity expansion.
- The results of previous clinical trials may not be predictive of future results, and our current and planned clinical trials may not satisfy the requirements of the United States ("U.S.") Food and Drug Administration ("FDA") or other non-U.S. regulatory authorities.
- We may require substantial additional funding, which may not be available to us on acceptable terms, or at all.
- We may finance future cash needs primarily through public or private offerings, debt financings or strategic collaborations, which may dilute your stockholdings in the Company.
- If our competitors develop and market products that are more effective, safer or less expensive than our future product candidates, our commercial opportunities will be negatively impacted.
- The regulatory approval process is expensive, time consuming and uncertain and may prevent us or our collaboration partners from obtaining approvals for the commercialization of some or all of our product candidates.
- Failure to recruit and enroll patients for clinical trials may cause the development of our product candidates to be delayed.
- Even if we obtain regulatory approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our product candidates, which could materially impair our ability to generate anticipated revenues.
- We may not meet regulatory quality standards applicable to our manufacturing and quality processes.
- Even if we receive regulatory approval to market our product candidates, the market may not be receptive to our products.
- The loss of Phillip Frost, M.D., our Chairman and Chief Executive Officer, could have a material adverse effect on our business and product development.
- If we fail to attract and retain key management and scientific personnel, we may be unable to successfully develop or commercialize our product candidates.
- In the event that we successfully evolve from a company primarily involved in development to a company also involved in commercialization, we may encounter difficulties in managing our growth and expanding our operations successfully.

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- If we fail to acquire and develop other products or product candidates, at all or on commercially reasonable terms, we may be unable to diversify or grow our business.
- We have no experience manufacturing our pharmaceutical product candidates other than at one of our Israeli facilities, and at our Mexican, and Spanish facilities, and we have no experience in manufacturing our diagnostic product candidates. We will therefore likely rely on third parties to manufacture and supply our pharmaceutical and diagnostics product candidates, and we would need to meet various standards to satisfy FDA regulations in order to manufacture on our own.
- We currently have no pharmaceutical or diagnostic marketing, sales or distribution capabilities other than in Chile, Mexico, Spain, and Uruguay for sales in those countries and our active pharmaceutical ingredients ("APIs") business in Israel, and the sales force for our laboratory business based in Nashville, Tennessee. If we are unable to develop our sales and marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing our pharmaceutical and diagnostic product candidates.
- Certain elements of our business are dependent on the success of ongoing and planned phase 3 clinical trials for Alpharen (Fermagate Tablets), and hGH-CTP.
- Independent clinical investigators and contract research organizations that we engage to conduct our clinical trials may not be diligent, careful or timely.
- The success of our business is dependent on the actions of our collaborative partners.
- Our exclusive worldwide agreement with Pfizer Inc. ("Pfizer") is important to our business. If we do not successfully develop hGH-CTP and/or Pfizer does not successfully commercialize hGH-CTP, our business could be adversely affected.
- If we are unable to obtain and enforce patent protection for our products, our business could be materially harmed.
- If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected.
- We rely heavily on licenses from third parties.
- We license patent rights to certain of our technology from third-party owners. If such owners do not properly maintain or enforce the patents underlying such licenses, our competitive position and business prospects will be harmed.
- Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties.
- Adverse results in material litigation matters or governmental inquiries could have a material adverse effect upon our business and financial condition.
- If our products have undesirable effects on patients, we could be subject to litigation or product liability claims that could impair our reputation and have a material adverse effect upon our business and financial condition.
- Medicare prescription drug coverage legislation and future legislative or regulatory reform of the health care system may adversely affect our ability to sell our products or provide our services profitably.
- Failure to obtain and maintain regulatory approval outside the U.S. will prevent us from marketing our product candidates abroad.
- We may not have the funding available to pursue acquisitions.
- Acquisitions may disrupt our business, distract our management, may not proceed as planned, and may also increase the risk of potential third party claims and litigation.
- We may encounter difficulties in integrating acquired businesses.
- Non-U.S. governments often impose strict price controls, which may adversely affect our future profitability.
- Political and economic instability in Europe and Latin America and political, economic, and military instability in Israel or neighboring countries could adversely impact our operations.
- We are subject to fluctuations in currency exchange rates in connection with our international businesses.

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- We have a large amount of goodwill and other intangible assets as a result of acquisitions and a significant write-down of goodwill and/or other intangible assets would have a material adverse effect on our reported results of operations and net worth.
- Our business may become subject to legal, economic, political, regulatory and other risks associated with international operations.
- The market price of our Common Stock may fluctuate significantly.
- The conversion and redemption features of our January 2013 convertible senior notes due in 2033 are classified as embedded derivatives and may continue to result in volatility in our financial statements, including having a material impact on our result of operations and recorded derivative liability.
- We have previously reported a material weakness in our internal control over financing reporting which may cause investors and stockholders to lose confidence in our financial reporting.
- Directors, executive officers, principal stockholders and affiliated entities own a significant percentage of our capital stock, and they may make decisions that you may not consider to be in your best interests or in the best interests of our stockholders.
- Compliance with changing regulations concerning corporate governance and public disclosure may result in additional expenses.
- If we are unable to satisfy the requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as they apply to us, or our internal controls over financial reporting are not effective, the reliability of our financial statements may be questioned and our Common Stock price may suffer.
- We may be unable to maintain our listing on the New York Stock Exchange (“NYSE”), which could cause our stock price to fall and decrease the liquidity of our Common Stock.
- Future issuances of Common Stock and hedging activities may depress the trading price of our Common Stock.
- Provisions in our charter documents and Delaware law could discourage an acquisition of us by a third party, even if the acquisition would be favorable to you.
- We do not intend to pay cash dividends on our Common Stock in the foreseeable future.

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PART I

Unless the context otherwise requires, all references in this Annual Report on Form 10-K to the "Company", "OPKO", "we", "our", "ours", and "us" refer to OPKO Health, Inc., a Delaware corporation, including our wholly-owned subsidiaries.

ITEM 1. BUSINESS

OVERVIEW

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

All product or service marks appearing in type form different from that of the surrounding text are trademarks or service marks owned, licensed to, promoted or distributed by OPKO, its subsidiaries or affiliates, except as noted. All other trademarks or services marks are those of their respective owners.

We own established pharmaceutical platforms in Chile, Spain, Mexico, and Uruguay which generate revenue and which we expect to facilitate future market entry for our products currently in development. We own a specialty active pharmaceutical ingredients ("APIs") manufacturer in Israel, which we expect may facilitate the development of our pipeline of molecules and compounds for our proprietary products. In the U.S., we own OPKO Lab, a laboratory certified under the Clinical Laboratory Improvement Amendments of 1988, as amended ("CLIA"), that operates as a full-service medical laboratory with a urologic focus and serves as the commercial platform for the U.S. launch of the 4Kscore test, our next generation prostate cancer test and the only blood test that accurately identifies risk for aggressive prostate cancer.

In March 2014, we began selling the 4Kscore test domestically through our CLIA-accredited laboratory in Nashville. In addition, we launched sales of the 4Kscore test in Europe in September 2014 and in Mexico in January 2015. The 4Kscore test measures the blood plasma levels of four different prostate-derived kallikrein proteins: Total PSA, Free PSA, Intact PSA and Human Kallikrein-2 ("hK2"). These biomarkers are combined with a patient's age, Digital Rectal Exam ("DRE") status (nodule / no nodule), and prior negative biopsy status (yes / no) using a proprietary algorithm to calculate the risk (probability) of finding an aggressive prostate cancer defined as Gleason Score 7 or higher prostate cancer. Recent data has also demonstrated potential that a high score using the 4Kscore test is associated with an increased risk of developing metastatic prostate cancer. The panel of biomarkers included in the OPKO 4Kscore is the result of more than a decade of research by scientists in Europe and the U.S. Extensive studies have shown that the use of this novel panel of kallikrein biomarkers and algorithm may not only improve the accuracy of identifying aggressive cancer, but may also reduce the number of unnecessary prostate biopsies by 50% or more and avoid diagnosis of indolent prostate cancer that can lead to over treatment with surgery or radiation. It is estimated that the 4Kscore test can provide $2-4 billion in healthcare savings in the U.S. each year.

The 4Kscore test is designed to be used as a reflex test after a finding of an abnormal DRE or elevated PSA, but before performing a prostate biopsy. There are approximately 1 million biopsies being performed annually in the U.S., with 80% of the results indicating no cancer or a low-grade, indolent form of prostate cancer. The test was developed by OPKO Lab and validated in a prospective, blinded study of 1,012 men in collaboration with 26 urology centers across the U.S. Results showed that the 4Kscore test was highly accurate for predicting the presence of high-grade cancer (Gleason score 7 or higher) prior to prostate biopsy. The full data from the blinded, prospective U.S. clinical validation study was presented at the AUA Annual Meeting in Orlando, FL on May 18, 2014 at Plenary Session and published in the online edition of European Urology in October 2014.

Our Claros1 immunoassay instrument system provides rapid, high performance blood test results and enables complex tests to be run in point-of-care settings. The instrument, a novel microfluidics-based system consisting of a credit card-sized disposable test cassette that works with a small desktop analyzer, can provide high performance, central laboratory-grade blood test results within minutes and permit the transition of complex immunoassays and other tests from the centralized reference laboratory to the physician's office or hospital nurses' station. We expect this

point-of-care instrument system to provide near-term commercialization opportunities through the transition of existing laboratory-based tests, including prostate specific antigen ("PSA"), testosterone and vitamin D, to our point-of-care system.

We intend to submit our application to the Food and Drug Administration (the "FDA") for clearance of a testosterone diagnostic test for our point-of-care system in the second half of 2015. We also intend to seek European certification related to

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health, safety and environmental legislation, also known as a CE Marking ("CE Mark") for the test in Europe at approximately the same time. We expect to begin marketing the testosterone test in the U.S. and Europe in 2016.

We have already obtained a CE Mark for our point-of-care diagnostic test for PSA using our system in Europe. We intend to update our CE Mark to reflect recent product improvements and launch the PSA test in Europe in 2016. We intend to submit our application to the FDA for pre-marketing authorization ("PMA") of the PSA test in the first quarter of 2016.

We are also presently working to add additional tests for our point-of-care system, including vitamin D and Lyme Disease, and we believe that there are many more applications for the technology, including infectious disease, cardiology, women's health, and companion diagnostics.

Our product pipeline also includes several pharmaceutical compounds and technologies in research and development for a broad range of indications and conditions.

In the third quarter of 2014, we announced successful top-line results from two identical randomized, double-blind, placebo-controlled, multi-site phase 3 trials of Rayaldee (CTAP101), our vitamin D prohormone to treat secondary hyperparathyroidism ("SHPT") in patients with stage 3 or 4 chronic kidney disease ("CKD") and vitamin D insufficiency. Vitamin D insufficiency often arises in CKD due to the abnormal upregulation of CYP24, an enzyme that destroys vitamin D and its metabolites. Studies in CKD patients have demonstrated that available over-the-counter and prescription vitamin D products cannot reliably raise blood vitamin D prohormone levels and effectively treat SHPT. Rayaldee was shown in the studies to effectively and safely treat SHPT and the underlying vitamin D insufficiency in pre-dialysis patients. A New Drug Application ("NDA") submission to the FDA is planned for the first quarter of 2015.

In addition to SHPT in CKD patients, we also are developing Rayaldee for other indications, and in August 2014, announced the submission of an Investigational New Drug application ("IND") to the FDA to evaluate Rayaldee as an adjunctive therapy for the prevention of skeletal-related events in patients with bone metastases undergoing anti-resorptive therapy. We commenced a phase 1 dose escalation study in the fourth quarter of 2014 in breast and prostate cancer patients with bone metastases who are receiving anti-resorptive therapy. The study will evaluate safety, markers of mineral metabolism and tumor progression.

We are also developing Alpharen (Fermagate Tablets), a new and potent non-absorbed phosphate binder to treat hyperphosphatemia in dialysis patients. Alpharen has been shown to be safe and effective in treating hyperphosphatemia in phase 2 and 3 trials in CKD patients undergoing chronic hemodialysis. Hyperphosphatemia contributes to soft tissue mineralization and affects approximately 90% of dialysis patients. Dialysis patients require ongoing phosphate binder treatment to maintain normal serum phosphorus levels.

The CKD patient population is large and growing as a result of obesity, hypertension and diabetes, representing a significant market opportunity. We intend to develop Rayaldee (CTAP101) and Alpharen (Fermagate Tablets) to constitute part of the foundation for a new and markedly improved standard of care for CKD patients having SHPT and/or hyperphosphatemia.

In August 2013, we acquired OPKO Biologics, formerly PROLOR Biotech, Inc., a biopharmaceutical company focused on developing and commercializing longer-acting proprietary versions of already approved therapeutic proteins utilizing a platform technology known as Carboxyl Terminal Peptide ("CTP") technology.

Our most advanced product in development using the platform technology is a long-acting version of human growth hormone, known as hGH-CTP, for the long-term treatment of children and adults with growth failure due to inadequate secretion of endogenous growth hormone (a $3.0 billion market opportunity growing 5% annually).

In December 2014, we entered into an exclusive worldwide agreement with Pfizer Inc. ("Pfizer") for the development and commercialization of our hGH-CTP for the treatment of growth hormone deficiency ("GHD") in adults and children, as well as for the treatment of growth failure in children born small for gestational age ("SGA"). In connection with the transaction, we granted Pfizer an exclusive license to commercialize hGH-CTP worldwide, and we received non-refundable and non-creditable upfront payments of $295 million and are eligible to receive up to an additional $275 million upon the achievement of certain regulatory milestones. In addition, we are eligible to receive initial royalty payments associated with the commercialization of hGH-CTP for Adult GHD. Upon the launch of hGH-CTP for Pediatric GHD, the royalties will transition to regional, tiered gross profit sharing for both hGH-CTP and Pfizer's

Genotropin®.

Pursuant to our agreement with Pfizer, we will lead the clinical activities for the hGH-CTP program and will be responsible for funding the development programs for the key indications, which includes Adult and Pediatric GHD and Pediatric SGA. Pfizer will be responsible for all development costs for additional indications as well as all post-marketing

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studies. In addition, Pfizer will fund the commercialization activities for all indications and lead the manufacturing activities covered by the global development plan.

The hGH-CTP product has been shown in a phase 2 clinical trial to have the potential to reduce the required dosing frequency of human growth hormone from the current standard of one injection per day to a single weekly injection. hGH-CTP is currently in a global phase 3 trial in adults and a global phase 2 trial in children and has orphan drug designation in the U.S. and Europe for both adults and children with GHD.

Factor VIIa-CTP is our novel, long-acting recombinant Factor VIIa which also utilizes CTP technology to extend circulatory half-life without the use of polymers, encapsulation techniques, or nanoparticles. Currently, Factor VIIa therapy is available only as an intravenous (IV) formulation which, due to Factor VIIa's short half-life, requires multiple infusions to treat a bleeding episode. Pre-clinical studies of intravenous and subcutaneous formulations of our product in hemophilic animal models demonstrated its duration of action and significantly increased survival. In January 2015, we submitted an IND to the FDA to conduct a Phase 2a study of Factor VII-CTP for the treatment of bleeding episodes in hemophilia A or B patients with inhibitors to Factor VIII or Factor IX. Factor VII-CTP has been granted orphan status in the U.S. and Europe.

In addition to hGH-CTP and Factor VII-CTP, our internal product development program is currently focused on extending the circulatory half life of oxyntomodulin. Oyxntomodulin, a natural appetite suppressor, is a peptide hormone secreted by the intestine following food intake that induces satiety when it reaches the brain. Oxyntomodulin activates both the glucagon-like peptide-1 receptor (GLP1R) and glucagon receptor (GCGR) and has been found to decrease food intake and body weight as well as lower glucose in overweight human volunteers.

The clinical utility of oxyntomodulin has been limited mostly because of its short circulating half life. We are developing a long-acting oxyntomdulin, GLP-1/glucagon dual receptor agonist comprising oxyntomodulin linked at its N-terminus to polyethylene glycol (PEG) linear chain through a proprietary bi-functional hydrolysable linker. Administration of the conjugate into the blood results in slow release of the authentic, non-modified natural oxyntomodulin. Our preclinical studies have shown that a single weekly injection of our compound in development significantly inhibited food intake and reduced body weight in obese and diabetic animal models, as well as improving the lipid profile by reducing cholesterol levels in obese and diabetic mice. In addition, the studies demonstrated improved glycemic control by inducing glucose dependent insulin secretion and by reducing fat, two biological effects related to type II diabetes. We expect to initiate a phase 1 study of our compound in the second half of 2015.

We believe that our up-regulating oligonucleotide therapeutics technology, or AntagoNAT, has the potential to create new drugs for the treatment of a wide variety of illnesses, including cancer, heart disease, metabolic disorders and a range of genetic disorders. We have a variety of therapeutic agents for respiratory disorders in clinical development, including products for asthma, chronic obstructive pulmonary disease ("COPD"), and chronic cough.

In addition to these development programs, we have pharmaceutical businesses in Chile, Spain, Mexico, Israel, and Uruguay.

We have a highly experienced management team that we believe has demonstrated an ability to successfully build and manage pharmaceutical businesses. Based on their experience in the industry, we believe that our management team has extensive development, regulatory and commercialization expertise and relationships that provide access to commercial opportunities.

GROWTH STRATEGY

We expect our future growth to come from leveraging our proprietary technology and development strengths, and opportunistically pursuing complementary, accretive, or strategic acquisitions and investments.

We have under development a broad and diversified portfolio of diagnostic tests, vaccines, small molecules, and biologics targeting a broad range of unmet medical needs. We intend to continue to leverage our proprietary technology and our strengths in all phases of research and development to further develop and commercialize our portfolio of proprietary pharmaceutical and diagnostic products. In support of our strategy, we intend to:

- obtain requisite regulatory approval and compile clinical data for our most advanced product candidates;
- develop a focused commercialization capability both internationally and in the U.S.; and
- expand into other medical markets that provide significant opportunities and that we believe are complementary to and synergistic with our business.

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We have and expect to continue to be opportunistic and to pursue complementary or strategic acquisitions, licenses and investments. Our management team has significant experience in identifying, executing and integrating these transactions. We expect to use well-timed, carefully selected acquisitions, licenses and investments to continue to drive our growth, including:

- Products and technologies. We intend to continue to pursue product and technology acquisitions and licenses that will complement our existing businesses and provide new product and market opportunities, improve our growth, enhance our profitability, leverage our existing assets, and contribute to our own organic growth.
- Commercial businesses. We intend to continue to pursue acquisitions of commercial businesses that will both drive our growth and provide geographically diverse sales and distribution opportunities, particularly outside of the U.S.
- Early stage investments. We have and may continue to make investments in early stage companies that we perceive to have valuable proprietary technology and significant potential to create value for OPKO as a shareholder.

CORPORATE INFORMATION

We were originally incorporated in Delaware in October 1991 under the name Cytoclonal Pharmaceutics, Inc., which was later changed to eXegenics, Inc. (“eXegenics”). On March 27, 2007, we were part of a three-way merger with Froptix Corporation (“Froptix”), a research and development company, and Acuity Pharmaceuticals, Inc. (“Acuity”), a research and development company. On June 8, 2007, we changed our name to OPKO Health, Inc.

Our shares are publicly traded on the NYSE under the ticker “OPK”. Effective as of August 2013, our stock also began trading on the Tel Aviv Stock Exchange. Our principal executive offices are located in leased office space in Miami, Florida. We lease office and lab space in Jupiter, Florida and Miramar, Florida, and Nes Ziona, Israel, which is where our molecular diagnostics research and development, oligonucleotide research and development and CTP research and development operations are based, respectively. We lease office, manufacturing, and warehouse space in Woburn, Massachusetts for our point-of-care diagnostics business, and in Nesher, Israel for our API business. We lease laboratory and office space in Nashville, Tennessee, Burlingame, California, and Miramar, Florida for our CLIA-certified laboratory business, and we lease office space in Bannockburn, Illinois, and Markham, Ontario for our pharmaceutical business directed to CKD. Our Chilean and Uruguayan operations are located in leased offices and warehouse facilities in Santiago and Montevideo, respectively. Our Mexican operations are based in owned offices, an owned manufacturing facility, and a leased warehouse facility in Guadalajara and in leased offices in Mexico City. Our Spanish operations are based in owned offices in Barcelona, in an owned manufacturing facility in Banyoles and a leased warehouse facility in Palol de Revardit. Our Brazilian operations are located in leased offices in Sao Paulo.

We currently manage our operations in two reportable segments, pharmaceutical and diagnostics. The pharmaceutical segment consists of two operating segments, our (i) pharmaceutical research and development segment, which is focused on the research and development of pharmaceutical products and vaccines, and (ii) the pharmaceutical operations we acquired in Chile, Spain, Mexico, Israel, Uruguay and Brazil. The diagnostics segment consists of two operating segments, our (i) pathology operations we acquired through the acquisition of OPKO Lab and (ii) point-of-care and molecular diagnostics operations. There are no significant inter-segment sales. We evaluate the performance of each segment based on operating profit or loss. There is no inter-segment allocation of interest expense and income taxes.

CURRENT PRODUCT CANDIDATES AND RELATED MARKETS

Diagnostics

4Kscore

We began selling the 4Kscore in the U.S. in March 2014 and in Europe and Mexico in September 2014 and January 2015, respectively. The 4Kscore measures the blood plasma levels of four different prostate-derived kallikrein proteins: Total PSA, Free PSA, Intact PSA and Human Kallikrein-2 (“hK2”). These biomarkers are then combined with a patient’s age, DRE status (nodule / no nodule), and prior negative biopsy status (yes / no) using a proprietary algorithm to calculate the risk (probability) of finding a Gleason Score 7 or higher prostate cancer.

The OPKO 4Kscore was developed by OPKO Lab and validated in 2014 in a prospective, blinded study of 1,012 men in collaboration with 26 urology centers across the U.S. Results showed that the 4Kscore test was highly accurate for predicting the presence of high-grade cancer (Gleason score 7 or higher) prior to prostate biopsy. The full data from the blinded, prospective U.S. clinical validation study were presented at the AUA Annual Meeting in Orlando, FL on

May 18, 2014 at Plenary Session and published in the online edition of European Urology in October 2014.

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The clinical data presented at the AUA annual meeting included 1,012 men scheduled for prostate biopsy. Patients were enrolled regardless of their PSA, age, DRE result, or primary versus repeat biopsy status, and represent contemporary practice in the U.S. The results demonstrated the ability of the 4Kscore test to discriminate between men with high-grade, aggressive prostate cancer and those men who had no findings of cancer or had low-grade or indolent form of the disease. The discrimination, measured by Area Under the Curve ("AUC") analysis, was 0.82 and was significantly higher than previously developed tests. Furthermore, the 4Kscore test demonstrated excellent risk calibration, indicating the accuracy of the result for an individual patient. The high value of AUC and the excellent risk calibration make the 4Kscore result valuable information for the shared decision-making between the urologist and patient on whether or not to perform a prostate biopsy, potentially reducing biopsies by more than 50%. Although quite specific to the prostate gland, PSA is not specific for prostate cancer. As a result, in the U.S., an estimated 750,000 men receive unnecessary prostate biopsies annually as a result of PSA testing. We believe that our novel 4Kscore test should yield significantly greater accuracy and should provide us with a unique opportunity to greatly improve the value of prostate cancer screening.

The four kallikrein panel of biomarkers utilized in the 4Kscore test is based on over a decade of research conducted by scientists at Memorial Sloan-Kettering Cancer Center and leading European institutions. Investigators at the University of Malmo, Sweden, University of Turku, Finland and Memorial Sloan Kettering Cancer Center, New York, have also demonstrated that an algorithm integrating these biomarkers along with patient data can predict prostate biopsy results, and that the use of this algorithm to determine whether to biopsy can reduce the number of prostate biopsies performed by over fifty percent (50%), avoiding the frequent complications from biopsies of pain, bleeding, and infection, which sometimes require hospitalization.

In December 2012, we completed the acquisition of OPKO Lab, our CLIA-certified laboratory with several phlebotomy sites throughout the U.S. and an experienced national sales force calling primarily on urologists. In addition to continuing to operate as a full-service medical laboratory specializing in urologic pathology, OPKO Lab provides us with the commercial platform to support the U.S. commercial launch of the 4Kscore for the detection of prostate cancer as an LDT.

Point-of-Care Diagnostics

In October 2011, we acquired Claros Diagnostics, Inc. ("OPKO Diagnostics"), which developed a novel diagnostic instrument system that provides rapid, high performance blood test results and enables tests to be run in point-of-care settings. The instrument, a microfluidics-based diagnostic test system consisting of a credit card-sized disposable test cassette that works with a small but sophisticated desktop analyzer, provides high performance quantitative blood test results within minutes and permits the transition of complex immunoassays and other tests from the centralized reference laboratory to the physician's office or hospital nurses station. The technology only requires a finger stick drop of blood introduced into the test cassette which can simultaneously run multiple tests (multiplex) on the single droplet of blood.

We intend to submit our application to the FDA for clearance of a testosterone diagnostic test for our point-of-care system in the second half of 2015. We also intend to seek a CE Mark for the test in Europe at approximately the same time. We expect to begin marketing the testosterone test in the U.S. and Europe in 2016.

We have already obtained a CE Mark for our point-of-care diagnostic test for PSA using this system in Europe. We intend to update our CE Mark to reflect recent product improvements and launch the PSA test in Europe in 2016. We intend to submit our PMA application to the FDA for the PSA test in the first quarter of 2016.

We are also presently working to add additional tests for our point-of-care system, including Lyme Disease and vitamin D, and we believe that there are many more applications for the technology, including infectious disease, cardiology, women's health, and companion diagnostics.

Molecular Diagnostics

In June 2009, we acquired exclusive, worldwide rights from the University of Texas Southwestern to an innovative platform technology for the rapid identification of molecules or immunobiomarkers that may be useful in the creation of accurate, easy-to-use diagnostic tests as well as the development of vaccines and highly targeted therapeutic agents for immune system-driven diseases. The technology is based on an innovative method for the identification in small

blood samples of disease-specific antibodies that can serve as diagnostic biomarkers for various diseases. We jointly own patent applications covering certain aspects of the technology and hold an exclusive license to the technology. After gaining extensive experience with the technology in the field of commercial diagnostic tests, we have concluded that other opportunities in the life science tools area may be a more promising use of the platform technology and are actively exploring the best way to realize the platform's potential.

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Pharmaceutical Business

We presently have several pharmaceutical compounds and technologies in research and development for a broad range of indications and conditions. Our product development candidates are in various stages of development and include the following:

Renal Products

In March 2013, we acquired Cytochroma Inc. ("Cytochroma" or "OPKO Renal"), a clinical stage specialty pharmaceutical company focused on developing and commercializing proprietary products to treat vitamin D insufficiency, hyperphosphatemia and SHPT associated with CKD, a condition characterized by progressive decline in renal function. CKD is classified in five stages — mild (stage 1) to severe (stage 5) disease. Our two lead renal products are Rayaldee (CTAP101), a vitamin D prohormone to treat SHPT in patients with stage 3 or 4 CKD and vitamin D insufficiency, and Alpharen (Fermagate Tablets), a new and potent non-absorbed phosphate binder to treat hyperphosphatemia in Stage 5 patients on chronic hemodialysis.

We announced successful top-line results from two pivotal phase 3 trials of Rayaldee in the third quarter of 2014. These trials were identical randomized, double-blind, placebo-controlled, multi-site studies intended to establish the safety and efficacy of Rayaldee as a new treatment for SHPT in patients with stage 3 or 4 CKD and vitamin D insufficiency. Vitamin D insufficiency arises in CKD due to the abnormal upregulation of CYP24, an enzyme that destroys vitamin D and its metabolites. Studies in CKD patients have demonstrated that currently available over-the-counter and prescription vitamin D products cannot reliably raise blood vitamin D prohormone levels and effectively treat SHPT, a condition commonly associated with CKD in which the parathyroid glands secrete excessive amounts of parathyroid hormone ("PTH"). Prolonged elevation of blood PTH causes excessive calcium and phosphorus to be released from bone, leading to elevated serum calcium and phosphorus levels, softening of the bones (osteomalacia) and calcification of vascular and renal tissues. SHPT affects 40-82% of patients with stage 3 or 4 CKD and approximately 95% of patients with stage 5.

The completed pivotal trials for Rayaldee successfully met all primary efficacy and safety endpoints. The primary efficacy endpoint was a responder analysis in which "responder" was defined as any treated subject who demonstrated an average 30% decrease in PTH from pre-treatment baseline during the last six weeks of the 26-week treatment period. A significantly higher response rate was observed with Rayaldee which steadily increased with treatment duration. The response rate with Rayaldee was similar in CKD stages 3 and 4. Safety and tolerability data were comparable in both treatment groups. Patients completing the two pivotal trials were treated, at their election, for an additional six months with Rayaldee during an open-label extension study. A new drug application ("NDA") submission to the FDA is planned for the first quarter of 2015.

In addition to SHPT in CKD patients, we also are developing Rayaldee for other indications, and in August 2014, announced the submission of an IND to the FDA to evaluate Rayaldee as an adjunctive therapy for the prevention of skeletal-related events in patients with bone metastases undergoing anti-resorptive therapy. We commenced a phase 1 dose escalation study in the fourth quarter of 2014 in breast and prostate cancer patients with bone metastases who are receiving anti-resorptive therapy. The study will evaluate safety, markers of mineral metabolism and tumor progression.

Our phosphate binder, Alpharen (Fermagate Tablets), has been shown to be safe and effective in treating hyperphosphatemia in phase 2 and 3 trials in stage 5 CKD patients undergoing chronic hemodialysis. Hyperphosphatemia, or elevated serum phosphorus, is common in dialysis patients and tightly linked to the progression of SHPT. The kidneys provide the primary route of excretion for excess phosphorus absorbed from ingested food. As kidney function worsens, serum phosphorus levels increase and directly stimulate PTH secretion. Stage 5 CKD patients must reduce their dietary phosphate intake and usually require regular treatment with phosphate binding agents to lower serum phosphorus to meet the recommendations of the National Kidney Foundation's Clinical Practice Guidelines that serum phosphorus levels should be maintained at or below 5.5 mg/dL. Hyperphosphatemia contributes to soft tissue mineralization and affects approximately 90% of dialysis patients. Dialysis patients require ongoing phosphate binder treatment to maintain controlled serum phosphorus levels.

We believe the CKD patient population is large and growing as a result of obesity, hypertension and diabetes; therefore this patient population represents a significant market opportunity. According to the National Kidney

Foundation, CKD afflicts over 26 million people in the U.S., including more than 20 million patients with stage 3 or 4 CKD. In stage 5, kidney function is minimal to absent and patients require regular dialysis or a kidney transplant for survival. An estimated 71-97% of CKD patients have vitamin D insufficiency which can lead to SHPT and its debilitating consequences. CKD continues to be associated with poor outcomes, reflecting the inadequacies of the current standard of care. Vitamin D insufficiency, hyperphosphatemia and SHPT, when inadequately treated, are major contributors to poor CKD outcomes. We intend to develop Rayaldee (CTAP101) and Alpharen (Fermagate Tablets) to constitute part of the foundation for a new and markedly improved standard of care for CKD patients having SHPT and/or hyperphosphatemia.

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OPKO Biologics

In August 2013, we acquired OPKO Biologics, formerly PROLOR Biotech, Inc., a biopharmaceutical company focused on developing and commercializing longer-acting proprietary versions of already approved therapeutic proteins utilizing a patented platform technology. The technology uses 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 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. We are using the CTP technology to develop new, proprietary versions of certain existing therapeutic proteins that have longer life spans than therapeutic proteins without CTP. We believe that our products will have greatly improved therapeutic profiles and distinct market advantages.

There are two existing biopharmaceuticals on the market that currently utilize CTP technology. The first product is human chorionic gonadotropin (hCG), of which CTP is naturally a part. Besides being present normally in high amounts during pregnancy, it is also given therapeutically to women or men as a fertility treatment (sold by Merck-Serono, Merck & Co. and Ferring). The second product is ELONVA® (FSH-CTP), which is approved for marketing in Europe. The data from the clinical use of these two products give us confidence that the CTP technology may be able to address the major problems faced by the other attempted approaches to increase protein lifespan. Clinical data from these products reassure us that CTP can be used safely and that it is effective in extending the serum lifetime and activity. We are now the exclusive licensee for the utilization of CTP technology in all therapeutic proteins, peptides and their modified forms except for human FSH, LH, TSH and hCG.

Our lead product candidate utilizing CTP, hGH-CTP, is a recombinant human growth hormone product under development for the treatment of GHD, which is a pituitary disorder resulting in short stature in children and other physical ailments in both children and adults.

In December 2014, we entered into an exclusive worldwide agreement with Pfizer for the development and commercialization of hGH-CTP for the treatment of GHD in adults and children, as well as for the treatment of growth failure in children born SGA. In connection with the transaction, we granted Pfizer an exclusive license to commercialize hGH-CTP worldwide, and we received non-refundable and non-creditable upfront payments of $295 million and are eligible to receive up to an additional $275 million upon the achievement of certain regulatory milestones. In addition, we are eligible to receive initial royalty payments associated with the commercialization of hGH-CTP for Adult GHD. Upon the launch of hGH-CTP for Pediatric GHD, the royalties will transition to regional, tiered gross profit sharing for both hGH-CTP and Pfizer’s Genotropin®.

Pursuant to our agreement with Pfizer, we will lead the clinical development activities for the hGH-CTP program and will be responsible for funding the development programs for the key indications, which includes Adult and Pediatric GHD and Pediatric SGA. Pfizer will be responsible for all development costs for additional indications as well as all post-marketing studies. In addition, Pfizer will fund the commercialization activities for all indications and lead the manufacturing activities covered by the global development plan.

GHD occurs when the production of growth hormone, secreted by the pituitary gland, is disrupted. Since growth hormone plays a critical role in stimulating body growth and development, and is involved in the production of muscle protein and in the breakdown of fats, a decrease in the hormone affects numerous body processes. hGH is used for the long-term treatment of children and adults with inadequate secretion of endogenous growth hormone. The primary indications it treats in children are GHD, kidney disease, Prader-Willi Syndrome and Turner’s Syndrome. In adults, the primary indications are replacement of endogenous growth hormone and the treatment of AIDS-induced weight loss. Patients using hGH receive daily injections six or seven times a week. This is particularly burdensome for pediatric patients. We believe a significant market opportunity exists for a longer-lasting version of hGH that would require fewer injections.

hGH-CTP is currently in a global phase 3 trial in adults and a global phase 2 trial in children and has orphan drug designation in the U.S. and Europe for both adults and children with GHD.

In addition to hGH-CTP, we are focused on products extending the life span of Factor VIIa (hemophilia) using the CTP technology. In February 2013, the FDA granted orphan drug designation to our longer-acting version of clotting Factor VIIa, Factor VIIa-CTP, for the treatment of bleeding episodes in patients with hemophilia A or B with

inhibitors to Factor VIII or Factor IX. These patients are currently being treated by commercially-available Factor VIIa, with estimated 2013 worldwide sales of $1.7 billion. Currently, Factor VIIa therapy is available only as an intravenous (IV) formulation which, due to Factor VIIa's short half-life, requires multiple infusions to treat a bleeding episode. In addition, frequent infusions are onerous when used as preventative prophylactic therapy, especially for children. Pre-clinical studies of IV and subcutaneous formulations of our product in hemophilic animal models demonstrated its duration of action and significantly increased survival. In January 2015, we submitted an IND to the FDA to conduct a Phase 2a study of Factor VIIa-CTP for the treatment of bleeding episodes

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in hemophilia A or B patients with inhibitors to Factor VIII or Factor IX. Factor VIIa-CTP has been granted orphan designation in Europe as well as the U.S.

We believe that the CTP technology may also be broadly applicable to other best-selling therapeutic proteins in the market and provide several key advantages over our competitor's existing products: significant reduction in the number of injections required to achieve the same or superior therapeutic effect from the same dosage; faster commercialization with greater chance of success and lower costs than those typically associated with a new therapeutic protein; and manufacturing using industry-standard biotechnology-based protein production processes.

In addition to hGH-CTP and Factor VII-CTP, our internal product development program is currently focused on extending the circulatory half life of oxyntomodulin. Oyxntomodulin, a natural appetite suppressor, is a peptide hormone secreted by the intestine following food intake that induces satiety when it reaches the brain. Oxyntomodulin activates both the glucagon-like peptide-1 receptor (GLP1R) and glucagon receptor (GCGR) and has been found to decrease food intake and body weight as well as lower glucose in overweight human volunteers.

We believe oxyntomodulin has potential to be a safe, long term therapy for obese and diabetes type II patients, representing significant market opportunities. More than 380 million are living with diabetes worldwide, of which approximately 90% have type II diabetes. According to the World Health Organization, there are more than 500 million severely overweight or obese people.

The clinical utility of oxyntomodulin has been limited mostly because of its short circulating half life. We are developing a long-acting oxyntomdulin comprising oxyntomodulin linked at its N-terminus to polyethylene glycol (PEG) linear chain through a proprietary bi-functional hydrolysable linker. Administration of the conjugate into the blood results in slow release of the authentic, non-modified natural oxyntomodulin. Our preclinical studies have shown that a single weekly injection of our compound in development significantly inhibited food intake and reduced body weight in obese and diabetic animal models, as well as improving the lipid profile by reducing cholesterol levels in obese and diabetic mice.

We expect to initiate a phase 1 study of our compound in the second half of 2015.

APIs

In December 2011, we acquired FineTech Pharmaceutical, Ltd. ("FineTech"), an Israeli company that develops and produces high value, high potency specialty APIs. Through its FDA registered facility in Nesher, Israel, FineTech currently manufactures commercial APIs for sale or license to pharmaceutical companies in the U.S., Canada, Europe and Israel. We believe that FineTech's significant know-how and experience with analytical chemistry and organic syntheses, together with its production capabilities, may play a valuable role in the development of our pipeline of proprietary molecules and compounds for diagnostic and therapeutic products, while providing revenues and profits from its existing API business.

Oligonucleotide Therapeutics

In January 2011, we acquired CURNA, Inc. ("CURNA"), a privately-held company based in Jupiter, Florida, engaged in the discovery of new drugs for the treatment of a wide variety of illnesses, including cancer, heart disease, metabolic disorders and a range of genetic anomalies. CURNA's broad platform technology utilizes a short, single strand oligonucleotide and is based on the up-regulation of protein production through interference with non-coding RNA's, or natural antisense. This strategy contrasts with established approaches which down-regulate protein production. CURNA has designed a novel type of therapeutic modality, termed AntagoNAT, and has initially demonstrated this approach for up-regulation of several therapeutically relevant proteins in in vitro and animal models. We believe that this short, single strand oligonucleotide can be delivered intravenously or subcutaneously without the drug delivery or cell penetration complications typically associated with double stranded siRNA therapeutics. CURNA has identified and developed compounds which increase the production of over 80 key proteins involved in a large number of individual diseases. We have ongoing pre-clinical studies for several of these compounds, with an initial focus on orphan diseases including Dravet Syndrome, Rett Syndrome and MPS-1.

Asthma and COPD

In May 2010, we acquired worldwide rights to a novel heparin-derived oligosaccharide which has significant potential in treating asthma and COPD. Over 22 million people in the U.S. live with asthma, including nearly 6 million children. Additionally, there are more than 12 million people in the U.S. who have COPD. Currently available

therapies often include unwanted side effects and may have limited efficacy. We believe that our product may have an improved efficacy and side effect profile. Our initial studies have demonstrated anti-inflammatory and anti-allergic activity when administered orally or inhaled with inhalers or nebulizers in sheep and mice asthma models. We have also successfully completed human feasibility studies in asthma.

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To complement our portfolio of respiratory products, we acquired in 2014 Inspiro Medical Ltd., a medical device firm developing a new platform to deliver small molecule drugs like corticosteroids and beta agonists or larger molecules to treat respiratory disease. Inspiro's Inspiromatic is a "smart" easy-to-use dry powder inhaler with several advantages over existing devices. In a First In Man double blinded clinical study conducted in 30 asthmatic children comparing Inspiromatic to a market leading dry powder inhaler, Inspiromatic demonstrated superior pulmonary delivery of the active drug.

NK-1 Program

In November 2009, we acquired rolapitant and other neurokinin-1 ("NK-1") assets from Schering Plough Corporation. In December 2010, we exclusively out-licensed the development, manufacture and commercialization of our lead NK-1 candidate, rolapitant, to TESARO, Inc. ("TESARO"). Rolapitant, a potent and selective competitive antagonist of the NK-1 receptor, had successfully completed phase 2 clinical testing for prevention of chemotherapy induced nausea and vomiting, or CINV, and post-operative induced nausea and vomiting. In December 2013, TESARO also announced successful achievement of the primary endpoint in each of two phase 3 trials of rolapitant for prevention of CINV. TESARO submitted its NDA to the FDA for approval of oral rolapitant in September 2014. Under the terms of the license, we are eligible to receive up-front and milestone payments of up to $121 million, double digit tiered royalties on sales of licensed product, as well as a share of future profits from the commercialization of licensed products in Japan, and an option to market the products in Latin America. In addition, we acquired an equity position in TESARO.

Commercial Operations

We also intend to continue to leverage our global commercialization expertise to pursue acquisitions of commercial businesses that will both drive our growth and provide geographically diverse sales and distribution opportunities, particularly outside of the U.S. At a time of slowing pharmaceutical sales growth in many mature countries, the expansion in many emerging markets has led to higher sales growth rates and an increasing contribution to the industry's global performance. As a result, we expect that emerging markets will continue to be a growing part of our business strategy, contributing both attractive revenue growth and cash flow to support our development programs.

In January 2014 and February 2013, we completed the acquisitions of Laboratorio Arama de Uruguay Limitada ("OPKO Uruguay Ltda."), an Uruguayan entity domiciled in Montevideo, and Silcon Comércio, Importacao E Exportacao de Produtos Farmaceuticos e Cosmeticos Ltda. ("OPKO Brazil"), a Brazilian entity domiciled in Sao Paulo, respectively. OPKO Uruguay Ltda. and OPKO Brazil will expand our presence in Latin America and complement the business activities of our operations in Chile and Mexico, as well as facilitate future market entry for our products in development.

In December 2012, we completed the acquisition of OPKO Lab, a Nashville-based CLIA-certified laboratory with several phlebotomy sites throughout the U.S. and an experienced national sales force calling primarily on urologists. In addition to continuing to operate as a full-service medical laboratory specializing in urologic pathology, OPKO Lab provides us with a commercial platform to support the U.S. commercial launch of the 4Kscore as an LDT and may be helpful in speeding the development and introduction of other important tests.

In August 2012, we completed the acquisition of Farmadiet Group Holding, S.L. ("OPKO Health Europe"), a Spanish company with 20 years of experience engaged in the development, manufacture, marketing, and sale of pharmaceutical, nutraceutical, and veterinary products in Europe.

In April 2012, we completed the acquisition of ALS Distribuidora Limitada ("ALS"), a privately-held Chilean pharmaceutical company engaged in the business of importation, commercialization and distribution of pharmaceutical products for private markets in Chile. ALS started operations in 2009 as the exclusive product distributor of Arama Laboratorios y Compañía Limitada ("Arama"), a company with more than 20 years of experience in the pharmaceutical products market. In connection with the transaction, OPKO acquired all of the product registrations and trademarks previously owned by Arama, as well as the Arama name.

In February 2010, we completed the acquisition of Pharmacos Exakta S.A. de C.V. ("Exakta-OPKO"), a Mexican pharmaceutical business engaged in the manufacture, marketing, sale, and distribution of ophthalmic and other pharmaceutical products to private and public customers in Mexico. Exakta-OPKO manufacturers and sells products primarily in the generics market in Mexico, although it has recently increased its focus on the development of

proprietary products as well.

In October 2009, we completed the acquisition of Pharma Genexx, S.A. (“OPKO Chile”). OPKO Chile markets, sells and distributes pharmaceutical and natural products to the private, hospital, pharmacy and public institutional markets in Chile for a wide range of indications, including, cardiovascular products, vaccines, antibiotics, gastro-intestinal products, and hormones, among others.

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Strategic Investments

We have and may continue to make investments in other early stage companies that we perceive to have valuable proprietary technology and significant potential to create value for OPKO as a shareholder. At December 31, 2014, we also hold investments in Zebra Biologics, Inc. ("Zebra"), a biotechnology company focused on the discovery and development of biosuperior antibody therapeutics and complex drugs, ARNO Therapeutics, Inc., a clinical stage company focused on the development of oncology drugs, OAO Pharmsynthez, a Russian pharmaceutical company traded on the Moscow Stock Exchange, RXi Pharmaceuticals Corporation, a biotechnology company focused on discovering, developing and commercializing innovative therapies using RNA-targeted technologies, SciVac Ltd, an Israeli company that produces a third-generation hepatitis B vaccine, Cocrystal Pharma, Inc., a biotechnology company developing new treatments for viral diseases, ChromaDex Corporation, a provider of proprietary ingredients and products for the dietary supplement, food and beverage, animal health, cosmetic and pharmaceutical industries, Neovasc Inc. ("Neovasc"), a publicly-traded medical technology company, Sevion Therapeutics, Inc., a biopharmaceutical company which discovers and develops entirely new therapeutic classes for the treatment of cancer and immunological diseases, and Non-Invasive Monitoring Systems, Inc., a company engaged in the research, development, manufacturing and marketing of a line of motorized, non-invasive, whole body, periodic acceleration platforms.

Instrumentation Business

In October 2011, we completed the sale of our ophthalmic instrumentation business to OPTOS, Inc., a subsidiary of Optos plc.

RESEARCH AND DEVELOPMENT EXPENSES

During the years ended December 31, 2014, 2013, and 2012, we incurred $83.6 million, $53.9 million, and $19.5 million, respectively, of research and development expenses related to our various product candidates. During the years ended December 31, 2014 and 2013, our research and development expenses primarily consisted of OPKO Renal and OPKO Biologics development programs including expenses related to the ongoing phase 3 clinical trials for Rayaldee (CTAP101) and the development of hGH-CTP. During the year ended December 31, 2012, our research and development expenses primarily consisted of our molecular diagnostic programs and activities related to the development programs acquired from OPKO Diagnostics and CURNA.

INTELLECTUAL PROPERTY

We believe that technology innovation is driving breakthroughs in healthcare. We have adopted a comprehensive intellectual property strategy which blends the efforts to innovate in a focused manner with the efforts of our business development activities to strategically in-license intellectual property rights. We develop, protect, and defend our own intellectual property rights as dictated by the developing competitive environment. We value our intellectual property assets and believe we have benefited from early and insightful efforts at understanding diagnostics, as well as the disease and the molecular basis of potential pharmaceutical intervention.

We actively seek, when appropriate and available, protection for our products and proprietary information by means of U.S. and foreign patents, trademarks, trade secrets, copyrights, and contractual arrangements. Patent protection in the pharmaceutical and diagnostic fields, however, can involve complex legal and factual issues. There can be no assurance that any steps taken to protect such proprietary information will be effective.

Because the patent positions of pharmaceutical, biotechnology, and diagnostics companies are highly uncertain and involve complex legal and factual questions, the patents owned and licensed by us, or any future patents, may not prevent other companies from developing similar or therapeutically equivalent products or ensure that others will not be issued patents that may prevent the sale of our products or require licensing and the payment of significant fees or royalties. Furthermore, to the extent that any of our future products or methods are not patentable, that such products or methods infringe upon the patents of third parties, or that our patents or future patents fail to give us an exclusive position in the subject matter claimed by those patents, we will be adversely affected. We may be unable to avoid infringement of third party patents and may have to obtain a license, defend an infringement action, or challenge the validity of the patents in court. A license may be unavailable on terms and conditions acceptable to us, if at all. Patent litigation is costly and time consuming, and we may be unable to prevail in any such patent litigation or devote sufficient resources to even pursue such litigation.

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LICENSES AND COLLABORATIVE RELATIONSHIPS

Our strategy is to develop a portfolio of product candidates through a combination of internal development, acquisition, and external partnerships. Collaborations are key to our strategy and we continue to build relationships and forge partnerships in various areas where unmet medical need and commercial opportunities exist. In December 2014, we entered into an exclusive agreement with Pfizer for the development and commercialization of our long-acting hGH-CTP for the treatment of GHD in adults and children, as well as for the treatment of growth failure in children born small for gestational age. Previously, we (or entities we have acquired) have completed strategic licensing transactions with the University of Texas Southwestern Medical Center at Dallas, the President and Fellows of Harvard College, Academia Sinica, The Scripps Research Institute, TESARO, INEOS Healthcare, Arctic Partners, and Washington University, among others.

COMPETITION

The pharmaceutical and diagnostic industries are highly competitive and require an ongoing, extensive search for technological innovation. The industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. They also require, among other things, the ability to effectively discover, develop, test and obtain regulatory approvals for products, as well as the ability to effectively commercialize, market and promote approved products.

We intend to leverage our technological innovation and proprietary position to effectively compete in the pharmaceutical and biopharmaceutical markets. We are seeking to commercialize our 4Kscore product in the U.S. in a laboratory setting and to capitalize on near-term commercialization opportunities for our proprietary diagnostic point-of-care system by transitioning laboratory-based tests, including the 4Kscore, PSA, vitamin D, and testosterone, to our point-of-care system. Numerous companies, however, including major pharmaceutical companies, specialty pharmaceutical companies and specialized biotechnology companies, are engaged in the development, manufacture and marketing of pharmaceutical products competitive with those that we intend to commercialize ourselves and through our partners. Competitors to our diagnostics business and laboratory business are many and include major diagnostic companies, reference laboratories, molecular diagnostic firms, universities and research institutions. Most of these companies have substantially greater financial and other resources, larger research and development staffs and more extensive marketing and manufacturing organizations than ours. This enables them, among other things, to make greater research and development investments and efficiently utilize their research and development costs, as well as their marketing and promotion costs, over a broader revenue base. This also provides our competitors with a competitive advantage in connection with the highly competitive product acquisition and product in-licensing process, which may include auctions in which the highest bidder wins. Our competitors may also have more experience and expertise in obtaining marketing approvals from the FDA and other regulatory authorities. In addition to product development, testing, approval, and promotion, other competitive factors in the pharmaceutical industry include industry consolidation, product quality and price, product technology, reputation, customer service, and access to technical information.

Our ability to commercialize our pharmaceutical and diagnostic test product candidates and compete effectively will depend, in large part, on:

- our ability to meet all necessary regulatory requirements to advance our product candidates through clinical trials and the regulatory approval process in the U.S. and abroad;
- the perception by physicians and other members of the health care community of the safety, efficacy, and benefits of our products compared to those of competing products or therapies;
- our ability to manufacture products we may develop on a commercial scale;
- the effectiveness of our sales and marketing efforts;
- the willingness of physicians to adopt a new diagnostic or treatment regimen represented by our technology;
- our ability to secure reimbursement for our product candidates,
- the price of the products we may develop and commercialize relative to competing products;
- our ability to accurately forecast and meet demand for our product candidates if regulatory approvals are achieved;
- our ability to develop a commercial scale infrastructure either on our own or with a collaborator, which would include expansion of existing facilities, including our manufacturing facilities, development of a sales and distribution

network, and other operational and financial systems necessary to support our increased scale;

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- our ability to maintain a proprietary position in our technologies; and
- our ability to rapidly expand the existing information technology infrastructure and configure existing operational, manufacturing, and financial systems (on our own or with third party collaborators) necessary to support our increased scale, which would include existing or additional facilities and or partners.

GOVERNMENT REGULATION

The U.S. government regulates healthcare through various agencies, including but not limited to the following: (i) the FDA, which administers the Federal Food, Drug and Cosmetic Act ("FDCA"), as well as other relevant laws; (ii) the Centers for Medicare & Medicaid Services ("CMS"), which administers the Medicare and Medicaid programs; (iii) the Office of Inspector General ("OIG"), which enforces various laws aimed at curtailing fraudulent or abusive practices, including by way of example, the Anti-Kickback Statute, the Physician Self-Referral Law, commonly referred to as the Stark law, the Anti-Inducement Law, the Civil Money Penalty Law, and the laws that authorize the OIG to exclude healthcare providers and others from participating in federal healthcare programs; and (iv) the Office of Civil Rights, which administers the privacy aspects of the Health Insurance Portability and Accountability Act of 1996. All of the aforementioned are agencies within the Department of Health and Human Services ("HHS"). Healthcare is also provided or regulated, as the case may be, by the Department of Defense through its TriCare program, the Department of Veterans Affairs, especially through the Veterans Health Care Act of 1992, the Public Health Service within HHS under Public Health Service Act § 340B (42 U.S.C. § 256b), the Department of Justice through the Federal False Claims Act and various criminal statutes, and state governments under the Medicaid and other state sponsored or funded programs and their internal laws regulating all healthcare activities.

The testing, manufacture, distribution, advertising, and marketing of drug and diagnostic products and medical devices are subject to extensive regulation by federal, state, and local governmental authorities in the U.S., including the FDA, and by similar agencies in other countries. Any drug, diagnostic, or device product that we develop must receive all relevant regulatory approvals or clearances, as the case may be, before it may be marketed in a particular country.

Drug Development

The regulatory process, which includes overseeing preclinical studies and clinical trials of each pharmaceutical compound to establish its safety and efficacy and confirmation by the FDA that good laboratory, clinical, and manufacturing practices were maintained during testing and manufacturing, can take many years, requires the expenditure of substantial resources, and gives larger companies with greater financial resources a competitive advantage over us. Delays or terminations of clinical trials that we undertake would likely impair our development of product candidates. Delays or terminations could result from a number of factors, including stringent enrollment criteria, slow rate of enrollment, size of patient population, having to compete with other clinical trials for eligible patients, geographical considerations, and others.

Although accelerated pathways for approval exist for certain drugs, generally, FDA review processes can be lengthy and unpredictable, and we may encounter delays or rejections of our applications when submitted. Generally, in order to gain FDA approval, we must first conduct preclinical studies in a laboratory and in animal models to obtain preliminary information on a compound and to identify any safety problems. The results of these studies are submitted as part of an IND application that the FDA must review before human clinical trials of an investigational drug can commence.

Clinical trials are normally done in three sequential phases and generally take two to five years or longer to complete. Phase 1 consists of testing the drug product in a small number of humans, normally healthy volunteers, to determine preliminary safety and tolerable dose range. Phase 2 usually involves studies in a limited patient population to evaluate the effectiveness of the drug product in humans having the disease or medical condition for which the product is indicated, determine dosage tolerance and optimal dosage, and identify possible common adverse effects and safety risks. Phase 3 consists of additional controlled testing at multiple clinical sites to establish clinical safety and effectiveness in an expanded patient population of geographically dispersed test sites to evaluate the overall benefit-risk relationship for administering the product and to provide an adequate basis for product labeling. Phase 4 clinical trials may be conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication.

After completion of clinical trials of a new drug product, FDA and foreign regulatory authority marketing approval must be obtained. Assuming that the clinical data support the product's safety and effectiveness for its intended use, a NDA is submitted to the FDA for its review. Generally, it takes one to three years to obtain approval. If questions arise during the FDA review process, approval may take a significantly longer period of time. The testing and approval processes require substantial time and effort and we may not receive approval on a timely basis, if at all, or the approval that we receive may be for a narrower indication than we had originally sought, potentially undermining the commercial viability of the product. Even if regulatory approvals are obtained, a marketed product is subject to continual review, and later discovery of previously unknown problems or failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a

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product or withdrawal of the product from the market as well as possible civil or criminal sanctions. For marketing outside the U.S., we also will be subject to foreign regulatory requirements governing human clinical trials and marketing approval for pharmaceutical products. The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary widely from country to country.

None of our pharmaceutical products under development have been approved for marketing in the U.S. or elsewhere. We may not be able to obtain regulatory approval for any such products under development in a timely manner, if at all. Failure to obtain requisite governmental approvals or failure to obtain approvals of the scope requested will delay or preclude us, or our licensees or marketing partners, from marketing our products, or limit the commercial use of our products, and thereby would have a material adverse effect on our business, financial condition, and results of operations. See “Risk Factors — The results of pre-clinical trials and previous clinical trials for our products may not be predictive of future results, and our current and planned clinical trials may not satisfy the requirements of the FDA or other non-U.S. regulatory authorities.”

Device Development

Devices are subject to varying levels of premarket regulatory control, the most comprehensive of which requires that a clinical evaluation be conducted before a device receives approval for commercial distribution. The FDA classifies medical devices into one of three classes: Class I devices are relatively simple and can be manufactured and distributed with general controls; Class II devices are somewhat more complex and require greater scrutiny; Class III devices are new and frequently help sustain life.

In the U.S., a company generally can obtain permission to distribute a new device in one of two ways. The first applies to any device that is substantially equivalent to a device first marketed prior to May 1976, or to another device marketed after that date, but which was substantially equivalent to a pre-May 1976 device. These devices are either Class I or Class II devices. To obtain FDA permission to distribute the device, a company generally must submit a section 510(k) submission, and receive an FDA order finding substantial equivalence to a predicate device (pre-May 1976 or post-May 1976 device that was substantially equivalent to a pre-May 1976 device) and permitting commercial distribution of that device for its intended use. A 510(k) submission must provide information supporting a claim of substantial equivalence to the predicate device. If clinical data from human experience are required to support the 510(k) submission, these data must be gathered in compliance with investigational device exemption (“IDE”), regulations for investigations performed in the U.S. The 510(k) process is normally used for products of the type that the Company proposes distributing. The FDA review process for premarket notifications submitted pursuant to section 510(k) takes, on average, about 90 days, but it can take substantially longer if the FDA has concerns, and there is no guarantee that the FDA will “clear” the device for marketing, in which case the device cannot be distributed in the U.S. There is also no guarantee that the FDA will deem the applicable device subject to the 510(k) process, as opposed to the more time-consuming, resource-intensive and problematic, PMA process described below.

The second, more comprehensive, PMA process, which can take a year or longer, applies to a new device that is not substantially equivalent to a pre-1976 product or that is to be used in supporting or sustaining life or preventing impairment. These devices are normally Class III devices. For example, most implantable devices are subject to the approval process. Two steps of FDA approval are generally required before a company can market a product in the U.S. that is subject to approval, as opposed to clearance. First, a company must comply with IDE regulations in connection with any human clinical investigation of the device. These regulations permit a company to undertake a clinical study of a “non-significant risk” device without formal FDA approval. Prior express FDA approval is required if the device is a significant risk device. Second, the FDA must review the company’s PMA application, which contains, among other things, clinical information acquired under the IDE. The FDA will approve the PMA application if it finds there is reasonable assurance that the device is safe and effective for its intended use. The PMA process takes substantially longer than the 510(k) process and it is conceivable that the FDA would not agree with our assessment that a device that we propose to distribute should be a Class I or Class II device. If that were to occur we would be required to undertake the more complex and costly PMA process. However, for either the 510(k) or the PMA process, the FDA could require us to run clinical trials, which would pose all of the same risks and uncertainties associated with the clinical trials of drugs, described above.

Even when a clinical study has been approved by the FDA or deemed approved, the study is subject to factors beyond a manufacturer's control, including, but not limited to the fact that the institutional review board at a given clinical site might not approve the study, might decline to renew approval which is required annually, or might suspend or terminate the study before the study has been completed. Also, the interim results of a study may not be satisfactory, leading the sponsor to terminate or suspend the study on its own initiative or the FDA may terminate or suspend the study. There is no assurance that a clinical study at any given site will progress as anticipated; there may be an insufficient number of patients who qualify for the study or who agree to participate in the study or the investigator at the site may have priorities other than the study. Also, there can be no assurance that the clinical study will provide sufficient evidence to assure the FDA that the product is safe and effective, a prerequisite for FDA approval of a PMA, or substantially equivalent in terms of safety and effectiveness to a predicate device, a

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prerequisite for clearance under 510(k). Even if the FDA approves or clears a device, it may limit its intended uses in such a way that manufacturing and distributing the device may not be commercially feasible. For marketing outside the U.S., we also will be subject to foreign regulatory requirements governing clinical trials and marketing approval for medical devices. The requirements governing the conduct of clinical trials, device clearance/approval, pricing, and reimbursement vary widely from country to country. In addition to the regulatory clearance and approval processes described herein, the FDA periodically issues draft guidance documents designed to provide additional detail on or reform aspects of the 510(k) and PMA clearance and approval processes. To the extent the FDA finalizes and implements these documents, the average 510(k) and PMA submission requirements and review times may change and devices that might previously have been cleared under the 510(k) process may require approval under the PMA process (and vice-versa). Additionally, the Medical User Fee Amendments of 2012 authorized the FDA to collect user fees for the review of certain premarket submissions received on or after October 1, 2012, including 510(k) and PMA applications. These fees are intended to improve the device review process, but it is still too early to assess the actual impact on the industry.

After clearance or approval to market is given, the FDA and foreign regulatory agencies, upon the occurrence of certain events, are authorized under various circumstances to withdraw the clearance or approval or require changes to a device, its manufacturing process or its labeling or additional proof that regulatory requirements have been met.

A manufacturer of a device approved through the PMA is not permitted to make changes to the device, which affects its safety or effectiveness without first submitting a supplement application to its PMA and obtaining FDA approval for that supplement. In some instances, the FDA may require clinical trials to support a supplement application. A manufacturer of a device cleared through the 510(k) process must submit another premarket notification if it intends to make a change or modification in the device that could significantly affect the safety or effectiveness of the device, such as a significant change or modification in design, material, chemical composition, energy source or manufacturing process. Any change in the intended uses of a PMA device or a 510(k) device requires an approval supplement or cleared premarket notification. Exported devices are subject to the regulatory requirements of each country to which the device is exported, as well as certain FDA export requirements.

A company that intends to manufacture medical devices is required to register with the FDA before it begins to manufacture the device for commercial distribution. As a result, we and any entity that manufactures products on our behalf will be subject to periodic inspection by the FDA for compliance with the FDA's Quality System Regulation requirements and other regulations. In the European Community, we will be required to maintain certain International Organization for Standardization ("ISO"), certifications in order to sell products and we or our manufacturers undergo periodic inspections by notified bodies to obtain and maintain these certifications. These regulations require us or our manufacturers to manufacture products and maintain documents in a prescribed manner with respect to design, manufacturing, testing and control activities. Further, we are required to comply with various FDA and other agency requirements for labeling and promotion. The Medical Device Reporting regulations require that we provide information to the FDA whenever there is evidence to reasonably suggest that a device may have caused or contributed to a death or serious injury or, if a malfunction were to occur, could cause or contribute to a death or serious injury. In addition, the FDA prohibits us from promoting a medical device for unapproved indications.

Diagnostic Products

Our diagnostic products in development are subject to regulation by the FDA and similar international health authorities. We have an obligation to adhere to the FDA's cGMP regulations. Additionally, we are subject to periodic FDA inspections, quality control procedures, and other detailed validation procedures. If the FDA finds deficiencies in the validation of our manufacturing and quality control practices, they may impose restrictions on marketing specific products until corrected.

Regulation by governmental authorities in the U.S. and other countries may be a significant factor in how we develop, test, produce and market our diagnostic test products. Diagnostic tests like ours may not fall squarely within the regulatory approval process for pharmaceutical or device products as described above, and the regulatory pathway is not as clear. Although the FDA regulates in vitro diagnostic devices, some companies have successfully commercialized diagnostic tests for various conditions and disease states without seeking clearance or approval for such tests through a 510(k) or PMA approval process. These tests are known as laboratory developed tests ("LDTs") and

are designed, manufactured, and used within a single laboratory that is certified under the Clinical Laboratory Improvement Amendments of 1988 (“CLIA”). CLIA is a federal law that regulates clinical laboratories that perform testing on specimens derived from humans for the purpose of providing information for diagnostic, preventative or treatment purpose. Such LDT testing is currently under the purview of CMS and state agencies that provide oversight of the safe and effective use of LDTs.

However, the FDA has consistently asserted that it has the regulatory authority to regulate LDTs despite historically exercising enforcement discretion. In furtherance of that position, the FDA issued two draft guidance documents in October

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2014: (1) Framework for Regulatory Oversight of Laboratory Developed Tests (the "Framework Guidance"); and (2) FDA Notification and Medical Device Reporting for Laboratory Developed Tests (the "Notification Guidance"). The Framework Guidance outlines the FDA's plan to adopt over time a risk-based approach to regulating LDTs whereby different classifications of LDTs would be subject to different levels of FDA oversight and enforcement, including, for example, prohibitions on adulteration and misbranding, establishment registration and device listing, premarket notification, banned devices, records and reports, good manufacturing practices, adverse event reporting, premarket review of safety, effectiveness, and clinical validity, and quality system requirements. The Notification Guidance is intended to explain how clinical laboratories should notify the FDA of the LDTs they develop and how to satisfy Medical Device Reporting requirements.

If finalized, the Framework Guidance and the Notification Guidance may have a materially adverse affect on the time, cost, and risk associated with the Company's development and commercialization of LDTs for the U.S. market, and there can be no assurance that clearances or approvals sought by the Company will be granted and maintained. However, the FDA's authority to regulate LDTs continues to be challenged, and the timeline and process for finalizing the draft guidance documents is unknown. We will continue to monitor changes to all domestic and international LDT regulatory policy so as to ensure compliance with the current regulatory scheme.

CLIA Laboratories

Our CLIA certified laboratories are subject to CLIA regulations, which are designed to ensure the quality and reliability of clinical laboratories by mandating specific standards in the areas of personnel qualifications, administration and participation in proficiency testing, patient test management, quality control, quality assurance and inspections. Laboratories must undergo on-site surveys at least every two years, which may be conducted by the Federal CLIA program or by a private CMS approved accrediting agency. The sanction for failure to comply with CLIA requirements may be suspension, revocation or limitation of a laboratory's CLIA certificate, which is necessary to conduct business, as well as significant fines and/or criminal penalties. We are also subject to regulation of laboratory operations under state clinical laboratory laws. State clinical laboratory laws may require that laboratories and/or laboratory personnel meet certain qualifications, specify certain quality controls or require maintenance of certain records. Certain states, such as California and Florida, each require that we obtain licenses to test specimens from patients residing in those states and additional states may require similar licenses in the future. Only Washington and New York State are exempt under CLIA, as these states have established laboratory quality standards at least as stringent as CLIA's. Potential sanctions for violation of these statutes and regulations include significant fines and the suspension or loss of various licenses, certificates and authorizations.

Impact of Regulation

The FDA in the course of enforcing the FDCA may subject a company to various sanctions for violating FDA regulations or provisions of the FDCA, including requiring recalls, issuing Warning Letters, seeking to impose civil money penalties, seizing devices that the agency believes are non-compliant, seeking to enjoin distribution of a specific type of device or other product, seeking to revoke a clearance or approval, seeking disgorgement of profits and seeking to criminally prosecute a company and its officers and other responsible parties.

The levels of revenues and profitability of biopharmaceutical companies may be affected by the continuing efforts of government and third party payers to contain or reduce the costs of health care through various means. For example, in certain foreign markets, pricing or profitability of therapeutic and other pharmaceutical products is subject to governmental control. In the U.S., there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental control. In addition, in the U.S. and elsewhere, sales of therapeutic and other pharmaceutical products are dependent in part on the availability and adequacy of reimbursement from third party payers, such as the government or private insurance plans. Third party payers are increasingly challenging established prices, and new products that are more expensive than existing treatments may have difficulty finding ready acceptance unless there is a clear therapeutic benefit. On April 1, 2014, the Protecting Access to Medicare Act of 2014 ("PAMA") was enacted into law. Under PAMA, Medicare payment for clinical diagnostic laboratory tests will be established by calculating a weighted mean of private payer rates starting in 2017. Further, applicable laboratories will be required to report payment rates for covered tests starting in 2016. Failure to report such data may result in a civil money penalty in an amount of up to $10,000 per day. It is anticipated that the

market-based payment system will result in lower reimbursement rates for clinical diagnostic laboratory tests. Even though the permitted annual decrease will be capped through 2022, the cap does not apply to new tests or new advanced diagnostic tests. We cannot assure you that any of our products will be considered cost effective, or that reimbursement will be available or sufficient to allow us to sell them competitively and profitably.

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State and Federal Security and Privacy Regulations

The privacy and security regulations under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (the "HITECH Act", and collectively, "HIPAA"), establish comprehensive federal standards with respect to the uses and disclosures of protected health information, or PHI, by health plans and health care providers, in addition to setting standards to protect the confidentiality, integrity and availability of electronic PHI. The regulations establish a complex regulatory framework on a variety of subjects, including:

- the circumstances under which uses and disclosures of PHI are permitted or required without a specific authorization by the patient, including but not limited to treatment purposes, to obtain payments for services and health care operations activities;
- a patient's rights to access, amend and receive an accounting of certain disclosures of PHI;
- the content of notices of privacy practices for PHI; and
- administrative, technical and physical safeguards required of entities that use or receive PHI electronically.

The final "omnibus" rule implementing the HITECH Act took effect on March 26, 2013. The rule is broad in scope, but certain provisions are particularly significant in light of our business operations. For example, the final "omnibus" rule implementing the HITECH Act:

- Makes clear that situations involving impermissible access, acquisition, use or disclosure of protected health information are now presumed to be a breach unless the covered entity or business associate is able to demonstrate that there is a low probability that the information has been compromised;
- Defines the term "business associate" to include subcontractors and agents that receive, create, maintain or transmit protected health information on behalf of the business associate;
- Establishes new parameters for covered entities and business associates on uses and disclosures of PHI for fundraising and marketing; and
- Establishes clear restrictions on the sale of PHI without patient authorization.

As a provider of clinical laboratory services and as we launch commercial diagnostic tests, we must continue to implement policies and procedures related to compliance with the HIPAA privacy and security regulations, as required by law. The privacy and security regulations provide for significant fines and other penalties for wrongful use or disclosure of PHI, including potential civil and criminal fines and penalties.

Anti-Kickback Laws, Physician Self-Referral Laws, False Claims Act, Civil Monetary Penalties

We are also subject to various federal, state, and international laws pertaining to health care "fraud and abuse," including anti-kickback laws and false claims laws. The federal Anti-Kickback Statute prohibits anyone from knowingly and willfully soliciting, receiving, offering, or paying any remuneration with the intent to refer, or to arrange for the referral or order of, services or items payable under a federal health care program, including the purchase or prescription of a particular drug or the use of a service or device. Recognizing that the Anti-Kickback Statute is broad and may technically prohibit many innocuous or beneficial arrangements, Congress authorized the U.S. Department of Health and Human Services Office of Inspector General, or OIG, to issue a series of regulations, known as "safe harbors." These safe harbors set forth requirements that, if met in their entirety, will assure health care providers and other parties that they will not be prosecuted under the Anti-Kickback Statute. The failure of a transaction or arrangement to fit precisely within one or more safe harbors does not necessarily mean that it is illegal, or that prosecution will be pursued. However, conduct and business arrangements that do not fully satisfy each applicable safe harbor may result in increased scrutiny by government enforcement authorities, such as the OIG.

Violations of the Anti-Kickback Statute are punishable by the imposition of criminal fines, civil money penalties, treble damages, and/or exclusion from participation in federal health care programs. Many states have also enacted similar anti-kickback laws. The Anti-Kickback Statute and similar state laws and regulations are expansive. If the government were to allege against or convict us of violating these laws, there could be a material adverse effect on our business, results of operations, financial condition, and our stock price. Even an unsuccessful challenge could cause adverse publicity and be costly to respond to, which could have a materially adverse effect on our business, results of operations and financial condition. We will consult counsel concerning the potential application of these and other

laws to our business and our sales, marketing and other activities and will make good faith efforts to comply with them. However, given the broad reach of federal and state

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anti-kickback laws and the increasing attention given by law enforcement authorities, we are unable to predict whether any of our activities will be challenged or deemed to violate these laws.

We are also subject to the physician self-referral laws, commonly referred to as the Stark law, which is a strict liability statute that generally prohibits physicians from referring Medicare patients to providers of "designated health services," including clinical laboratories, with whom the physician or the physician's immediate family member has an ownership interest or compensation arrangement, unless an applicable exception applies. Moreover, many states have adopted or are considering adopting similar laws, some of which extend beyond the scope of the Stark law to prohibit the payment or receipt of remuneration for the prohibited referral of patients for designated healthcare services and physician self-referrals, regardless of the source of the payment for the patient's care. If it is determined that certain of our practices or operations violate the Stark law or similar statutes, we could become subject to civil and criminal penalties, including exclusion from the Medicare programs and loss of government reimbursement. The imposition of any such penalties could harm our business.

Another development affecting the health care industry is the increased use of the federal civil False Claims Act and, in particular, actions brought pursuant to the False Claims Act's "whistleblower" or "qui tam" provisions. The False Claims Act, as amended by the Fraud Enforcement and Recovery Act of 2009 and the Patient Protection and Affordable Care Act of 2010, imposes liability on any person or entity who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal health care program. We submit claims for services performed at our laboratories. The qui tam provisions of the False Claims Act allow a private individual to bring actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically. In addition, various states have enacted false claim laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third-party payor and not merely a federal health care program. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties for each separate false claim. There are many potential bases for liability under the False Claims Act. Liability arises, primarily, when an entity knowingly submits, or causes another to submit, a false claim for reimbursement to the federal government. The False Claims Act has been used to assert liability on the basis of inadequate care, kickbacks and other improper referrals, improper use of Medicare numbers when detailing the provider of services, and allegations as to misrepresentations with respect to the services rendered. Our activities relating to the sale and marketing of our products may be subject to scrutiny under these laws. We are unable to predict whether we would be subject to actions under the False Claims Act or a similar state law, or the impact of such actions. However, the costs of defending such claims, as well as any sanctions imposed, could significantly adversely affect our financial performance.

Further, federal law prohibits any entity from offering or transferring to a Medicare or Medicaid beneficiary any remuneration that the entity knows or should know is likely to influence the beneficiary's selection of a particular provider, practitioner or supplier of Medicare or Medicaid payable items or services, including waivers of copayments and deductible amounts (or any part thereof) and transfers of items or services for free or for other than fair market value. Entities found in violation may be liable for civil monetary penalties of up to $10,000 for each wrongful act. Although we believe that our sales and marketing practices are in material compliance with all applicable federal and state laws and regulations, relevant regulatory authorities may disagree and violation of these laws, or, our exclusion from such programs as Medicaid and other governmental programs as a result of a violation of such laws, could have a material adverse effect on our business, results of operations, financial condition and cash flows.

Foreign Corrupt Practices Act

We are also subject to the U.S. Foreign Corrupt Practices Act ("FCPA"), which prohibits corporations and individuals from paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect their transactions and to devise and maintain an adequate system of internal accounting controls. Our international activities create the risk of unauthorized payments or offers of payments by our employees, consultants, sales agents or distributors, even though they may not always be subject

to our control. We discourage these practices by our employees and agents. However, our existing safeguards and any future improvements may prove to be less than effective, and our employees, consultants, sales agents or distributors may engage in conduct for which we might be held responsible. Any failure by us to adopt appropriate compliance procedures and ensure that our employees and agents comply with the FCPA and applicable laws and regulations in foreign jurisdictions could result in substantial penalties or restrictions on our ability to conduct business in certain foreign jurisdictions.

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MANUFACTURING AND QUALITY

Other than our facilities in Guadalajara, Mexico, Nesher, Israel, and Banyoles, Spain, we currently have no pharmaceutical manufacturing facilities. We have entered into agreements with various third parties for the formulation and manufacture of our pharmaceutical clinical supplies. These suppliers and their manufacturing facilities must comply with FDA regulations, current good laboratory practices ("cGLPs") and current good manufacturing practices ("cGMPs"). We plan to outsource the manufacturing and formulation of our clinical supplies. The FDA and similar regulatory bodies may inspect our facilities and the facilities of those who manufacture on our behalf worldwide. If the FDA or similar regulatory bodies inspecting our facilities or the facilities of our suppliers find regulatory violations in manufacturing and quality control practices or procedures they may require us to cease partial or complete manufacturing operations until the violations are corrected. They may also impose restrictions on distribution of specific products until the violations are corrected.

Our point-of-care diagnostic system consists of a disposable test cassette and an analyzer. We prepare all necessary test reagents and assemble and package the disposable cassettes at our facility in Woburn, Massachusetts. We rely on third parties for the manufacture of the analyzer.

We are committed to providing high quality products to our customers, and we plan to meet this commitment by working diligently to continue implementing updated and improved quality systems and concepts throughout our organization.

SALES & MARKETING

We currently do not have pharmaceutical or diagnostics sales or marketing personnel in the U.S. other than the sales force for the OPKO Lab business, and we have limited personnel in Chile, Spain, Mexico, Israel, Uruguay and Brazil. In order to commercialize any pharmaceutical or diagnostic products that are approved for commercial sale, we must either build a sales and marketing infrastructure or collaborate with third parties with sales and marketing experience.

EMPLOYEES

As of December 31, 2014, we had 674 full-time employees worldwide. None of our employees are represented by a collective bargaining agreement.

Code of Ethics

We have adopted a Code of Business Conduct and Ethics. We require all employees, including our principal executive officer and principal accounting officer and other senior officers and our employee directors, to read and to adhere to the Code of Business Conduct and Ethics in discharging their work-related responsibilities. Employees are required to report any conduct that they believe in good faith to be an actual or apparent violation of the Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics is available on our website at http://www.OPKO.com.

Available Information

We make available free of charge on or through our web site, at www.opko.com, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports as soon as reasonably practicable after such material is electronically filed with the SEC. Additionally, the public may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Room 1580, Washington, D.C., 20549. Information regarding operation of the Public Reference Room is available by calling the SEC at 1-800-SEC-0330. Information that we file with the SEC is also available at the SEC's Web-site at www.sec.gov.

ITEM 1A. RISK FACTORS.

You should carefully consider the risks described below, as well as other information contained in this report, including the consolidated financial statements and the notes thereto and "Management's Discussion and Analysis of Financial Condition and Results of Operations." The occurrence of any of the events discussed below could significantly and adversely affect our business, prospects, results of operations, financial condition, and cash flows.

RISKS RELATED TO OUR BUSINESS

We have a history of operating losses and we do not expect to become profitable in the near future.

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We are a healthcare company with a limited operating history. We are not profitable and have incurred losses since our inception. We do not anticipate that we will generate revenue from the sale of proprietary pharmaceutical products or certain of our diagnostic products for some time and we have generated only limited revenue from our pharmaceutical operations in Chile, Mexico, Israel, Spain, and Uruguay, from our ophthalmic instrumentation business, which we sold in October 2011, and from sale of the 4Kscore. Although we launched sales of 4Kscore in 2014, and we plan to launch certain other diagnostics products in the near future, we may not generate substantial revenue from the sale of these products for some time or at all. We have not yet submitted any pharmaceutical products for marketing approval or clearance by regulatory authorities and we do not currently have rights to any pharmaceutical product candidates that have been approved for marketing, other than those products sold by our Chilean, Mexican, Israeli, Spanish, and Uruguayan subsidiaries. We continue to incur research and development and general and administrative expenses related to our operations and, to date, we have devoted most of our financial resources to research and development, including our pre-clinical development activities and clinical trials. We expect to continue to incur losses from our operations for the foreseeable future, and we expect these losses to increase as we continue our research activities and conduct development of, and seek regulatory approvals and clearances for, our product candidates, and prepare for and begin to commercialize any approved or cleared products. If our product candidates fail in clinical trials or do not gain regulatory approval or clearance, or if our product candidates do not achieve market acceptance, we may never become profitable. In addition, if we are required by the U.S. Food and Drug Administration ("FDA"), to perform studies in addition to those we currently anticipate, our expenses will increase beyond current expectations and the timing of any potential product approval may be delayed. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

We may require substantial additional funding, which may not be available to us on acceptable terms, or at all.

We are advancing and intend to continue to advance multiple product candidates through clinical and pre-clinical development. As of December 31, 2014, we have cash and cash equivalents of $96.9 million. In January 2015, we completed our exclusive worldwide agreement with Pfizer for the development and commercialization of our long-acting hGH-CTP. Under the terms of the agreements with Pfizer, we received non-refundable and non-creditable upfront payments of $295 million and are eligible to receive up to an additional $275 million upon the achievement of certain regulatory milestones. In addition, we are eligible to receive initial royalty payments associated with the commercialization of hGH-CTP for Adult GHD. Upon the launch of hGH-CTP for Pediatric GHD, the royalties will transition to a regional, tiered gross profit sharing for both hGH-CTP and Pfizer's Genotropin®. We are responsible for development expense under the agreement up to an agreed cap which may be exceeded in certain circumstances.

We believe we have sufficient cash and cash equivalents on hand or available to us through lines of credit to meet our anticipated cash requirements for operations and debt service beyond the next 12 months. We have based this estimate on assumptions that may prove to be wrong or subject to change, and we may be required to use our available capital resources sooner than we currently expect or curtail aspects of our operations in order to preserve our capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates and the success of our relationship with Pfizer, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials. Our future capital requirements will depend on a number of factors, including the continued progress of our research and development of product candidates, the timing and outcome of clinical trials and regulatory approvals, the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing patent claims and other intellectual property rights, the status of competitive products, the availability of financing, and our success in developing markets for our product candidates.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to finance future cash needs primarily through public or private equity offerings, debt financings, or strategic collaborations. Our ability to obtain additional capital may depend on prevailing economic conditions and financial, business and other factors beyond our control. Disruptions in the U.S. and global financial markets may adversely impact the availability and cost of credit, as well as our ability to raise money in the capital markets. Economic conditions have been, and continue to be, volatile. Continued instability in these market conditions may limit our ability to replace, in a timely manner, maturing liabilities and access the capital necessary to fund and grow

our business. There can be no assurance that additional capital will be available to us on acceptable terms, or at all, which could adversely impact our business, results of operations, liquidity, capital resources and financial condition. If we are not able to secure additional funding when needed, we may have to delay, reduce the scope of, or eliminate one or more of our clinical trials or research and development programs. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience additional significant dilution, and debt financing, if available, may involve restrictive covenants. To the extent that we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish some rights to our technologies or our product candidates or grant licenses on terms that may not be favorable to us. We may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time.

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The conversion and redemption features of our 2033 Senior Notes are classified as embedded derivatives and may continue to result in volatility in our financial statements, including having a material impact on our results of operations and the derivative liability recorded.

The conversion rights and redemption options of our 2033 Senior Notes are classified as embedded derivatives and as a result, are marked-to-market to reflect their fair value at each reporting period. The fair value of the embedded derivatives is influenced by a variety of factors, including the actual and anticipated behavior of the holders of the 2033 Senior Notes, the expected volatility of our Common Stock price and our Common Stock price as of the fair value measurement date. Some of these factors are outside of our control. As a result, changes in these factors may have a material impact on our results of operations and the derivative liability recorded in our Consolidated Balance Sheets. Consequently, our financial statements may vary periodically, based on factors other than our revenues and expenses.

Our technologies are in an early stage of development and are unproven.

The effectiveness of our technologies is not well-known in, or accepted generally by, the clinical medical community. There can be no assurance that we will be able to successfully employ our technologies as therapeutic, diagnostic, or preventative solutions for any disease or condition. Our failure to establish the efficacy or safety of our technologies would have a material adverse effect on our business.

In addition, we have a limited operating history. Our operations to date have been primarily limited to organizing and staffing our company, developing our technology, and undertaking pre-clinical studies and clinical trials of our product candidates. We have not yet obtained regulatory approvals for any of our pharmaceutical product or diagnostic candidates other than those products sold by our Chilean, Mexican, Israeli, Spanish, and Uruguayan subsidiaries. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Our research and development activities may not result in commercially viable products.

Many of our product candidates are in the early stages of development and are prone to the risks of failure inherent in drug, diagnostic, and medical device product development. These risks further include the possibility that such products would:

- be found to be ineffective, unreliable, or otherwise inadequate or otherwise fail to receive regulatory approval;
- be difficult or impossible to manufacture on a commercial scale;
- be uneconomical to market or otherwise not be effectively marketed;
- fail to be successfully commercialized if adequate reimbursement from government health administration authorities, private health insurers, and other organizations for the costs of these products is unavailable;
- be impossible to commercialize because they infringe on the proprietary rights of others or compete with products marketed by others that are superior; or
- fail to be commercialized prior to the successful marketing of similar products by competitors.

The results of pre-clinical trials and previous clinical trials for our products may not be predictive of future results, and our current and planned clinical trials may not satisfy the requirements of the FDA or other non-U.S. regulatory authorities.

Positive results from pre-clinical studies and early clinical trial experience should not be relied upon as evidence that later-stage or large-scale clinical trials will succeed. Likewise, there can be no assurance that the results of studies conducted by collaborators or other third parties will be viewed favorably or are indicative of our own future study results. We may be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are either (i) with respect to drugs or Class III devices, safe and effective for use in a diverse population of their intended uses or (ii) with respect to Class I or Class II devices, are substantially equivalent in terms of safety and effectiveness to devices that are already marketed under section 510(k) of the Food, Drug and Cosmetic Act. Success in early clinical trials does not mean that future clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and other non-U.S. regulatory authorities despite having progressed through initial clinical trials.

Further, our drug candidates may not be approved or cleared even if they achieve their primary endpoints in phase 3 clinical trials or registration trials. In addition our diagnostic test candidates may not be approved or cleared, as the

case may be, even though clinical or other data are, in our view, adequate to support an approval or clearance. The FDA or other non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from pre-clinical studies and

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clinical trials. In addition, any of these regulatory authorities may change requirements for the approval or clearance of a product candidate even after reviewing and providing comment on a protocol for a pivotal clinical trial that has the potential to result in FDA and other non-U.S. regulatory authorities' approval. Any of these regulatory authorities may also approve or clear a product candidate for fewer or more limited indications or uses than we request or may grant approval or clearance contingent on the performance of costly post-marketing clinical trials. The FDA or other non-U.S. regulatory authorities may not approve the labeling claims necessary or desirable for the successful commercialization of our product candidates.

The results of our clinical trials may show that our product candidates may cause undesirable side effects, which could interrupt, delay or halt clinical trials, resulting in the denial of regulatory approval by the FDA and other non-U.S. regulatory authorities.

In light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of Congress, the Government Accounting Office, medical professionals, and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products, and establishment of risk management programs that may, for instance, restrict distribution of drug products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

Our business is substantially dependent on our ability to develop, launch and generate revenue from our diagnostic programs.

Our business is substantially dependent on our ability to develop and launch diagnostic tests based on our point-of-care diagnostics platform. In addition, our business is dependent on our ability to successfully commercialize the 4Kscore. We are committing significant research and development resources to the development of diagnostic tests, and there is no guarantee that we will be able to successfully launch these tests on anticipated timelines or at all. We have limited experience in developing, manufacturing, selling, marketing or distributing diagnostic tests. If we are not able to successfully develop, market or sell diagnostic tests we develop for any reason, including the failure to obtain any required regulatory approvals, we will not generate any revenue from the sale of such tests. Even if we are able to develop effective diagnostic tests for sale in the marketplace, a number of factors could impact our ability to sell such tests or generate any significant revenue from the sale of such tests, including without limitation:

- our ability to establish and maintain adequate infrastructure to support the commercial launch and sale of our diagnostic tests, including establishing adequate laboratory space, information technology infrastructure, sample collection and tracking systems, electronic ordering and reporting systems and other infrastructure and hiring adequate laboratory and other personnel;
- the success of the validation studies for our diagnostic tests under development and our ability to publish study results in peer-reviewed journals;
- the availability of alternative and competing tests or products and technological innovations or other advances in medicine that cause our technologies to be less competitive;
- the accuracy rates of such tests, including rates of false-negatives and/or false-positives;
- concerns regarding the safety or effectiveness or clinical utility of our diagnostic tests;
- changes in the regulatory environment affecting health care and health care providers, including changes in laws regulating laboratory testing and/or device manufacturers;
- the extent and success of our sales and marketing efforts and ability to drive adoption of our diagnostic tests;
- coverage and reimbursement levels by government payors and private insurers;
- pricing pressures and changes in third-party payor reimbursement policies; and
- intellectual property rights held by others or others infringing our intellectual property rights.

Our ability to successfully develop and commercialize certain of our diagnostic tests and LDTs will depend on our ability to successfully operate our CLIA-certified laboratory and maintain required regulatory licensures.

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In December 2012, we acquired a CLIA-certified laboratory through our acquisition of OPKO Lab. In order to successfully develop and commercialize certain diagnostic tests and LDTs, we must maintain our CLIA-certified laboratory and comply with all the CLIA requirements.

CLIA is designed to ensure the quality and reliability of clinical laboratories by mandating specific standards in the areas of personnel qualifications, administration and participation in proficiency testing, patient test management, quality control, quality assurance and inspections. The sanction for failure to comply with CLIA requirements may be suspension, revocation or limitation of a laboratory's CLIA certificate, which is necessary to conduct business, as well as significant fines and/or criminal penalties. Laboratories must undergo on-site surveys at least every two years, which may be conducted by the Federal CLIA program or by a private CMS approved accrediting agency such as CAP, among others. OPKO Lab is also subject to regulation of laboratory operations under state clinical laboratory laws as will be any new CLIA-certified laboratory that we establish or acquire. State clinical laboratory laws may require that laboratories and/or laboratory personnel meet certain qualifications, specify certain quality controls or require maintenance of certain records. Certain states, such as California, Florida, Maryland, New York, Pennsylvania and Rhode Island, require that laboratories obtain licenses to test specimens from patients residing in those states and additional states may require similar licenses in the future. If we are unable to obtain and maintain licenses from states where required, we will not be able to process any samples from patients located in those states. Only Washington and New York States are exempt under CLIA, as these states have established laboratory quality standards at least as stringent as CLIA's. Potential sanctions for violation of these statutes and regulations include significant fines and the suspension or loss of various licenses, certificates and authorizations, which could adversely affect our business and results of operations.

If we fail to comply with CLIA requirements, HHS or state agencies could require us to cease diagnostic testing. Even if it were possible for us to bring our laboratory back into compliance after failure to comply with such requirements, we could incur significant expenses and potentially lose revenues in doing so. Moreover, new interpretations of current regulations or future changes in regulations under CLIA may make it difficult or impossible for us to comply with the CLIA classification, which would significantly harm our business and materially adversely affect our financial condition.

It is also possible that we do not currently have adequate infrastructure in place for the demand of future LDTs or other diagnostic tests we develop. Failure to expand our current infrastructure and laboratories to support the development and commercialization of certain diagnostic tests could adversely affect our business and results of operations.

If our competitors develop and market products that are more effective, safer or less expensive than our future product candidates, our commercial opportunities will be negatively impacted.

The pharmaceutical and diagnostic industries are highly competitive and require an ongoing, extensive search for technological innovation. Numerous companies, including major pharmaceutical companies, specialty pharmaceutical companies and specialized biotechnology companies, are engaged in the development, manufacture and marketing of pharmaceutical products competitive with those that we intend to commercialize ourselves and through our partners. Competitors to our diagnostics business are many and include major diagnostic companies, reference laboratories, molecular diagnostic firms, universities and research institutions. Most of these companies have substantially greater financial and other resources, larger research and development staffs and more extensive marketing and manufacturing organizations than ours. Large pharmaceutical and diagnostic companies, in particular, have extensive experience in clinical testing and in obtaining regulatory approvals or clearances for drugs, diagnostic tests, or medical devices. These companies also have significantly greater research and marketing capabilities than we do. Compared to us, many of our potential competitors have substantially greater capital resources, development resources, including personnel and technology, clinical trial experience, regulatory experience, expertise in prosecution of intellectual property rights, manufacturing and distribution experience, and sales and marketing experience.

We believe that our ability to successfully compete will depend on, among other things:

- the results of our clinical trials;
- our ability to recruit and enroll patients for our clinical trials;
- the efficacy, safety and reliability of our product candidates;

- the speed at which we develop our product candidates;
- our ability to design and successfully execute appropriate clinical trials;
- the timing and scope of regulatory approvals or clearances;
- our ability to commercialize and market any of our product candidates that may receive regulatory approval or clearance;

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- appropriate coverage and adequate levels of reimbursement under private and governmental health insurance plans, including Medicare;
- our ability to protect intellectual property rights related to our products;
- our ability to have our partners manufacture and sell commercial quantities of any approved products to the market; and
- acceptance of future product candidates by physicians and other health care providers.

If our competitors market products that are more effective, safer, easier to use or less expensive than our future product candidates, if any, or that reach the market sooner than our future product candidates, if any, we may not achieve commercial success. In addition, the biopharmaceutical, diagnostic, and medical device industries are characterized by rapid technological change. Because our research approach integrates many technologies, it may be difficult for us to stay abreast of the rapid changes in each technology. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete or less competitive.

Our product development activities could be delayed or stopped.

We do not know whether our current or planned pre-clinical and clinical studies will be completed on schedule, or at all. Furthermore, we cannot guarantee that our planned pre-clinical and clinical studies will begin on time or at all. The commencement of our planned clinical trials could be substantially delayed or prevented by several factors, including:

- a limited number of, and competition for, suitable patients with the particular types of disease required for enrollment in our clinical trials or that otherwise meet the protocol's inclusion criteria and do not meet any of the exclusion criteria;
- a limited number of, and competition for, suitable serum or other samples from patients with particular types of disease required for our validation studies;
- a limited number of, and competition for, suitable sites to conduct our clinical trials;
- delay or failure to obtain FDA or other non-U.S. regulatory authorities' approval or agreement to commence a clinical trial;
- delay or failure to obtain sufficient supplies of the product candidate for our clinical trials;
- requirements to provide the drugs, diagnostic tests, or medical devices required in our clinical trial protocols or clinical trials at no cost or cost, which may require significant expenditures that we are unable or unwilling to make;
- delay or failure to reach agreement on acceptable clinical trial agreement terms or clinical trial protocols with prospective sites or investigators; and
- delay or failure to obtain institutional review board ("IRB") approval to conduct or renew a clinical trial at a prospective site.

The completion of our clinical trials could also be substantially delayed or prevented by several factors, including:

- slower than expected rates of patient recruitment and enrollment;
- failure of patients to complete the clinical trial;
- unforeseen safety issues;
- lack of efficacy evidenced during clinical trials;
- termination of our clinical trials by one or more clinical trial sites;
- inability or unwillingness of patients or medical investigators to follow our clinical trial protocols; and
- inability to monitor patients adequately during or after treatment.

Our clinical trials may be suspended or terminated at any time by the FDA, other regulatory authorities, the IRB for any given site, or us. Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes with appropriate regulatory authorities. Amendments may require us to resubmit our clinical trial protocols to IRBs for re-examination, which may impact the costs, timing, or successful completion of a clinical

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trial. Any failure or significant delay in commencing or completing clinical trials for our product candidates could materially harm our results of operations and financial condition, as well as the commercial prospects for our product candidates.

The regulatory approval process is expensive, time consuming and uncertain and may prevent us or our collaboration partners from obtaining approvals for the commercialization of some or all of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, marketing, and distribution of drug products, diagnostic products, or medical devices are subject to extensive regulation by the FDA and other non-U.S. regulatory authorities, which regulations differ from country to country. In general, we are not permitted to market our product candidates in the U.S. until we receive approval of a NDA, a clearance letter under the premarket notification process, or 510(k) process, or an approval of a PMA from the FDA. We have not submitted a NDA or PMA application or premarket notification, nor have we received marketing approval or clearance for any of our proprietary pharmaceutical or diagnostic product candidates, other than a CE Mark for our point-of-care PSA test. Obtaining approval of a NDA or PMA can be a lengthy, expensive, and uncertain process. With respect to medical devices, while the FDA reviews and clears a premarket notification in as little as three months, there is no guarantee that our products will qualify for this more expeditious regulatory process, which is reserved for Class I and II devices, nor is there any assurance that even if a device is reviewed under the 510(k) process that the FDA will review it expeditiously or determine that the device is substantially equivalent to a lawfully marketed non-PMA device. If the FDA fails to make this finding, then we cannot market the device. In lieu of acting on a premarket notification, the FDA may seek additional information or additional data which would further delay our ability to market the product. Furthermore, we are not permitted to make changes to a device approved through the PMA or 510(k) which affects the safety or efficacy of the device without first submitting a supplement application to the PMA and obtaining FDA approval or cleared premarket notification for that supplement. In some cases, the FDA may require clinical trials to support a supplement application. In addition, failure to comply with FDA, non-U.S. regulatory authorities, or other applicable U.S. and non-U.S. regulatory requirements may, either before or after product approval or clearance, if any, subject our company to administrative or judicially imposed sanctions, including, but not limited to the following:

- restrictions on the products, manufacturers, or manufacturing process;
- adverse inspectional observations (Form 483), warning letters, or non-warning letters incorporating inspectional observations;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals or clearances;
- product seizures, detentions, or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production;
- imposition of restrictions on operations, including costly new manufacturing requirements; and
- refusal to approve or clear pending NDAs or supplements to approved NDAs, applications or pre-market notifications.

Regulatory approval of an NDA or NDA supplement, PMA, PMA supplement or clearance pursuant to a pre-market notification is not guaranteed, and the approval or clearance process, as the case may be, is expensive and may, especially in the case of an NDA or PMA application, take several years. The FDA also has substantial discretion in the drug and medical device approval and clearance process. Despite the time and expense exerted, failure can occur at any stage, and we could encounter problems that cause us to abandon clinical trials or to repeat or perform additional pre-clinical studies and clinical trials. The number of pre-clinical studies and clinical trials that will be required for FDA approval or clearance varies depending on the drug or medical device candidate, the disease or condition that the drug or medical device candidate is designed to address, and the regulations applicable to any particular drug or medical device candidate. The FDA can delay, limit or deny approval or clearance of a drug or medical device candidate for many reasons, including:

- a drug candidate may not be deemed safe or effective;
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a medical device candidate may not be deemed to be substantially equivalent to a lawfully marketed non-PMA device, in the case of a premarket notification;

- the FDA may not find the data from pre-clinical studies and clinical trials sufficient;
- the FDA may not approve our or our third-party manufacturer's processes or facilities; or

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- the FDA may change its approval or clearance policies or adopt new regulations.

Beyond these risks, there is also a possibility that our licensees or collaborators could decide to discontinue a study at any time for commercial, scientific or other reasons.

Regulation by governmental authorities in the U.S. and other countries may be a significant factor in how we develop, test, produce and market our diagnostic test products. Diagnostic tests like ours may not fall squarely within the regulatory approval process for pharmaceutical or device products as described above, and the regulatory pathway is not as clear. It is possible that the diagnostic products developed by us or our collaborators will be regulated as medical devices by the FDA and comparable agencies of other countries and require either PMA or 510(k) clearance from the FDA prior to marketing. Some companies that have successfully commercialized diagnostic tests for various conditions and disease states have not sought clearance or approval for such tests through the traditional 510(k) or PMA processes, and have instead utilized a process involving LDTs through a CLIA- certified laboratory. CLIA is a federal law that regulates clinical laboratories that perform testing on specimens derived from humans for the purpose of providing information for diagnostic, preventative or treatment purpose. In such instances, the CLIA lab is solely responsible for the development, validation and commercialization of the assay.

Such LDT testing is currently under the purview of CMS and state agencies that provide oversight of the safe and effective use of LDTs. However, the FDA has consistently asserted that it has the regulatory authority to regulate LDTs despite historically exercising enforcement discretion. In furtherance of that position, the FDA issued two draft guidance documents in October 2014: (1) Framework for Regulatory Oversight of Laboratory Developed Tests (the "Framework Guidance"); and (2) FDA Notification and Medical Device Reporting for Laboratory Developed Tests (the "Notification Guidance"). The Framework Guidance outlines the FDA's plan to adopt over time a risk-based approach to regulating LDTs whereby different classifications of LDTs would be subject to different levels of FDA oversight and enforcement, including, for example, prohibitions on adulteration and misbranding, establishment registration and device listing, premarket notification, banned devices, records and reports, good manufacturing practices, adverse event reporting, premarket review of safety, effectiveness, and clinical validity, and quality system requirements. The Notification Guidance is intended to explain how clinical laboratories should notify the FDA of the LDTs they develop and how to satisfy Medical Device Reporting requirements. If finalized, the Framework Guidance and the Notification Guidance may have a materially adverse affect on the time, cost, and risk associated with the Company's development and commercialization of LDTs for the U.S. market, and there can be no assurance that clearances or approvals sought by the Company will be granted and maintained. However, the FDA's authority to regulate LDTs continues to be challenged, and the timeline and process for finalizing the draft guidance documents is unknown. We will continue to monitor changes to all domestic and international LDT regulatory policy so as to ensure compliance with the current regulatory scheme.

Our product candidates may have undesirable side effects and cause our approved products to be taken off the market. If a product candidate receives marketing approval and we or others later identify undesirable side effects caused by such products:

- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication, or field alerts to physicians and pharmacies;
- regulatory authorities may withdraw their approval of the product and require us to take our approved product off the market;
- we may be required to change the way the product is administered, conduct additional clinical trials, or change the labeling of the product;
- we may have limitations on how we promote our products;
- sales of products may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase our commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from its sale.

If the validity of an informed consent from a subject was to be challenged, it may negatively impact our product development efforts.

We take steps to ensure that all clinical data and genetic and other biological samples are collected from subjects who provide informed consent for the data and samples and we work to ensure that the subjects from whom our data and samples

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are collected do not retain any proprietary or commercial rights to the data or samples or any discoveries derived from them. However, because we may collect data and samples from countries that are governed by a number of different regulatory regimes, there are many complex legal questions relating to the adequacy of informed consent that we must continually address. The adequacy of any given subject's informed consent may be challenged in the future, and any given informed consent may prove unlawful or otherwise inadequate for our purposes. Any findings against us, or our clinical collaborators, could obligate us to stop using some of our clinical samples, which in turn may hinder our product development efforts. Such a result would also likely involve legal challenges that may consume our management and financial resources.

Our business will be heavily dependent on the success of phase 3 clinical trials for hGH-CTP and Alpharen (Fermagate Tablets) and our ability to achieve regulatory approvals for the marketing of these products and Rayaldee. There is no assurance that phase 3 trials for hGH-CTP or Alpharen (Fermagate Tablets) will continue to be successful or support marketing approval, or that we will be able to obtain marketing approval for either product, Rayaldee or any other product candidate we are developing. Before they can be marketed, our products in development must be approved by the FDA or similar foreign governmental agencies. The process for obtaining FDA approval is both time-consuming and costly, with no certainty of a successful outcome. Before obtaining regulatory approval for the sale of any drug candidate, we must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Although hGH-CTP and Alpharen (Fermagate Tablets) have exhibited no serious adverse events associated with the drug administration in the clinical trials conducted to date, further testing or patient use may undermine those determinations or unexpected side effects may arise. A failure of any preclinical study or clinical trial can occur at any stage of testing. The results of preclinical and initial clinical testing of these products may not necessarily indicate the results that will be obtained from later or more extensive testing. It also is possible to suffer significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials. If phase 3 clinical trials for hGH-CTP and Alpharen (Fermagate Tablets) are not successful or we are unable to achieve regulatory approval for these products or Rayaldee, our business will be significantly adversely impacted, which could have a materially adverse effect on our business, financial condition and results of operations.

We have limited sales and marketing experience for pharmaceutical products.

We do not have significant experience in undertaking the commercial launch of pharmaceutical products and, to date, have limited sales and marketing infrastructure and expertise. Substantial resources will continue to be required for us to promote the sale of any pharmaceutical product for which we may receive marketing clearance. There can be no assurance that we will be able to devote the necessary resources to our products under development sufficient to achieve market acceptance. Our failure to acquire or develop the skills and personnel necessary to successfully commercialize our products under development would have a material adverse effect on our business.

Our inability to address quality control issues in a timely manner could delay the production and sale of our products.

We are committed to providing high quality products to our customers, and we plan to meet this commitment by working diligently to continue implementing updated and improved quality systems and concepts throughout our organization. We cannot assure you that we will not have quality control issues in the future, which may result in warning letters and citations from the FDA. If we receive any warning letters from the FDA in the future, there can be no assurances regarding the length of time or cost it will take us to resolve such quality issues to our satisfaction and to the satisfaction of the FDA. If our remedial actions are not satisfactory to the FDA, we may have to devote additional financial and human resources to our efforts, and the FDA may take further regulatory actions against us including, but not limited to, assessing civil monetary penalties or imposing a consent decree on us, which could result in further regulatory constraints, including the governance of our quality system by a third party. Our inability to resolve these issues or the taking of further regulatory action by the FDA may weaken our competitive position and have a material adverse effect on our business, results of operations and financial condition.

We manufacture pharmaceutical products in Mexico, Spain, and Israel. We also prepare necessary test reagents and assemble and package the cassettes for our point-of-care diagnostic system at our facility in Woburn, Massachusetts. Any quality control issues at our facilities may weaken our competitive position and have a material adverse effect on our business results of operations and financial condition.

We may not meet regulatory quality standards applicable to our manufacturing and quality processes, which could have an adverse effect on our business, results of operations and financial condition.

As a medical device manufacturer, we are required to register with the FDA and are subject to periodic inspection by the FDA for compliance with its Quality System Regulation ("QSR") requirements, which require manufacturers of medical devices to adhere to certain regulations, including testing, quality control and documentation procedures. Compliance with applicable regulatory requirements is subject to continual review and is monitored rigorously through periodic inspections by

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the FDA. In addition, most international jurisdictions have adopted regulatory approval and periodic renewal requirements for medical devices, and we must comply with these requirements in order to market our products in these jurisdictions. In the European Community, we are required to maintain certain ISO certifications in order to sell our products and must undergo periodic inspections by notified bodies to obtain and maintain these certifications. Further, some emerging markets rely on the FDA's Certificate for Foreign Government ("CFG") in lieu of their own regulatory approval requirements. Our failure, or our manufacturers' failure to meet QSR ISO, or any other regulatory requirements or industry standards could delay production of our products and lead to fines, difficulties in obtaining regulatory clearances, recalls or other consequences, which could, in turn, have a material adverse effect on our business, results of operations, and our financial condition.

Even if we obtain marketing approvals or clearances for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our product candidates, which could materially impair our ability to generate anticipated revenues.

Once regulatory approval has been granted to market a product, the approved or cleared product and its manufacturer are subject to continual review. Any approved or cleared product may only be promoted for its indicated uses. In addition, if the FDA or other non-U.S. regulatory authorities approve any of our product candidates for marketing, the labeling, packaging, adverse event reporting, storage, advertising, and promotion for the product will be subject to extensive regulatory requirements. We and the manufacturers of our products are also required to comply with current Good Manufacturing Practices ("cGMP") regulations or the FDA's QSR regulations, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Moreover, device manufacturers are required to report adverse events by filing Medical Device Reports with the FDA, which reports are publicly available. Further, regulatory agencies must approve manufacturing facilities before they can be used to manufacture our products, and these facilities are subject to ongoing regulatory inspection. If we fail to comply with the regulatory requirements of the FDA and other non-U.S. regulatory authorities, or if previously unknown problems with our products, manufacturers, or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions. Furthermore, any limitation on indicated uses for a product candidate or our ability to manufacture and promote a product candidate could significantly and adversely affect our business, results of operations, and financial condition.

In addition, the FDA and other non-U.S. regulatory authorities may change their policies and additional regulations may be enacted that could prevent or delay marketing approval or clearance of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are not able to maintain regulatory compliance, we would likely not be permitted to market our future product candidates and we may not achieve or sustain profitability, which would materially impair our ability to generate anticipated revenues.

Even if we receive regulatory approval or clearance to market our product candidates, the market may not be receptive to our products.

Even if our product candidates obtain marketing approval or clearance, our products may not gain market acceptance among physicians, patients, health care payors and/or the medical community. We believe that the degree of market acceptance will depend on a number of factors, including:

- timing of market introduction of competitive products;
- safety and efficacy of our product compared to other products;
- prevalence and severity of any side effects;
- potential advantages or disadvantages over alternative treatments;
- strength of marketing and distribution support;
- price of our products, both in absolute terms and relative to alternative treatments;
- availability of coverage and reimbursement from government and other third-party payors;
- potential product liability claims;
- limitations or warnings contained in a product's regulatory authority-approved labeling; and
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changes in the standard of care for the targeted indications for any of our product candidates, which could reduce the marketing impact of any claims that we could make following applicable regulatory authority approval.

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In addition, our efforts to educate the medical community and health care payors on the benefits of our product candidates may require significant resources and may never be successful. If our products do not gain market acceptance, it would have a material adverse effect on our business, results of operations, and financial condition.

If our future product candidates are not covered and eligible for reimbursement from government and third party payors, we may not be able to generate significant revenue or achieve or sustain profitability.

The coverage and reimbursement status of newly approved or cleared drugs and diagnostic tests is uncertain, and failure of our pharmaceutical products or diagnostic tests to be adequately covered by insurance and eligible for adequate reimbursement could limit our ability to market any future product candidates we may develop and decrease our ability to generate revenue from any of our existing and future product candidates that may be approved or cleared.

There is significant uncertainty related to the third-party coverage and reimbursement of newly approved or cleared drugs and diagnostic products. The commercial success of our existing and future product candidates in both domestic and international markets will depend in part on the availability of coverage and adequate reimbursement from third-party payors, including government payors, such as the Medicare and Medicaid programs, managed care organizations, and other third-party payors. The government and other third-party payors are increasingly attempting to contain health care costs by limiting both insurance coverage and the level of reimbursement for new drugs and diagnostic tests and, as a result, they may not cover or provide adequate payment for our product candidates. These payors may conclude that our product candidates are less safe, less effective, or less cost-effective than existing or later-introduced products. These payors may also conclude that the overall cost of the procedure using one of our devices exceeds the overall cost of the competing procedure using another type of device, and third-party payors may not approve our product candidates for insurance coverage and adequate reimbursement. The failure to obtain coverage and adequate or any reimbursement for our product candidates, or health care cost containment initiatives that limit or restrict reimbursement for our product candidates, may reduce any future product revenue. Even though a drug (not administered by a physician) may be approved by the FDA, this does not mean that a Prescription Drug Plan ("PDP"), a private insurer operating under Medicare Part D, will list that drug on its formulary or will set a reimbursement level. PDPs are not required to make every FDA-approved drug available on their formularies. If our drug products are not listed on sufficient number of PDP formularies or if the PDPs' levels of reimbursement are inadequate, our business, results of operations, and financial condition could be materially adversely affected. Additionally, our failure to comply with applicable Medicare, Medicaid and other governmental payor rules could result in our inability to participate in a governmental payor program, our returning funds already paid to us, civil monetary penalties, criminal penalties and/or limitations on the operational function of our laboratory. If we were unable to receive reimbursement under a governmental payor program, a substantial portion of our revenues would be lost, which would adversely affect our results of operations and financial condition.

Our success is dependent to a significant degree upon the involvement and efforts of our Chairman and Chief Executive Officer, Phillip Frost, M.D.

Our success is dependent to a significant degree upon the efforts of our Chairman and Chief Executive Officer, Phillip Frost, M.D., who is essential to our business. The departure of our CEO for whatever reason or the inability of our CEO to continue to serve in his present capacity could have a material adverse effect upon our business, financial condition, and results of operations. Our CEO has a highly regarded reputation in the pharmaceutical and medical industry and attracts business opportunities and assists both in negotiations with acquisition targets, investment targets, and potential joint venture partners. Our CEO has also provided financing to the Company, both in terms of a credit agreement and equity investments. If we lost his services, our relationships with acquisition and investment targets, joint ventures, and investors may suffer and could cause a material adverse impact on our operations, financial condition, and the value of our Common Stock.

If we fail to attract and retain key management and scientific personnel, we may be unable to successfully develop or commercialize our product candidates.

We will need to expand and effectively manage our managerial, operational, financial, development, and other resources in order to successfully pursue our research, development, and commercialization efforts for our product candidates. Our success depends on our continued ability to attract, retain, and motivate highly qualified management

and pre-clinical and clinical personnel. The loss of the services or support of any of our senior management, particularly Dr. Phillip Frost, our Chairman of the Board and CEO, could delay or prevent the development and commercialization of our product candidates. We do not maintain “key man” insurance policies on the lives of any of our employees. We will need to hire additional personnel as we continue to expand our research and development activities and build a sales and marketing function.

We have scientific and clinical advisors who assist us in formulating our research, development, and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities

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that may limit their availability to us. In addition, these advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical, medical device, diagnostic, and other similar businesses. If we are unable to attract and retain the necessary personnel to accomplish our business objectives, we may experience constraints that will impede significantly the achievement of our research and development objectives, our ability to raise additional capital and our ability to implement our business strategy, which will adversely affect our business, results of operations and financial condition. In particular, if we lose any members of our senior management team, we may not be able to find suitable replacements in a timely fashion or at all and our business may be harmed as a result.

As we evolve from a company primarily involved in development to a company also involved in commercialization, we may encounter difficulties in managing our growth and expanding our operations successfully.

As we advance our product candidates through clinical trials, research, and development we will need to expand our development, regulatory, manufacturing, marketing, and sales capabilities or contracts with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with such third parties, as well as additional collaborators and suppliers. Maintaining these relationships and managing our future growth will impose significant added responsibilities on members of our management. We must be able to: manage our development efforts effectively; manage our clinical trials effectively; hire, train and integrate additional management, development, administrative and sales and marketing personnel; improve our managerial, development, operational and finance systems; implement and manage an effective marketing strategy; and expand our facilities, all of which may impose a strain on our administrative and operational infrastructure.

Furthermore, we may acquire additional businesses, products or product candidates that complement or augment our existing business. Integrating any newly acquired business or product could be expensive and time-consuming. We may not be able to integrate any acquired business or product successfully or operate any acquired business profitably. Our future financial performance will depend, in part, on our ability to manage any future growth effectively and our ability to integrate any acquired businesses. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company, which would have a material adverse effect on our business, results of operations and financial condition.

If we fail to acquire and develop other products or product candidates at all or on commercially reasonable terms, we may be unable to diversify or grow our business.

We intend to continue to rely on acquisitions and in-licensing as the source of our products and product candidates for development and commercialization. The success of this strategy depends upon our ability to identify, select, and acquire pharmaceutical and diagnostic products, drug delivery technologies, and medical device product candidates. Proposing, negotiating, and implementing an economically viable product acquisition or license is a lengthy and complex process. We compete for partnering arrangements and license agreements with pharmaceutical, biotechnology and medical device companies, and academic research institutions. Our competitors may have stronger relationships with third parties with whom we are interested in collaborating and/or may have more established histories of developing and commercializing products. Most of our competitors also have substantially greater financial and other resources than us. As a result, our competitors may have a competitive advantage in entering into partnering arrangements with such third parties, as such partnering arrangements are often decided in an auction process in which the highest bidder wins. In addition, even if we find promising product candidates, and generate interest in a partnering or strategic arrangement to acquire such product candidates, we may not be able to acquire rights to additional product candidates or approved products on terms that we find acceptable, or at all.

We expect that any product candidate to which we acquire rights will require additional development efforts prior to commercial sale, including extensive clinical testing and approval or clearance by the FDA and other non-U.S. regulatory authorities. All product candidates are subject to the risks of failure inherent in pharmaceutical, diagnostic test or medical device product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. Even if the product candidates are approved or cleared for marketing, we cannot be sure that they would be capable of economically feasible production or

commercial success. If we fail to acquire or develop other product candidates that are capable of economically feasible production and commercial success, our business, results of operations and financial condition and cash flows may be materially adversely affected.

We have no experience manufacturing our pharmaceutical product candidates other than at our Israeli, Mexican, and Spanish facilities, and we have no experience in manufacturing our diagnostic product candidates; we therefore rely on third parties to manufacture and supply our pharmaceutical and diagnostic product candidates.

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If our manufacturing partners are unable to produce our products in the amounts that we require, we may not be able to establish a contract and obtain a sufficient alternative supply from another supplier on a timely basis and in the quantities we require. We expect to continue to depend on third-party contract manufacturers for the foreseeable future.

Our product candidates require precise, high quality manufacturing. Any of our contract manufacturers will be subject to ongoing periodic unannounced inspection by the FDA and other non-U.S. regulatory authorities to ensure strict compliance with QSR regulations for devices or cGMPs for drugs, and other applicable government regulations and corresponding standards relating to matters such as testing, quality control, and documentation procedures. If our contract manufacturers fail to achieve and maintain high manufacturing standards in compliance with QSR or cGMPs, we may experience manufacturing errors resulting in patient injury or death, product recalls or withdrawals, delays or interruptions of production or failures in product testing or delivery, delay or prevention of filing or approval of marketing applications for our products, cost overruns, or other problems that could seriously harm our business. Any performance failure on the part of our contract manufacturers could delay clinical development or regulatory approval or clearance of our product candidates or commercialization of our future product candidates, depriving us of potential product revenue and resulting in additional losses. In addition, our dependence on a third party for manufacturing may adversely affect our future profit margins. Our ability to replace an existing manufacturer may be difficult because the number of potential manufacturers is limited and the FDA must approve any replacement manufacturer before it can begin manufacturing our product candidates. Such approval would result in additional non-clinical testing and compliance inspections. It may be difficult or impossible for us to identify and engage a replacement manufacturer on acceptable terms in a timely manner, or at all.

We currently have limited marketing staff and no pharmaceutical or diagnostic sales or distribution capabilities in the U.S. other than our sales force for our laboratory business and 4Kscore product based in Nashville, Tennessee. If we are unable to develop our sales, marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing our pharmaceutical or diagnostic product candidates in the U.S.

We currently have no pharmaceutical or diagnostic test marketing, sales or distribution capabilities in the U.S. other than the sales force for the OPKO Lab business, and through our Mexican, Spanish, Chilean, and Uruguayan subsidiaries for sales in those countries and for sales of APIs by our Israeli subsidiary. If our pharmaceutical and diagnostic product candidates are approved, we intend to establish our sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our product candidates, which will be expensive and time-consuming. Any failure or delay in the development of any of our internal sales, marketing, and distribution capabilities would adversely impact the commercialization of our products. With respect to our existing and future product candidates, we may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. To the extent that we enter into co-promotion or other licensing arrangements, our product revenue and profit is likely to be lower than if we directly marketed or sold our products. In addition, any revenue we receive will depend in whole or in part upon the efforts of such third parties, which may not be successful and are generally not within our control. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our existing and future product candidates. If we are not successful in commercializing our existing and future product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

Independent clinical investigators and contract research organizations that we engage to conduct our clinical trials may not be diligent, careful or timely.

We depend on independent clinical investigators to conduct our clinical trials. Contract research organizations may also assist us in the collection and analysis of data. These investigators and contract research organizations will not be our employees, and we will not be able to control, other than by contract, the amount of resources, including time, that they devote to products that we develop. If independent investigators fail to devote sufficient resources to the development of product candidates or clinical trials, or if their performance is substandard, it will delay the marketing approval or clearance and commercialization of any products that we develop. Further, the FDA requires that we

comply with standards, commonly referred to as good clinical practice, for conducting, recording and reporting clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial subjects are protected. If our independent clinical investigators and contract research organizations fail to comply with good clinical practice, the results of our clinical trials could be called into question and the clinical development of our product candidates could be delayed. Failure of clinical investigators or contract research organizations to meet their obligations to us or comply with federal regulations and good clinical practice procedures could adversely affect the clinical development of our product candidates and harm our business, results of operations, and financial condition.

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If we fail to comply with complex and rapidly evolving laws and regulations, we could suffer penalties, be required to pay substantial damages or make significant changes to our operations.

We are subject to numerous federal and state regulations, including, but not limited to, the Anti-Kickback Statute, the Physician Self-Referral Law, the False Claims Act, and HIPAA. If we fail to comply with existing or future applicable laws and regulations, we could suffer civil or criminal penalties, including the loss of our licenses to operate our laboratories and our ability to participate in federal and state healthcare programs. Although we believe that we are substantially compliant with all existing statutes and regulations applicable to our business, different interpretations and enforcement policies of these laws and regulations could subject our current practices to allegations of impropriety or illegality, or could require us to make significant changes to our operations. In addition, we cannot predict the impact of future legislation and regulatory changes on our business or assure that we will be able to obtain or maintain the regulatory approvals required to operate our business.

As a result of political, economic, and regulatory influences, the healthcare delivery industry in the U.S. is under intense scrutiny and subject to fundamental changes. We cannot predict which reform proposals will be adopted, when they may be adopted, or what impact they may have on us. The costs associated with complying with federal and state regulations could be significant and the failure to comply with any such legal requirements could have a material adverse effect on our financial condition, results of operations, and liquidity.

Failure to timely or accurately bill for our services could have a material adverse effect on our business.

Billing for laboratory testing services is extremely complicated and is subject to extensive and non-uniform rules and administrative requirements. Depending on the billing arrangement and applicable law, we bill various payors, such as patients, insurance companies, Medicare, Medicaid, physicians, hospitals and employer groups. Changes in laws and regulations could increase the complexity and cost of our billing process. Additionally, in the U.S., third-party payors generally require billing codes on claims for reimbursement that describe the services provided. For laboratory services, the American Medical Association establishes most of the billing codes using a data code set called Current Procedural Terminology, or CPT, codes. Each third-party payor generally develops payment amounts and coverage policies for their beneficiaries or members that ties to the CPT code established for the laboratory test and, therefore, coverage and reimbursement may differ by payor even if the same billing code is reported for claims filing purposes. For laboratory tests without a specific billing code, payors often review claims on a claim-by-claim basis and there are increased uncertainties as to coverage and eligibility for reimbursement.

Incorrect or incomplete documentation and billing information could result in non-payment for services rendered or having to pay back amounts incorrectly billed and collected. Further, the failure to timely or correctly bill could lead to various penalties, including: (1) exclusion from participation in CMS and other government programs; (2) asset forfeitures; (3) civil and criminal fines and penalties; and (4) the loss of various licenses, certificates and authorizations necessary to operate our business, any of which could have a material adverse effect on our results of operations or cash flows.

The success of our business may be dependent on the actions of our collaborative partners.

We have entered into and expect in the future to enter into collaborative arrangements with established multi-national pharmaceutical, diagnostic, and medical device companies, which will finance or otherwise assist in the development, manufacture and marketing of products incorporating our technology. We anticipate deriving some revenues from research and development fees, license fees, milestone payments, and royalties from collaborative partners. Our prospects, therefore, may depend to some extent upon our ability to attract and retain collaborative partners and to develop technologies and products that meet the requirements of prospective collaborative partners. In addition, our collaborative partners may have the right to abandon research projects, guide strategy regarding prosecution of relevant patent applications and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed-upon research terms. There can be no assurance that we will be successful in establishing collaborative arrangements on acceptable terms or at all, that collaborative partners will not terminate funding before completion of projects, that our collaborative arrangements will result in successful product commercialization, or that we will derive any revenues from such arrangements. To the extent that we are unable to develop and maintain collaborative arrangements, we would need substantial additional capital to undertake research, development, and commercialization activities on our own.

Our exclusive worldwide agreement with Pfizer Inc. is important to our business. If we do not successfully develop hGH-CTP and/or Pfizer Inc. does not successfully commercialize hGH-CTP, our business could be adversely affected. In December 2014, we entered into a development and commercialization agreement with Pfizer relating to our long-acting hGH-CTP for the treatment of growth hormone deficiency in adults and children. Under the terms of the arrangement with Prizer, we are responsible for the development program and are obligated to pay for the development up to an agreed cap, which may be exceeded under certain circumstances. If we were required to exceed the agreed cap, it could have a material negative impact on the expected benefits to us from the Pfizer transaction and our overall financial condition. In the event that the

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parties are able to obtain regulatory approvals to market a product covered by the agreement, we will be substantially dependent on Pfizer for the successful commercialization of such product. The success of the collaboration arrangement with Pfizer is dependent in part on, among other things, the skills, experience and efforts of Pfizer's employees responsible for the project, Pfizer's commitment to the arrangement, and the financial condition of Pfizer, all of which are beyond our control. In the event that Pfizer, for any reason, including but not limited to early termination of the agreement, fails to devote sufficient resources to successfully develop and commercialize any product resulting from the collaboration arrangement, our ability to earn milestone payments or receive royalty or profit sharing payments would be adversely affected, which would have a material adverse affect on our financial condition and prospects.

If we are unable to obtain and enforce patent protection for our products, our business could be materially harmed. Our success depends, in part, on our ability to protect proprietary methods and technologies that we develop or license under the patent and other intellectual property laws of the U.S. and other countries, so that we can prevent others from unlawfully using our inventions and proprietary information. However, we may not hold proprietary rights to some patents required for us to commercialize our product candidates. Because certain U.S. patent applications are confidential until patents issue, such as applications filed prior to November 29, 2000, or applications filed after such date for which nonpublication has been requested, third parties may have filed patent applications for technology covered by our pending patent applications without our being aware of those applications, and our patent applications may not have priority over those applications. For this and other reasons, we or our third-party collaborators may be unable to secure desired patent rights, thereby losing desired exclusivity. If licenses are not available to us on acceptable terms, we may not be able to market the affected products or conduct the desired activities, unless we challenge the validity, enforceability, or infringement of the third-party patent or otherwise circumvent the third-party patent.

Our strategy depends on our ability to rapidly identify and seek patent protection for our discoveries. In addition, we will rely on third-party collaborators to file patent applications relating to proprietary technology that we develop jointly during certain collaborations. The process of obtaining patent protection is expensive and time-consuming. If our present or future collaborators fail to file and prosecute all necessary and desirable patent applications at a reasonable cost and in a timely manner, our business will be adversely affected. Despite our efforts and the efforts of our collaborators to protect our proprietary rights, unauthorized parties may be able to obtain and use information that we regard as proprietary.

The issuance of a patent does not guarantee that it is valid or enforceable. Any patents we have obtained, or obtain in the future, may be challenged, invalidated, unenforceable, or circumvented. Moreover, the U.S. Patent and Trademark Office ("USPTO") may commence interference proceedings involving our patents or patent applications. In addition, court decisions may introduce uncertainty in the enforceability or scope of patents owned by biotechnology, pharmaceutical, and medical device companies. Any challenge to, finding of unenforceability or invalidation or circumvention of, our patents or patent applications would be costly, would require significant time and attention of our management, and could have a material adverse effect on our business, results of operations and financial condition.

Our pending patent applications may not result in issued patents. The patent position of pharmaceutical, biotechnology, diagnostic, and medical device companies, including ours, is generally uncertain and involves complex legal and factual considerations. The standards that the U.S. Patent and Trademark Office and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable in pharmaceutical, biotechnology, diagnostic, or medical device patents. Accordingly, we do not know the degree of future protection for our proprietary rights or the breadth of claims that will be allowed in any patents issued to us or to others. The legal systems of certain countries do not favor the aggressive enforcement of patents, and the laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. Therefore, the enforceability or scope of our owned or licensed patents in the U.S. or in foreign countries cannot be predicted with certainty, and, as a result, any patents that we own or license may not provide sufficient protection against competitors. We may not be able to obtain or maintain patent protection for our pending patent applications, those we may file in the future, or those we may

license from third parties.

While we believe that our patent rights are enforceable, we cannot assure you that any patents that have issued, that may issue, or that may be licensed to us will be enforceable or valid, or will not expire prior to the commercialization of our product candidates, thus allowing others to more effectively compete with us. Therefore, any patents that we own or license may not adequately protect our product candidates or our future products, which could have a material adverse effect on our business, results of operations, and financial condition.

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If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected.

In addition to patent protection, we also rely on other proprietary rights, including protection of trade secrets, know-how, and confidential and proprietary information. To maintain the confidentiality of trade secrets and proprietary information, we will seek to enter into confidentiality agreements with our employees, consultants, and collaborators upon the commencement of their relationships with us. These agreements generally require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. Our agreements with employees also generally provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property.

However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants, or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our confidential information. The disclosure of our trade secrets would impair our competitive position and may materially harm our business, financial condition, and results of operations.

We will rely heavily on licenses from third parties. Failure to comply with the provisions of these licenses could result in the loss of our rights under the license agreements.

Many of the patents and patent applications in our patent portfolio are not owned by us, but are licensed from third parties. Such license agreements give us rights for the commercial exploitation of the patents resulting from the respective patent applications, subject to certain provisions of the license agreements. Failure to comply with these provisions could result in the loss of our rights under these license agreements. Our inability to rely on these patents and patent applications, which are the basis of our technology, would have a material adverse effect on our business, results of operations and financial condition.

We license patent rights to certain of our technology from third-party owners. If such owners do not properly maintain or enforce the patents underlying such licenses, our competitive position and business prospects will be harmed.

We have obtained licenses from, among others, INEOS Healthcare, Washington University, UT Southwestern, the President and Fellows of Harvard College, The Scripps Research Institute, Arctic Partners, and Academia Sinica, among others, that are necessary or useful for our business. In addition, we intend to enter into additional licenses of third-party intellectual property in the future. Although our goal is to obtain exclusivity in our licensing transactions, we cannot guarantee that no third parties will step forward and assert inventorship or ownership in our in-licensed patents. In some cases, we may rely on the assurances of our licensors that all ownership rights have been secured and that all necessary agreements are intact or forthcoming.

Our success will depend in part on our ability or the ability of our licensors to obtain, maintain, and enforce patent protection for our licensed intellectual property and, in particular, those patents to which we have secured exclusive rights in our field. We or our licensors may not successfully prosecute the patent applications which are licensed to us. Even if patents issue in respect of these patent applications, we or our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we would. Without protection for the intellectual property we have licensed, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business, results of operations and financial condition.

Some jurisdictions may require us, or those from whom we license patents, to grant licenses to third parties. Such compulsory licenses could be extended to include some of our product candidates, which may limit our potential revenue opportunities.

Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, most countries limit the enforceability of patents

against government agencies or government contractors. In these countries, the patent owner may be limited to monetary relief from an infringement and may be unable to enjoin infringement, which could materially diminish the value of the patent. If we or

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those from whom we license patents are required to issue compulsory licenses, it could materially adversely affect our business, results of operation and financial condition.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties.

Other entities may have or obtain patents or proprietary rights that could limit our ability to develop, manufacture, use, sell, offer for sale or import products, or impair our competitive position. In addition, other entities may have or obtain patents or proprietary rights that cover our current research and preclinical studies. While there are statutory exemptions to patent infringement for those who are using third party patented technology in the process of pursuing FDA regulatory approval, the U.S. case law pertaining to such exemptions changes over time. Lawsuits involving such exemptions are very fact intensive and it is currently unclear under U.S. case law whether preclinical studies would always qualify for such an exemption, and whether such exemptions would apply to research tools. To the extent that our current research and preclinical studies may be covered by the patent rights of others, the risk of suit may continue after such patents expire because the statute of limitations for patent infringement runs for six years. To the extent that a third party develops and patents technology that covers our products, we may be required to obtain licenses to that technology, which licenses may not be available or may not be available on commercially reasonable terms, if at all. If licenses are not available to us on acceptable terms, we will not be able to market the affected products or conduct the desired activities, unless we challenge the validity, enforceability or infringement of the third-party patent, or circumvent the third-party patent, which would be costly and would require significant time and attention of our management. Third parties may have or obtain by license or assignment valid and enforceable patents or proprietary rights that could block us from developing products using our technology. Our failure to obtain a license to any technology that we require may materially harm our business, financial condition, and results of operations.

If we become involved in patent litigation or other proceedings related to a determination of rights, we could incur substantial costs and expenses, substantial liability for damages or be required to stop our product development and commercialization efforts.

Third parties may sue us for infringing their patent rights. Likewise, we may need to resort to litigation to enforce a patent issued or licensed to us or to determine the scope and validity of proprietary rights of others. In addition, a third-party may claim that we have improperly obtained or used its confidential or proprietary information. Furthermore, in connection with our third-party license agreements, we generally have agreed to indemnify the licensor for costs incurred in connection with litigation relating to intellectual property rights. The cost to us of any litigation or other proceeding relating to intellectual property rights, even if resolved in our favor, could be substantial, and the litigation would divert our management's efforts. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of any litigation could limit our ability to continue our operations. Our involvement in patent litigation and other proceedings could have a material adverse effect on our business, results of operations, and financial condition.

If any parties successfully claim that our creation or use of proprietary technologies infringes upon their intellectual property rights, we might be forced to pay damages, potentially including treble damages, if we are found to have willfully infringed on such parties' patent rights. In addition to any damages we might have to pay, a court could require us to stop the infringing activity or obtain a license. Any license required under any patent may not be made available on commercially acceptable terms, if at all. In addition, such licenses are likely to be non-exclusive and, therefore, our competitors may have access to the same technology licensed to us. If we fail to obtain a required license and are unable to design around a patent, we may be unable to effectively market some of our technology and products, which could limit our ability to generate revenues or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations.

We may become subject to product liability for our diagnostic tests, clinical trials, pharmaceutical products and medical device products.

Our success depends on the market's confidence that we can provide reliable, high-quality pharmaceuticals, medical devices, and diagnostics tests. Our reputation and the public image of our products or technologies may be impaired if

our products fail to perform as expected or our products are perceived as difficult to use. Our products are complex and may develop or contain undetected defects or errors. Furthermore, if a future product candidate harms people, or is alleged to be harmful, we may be subject to costly and damaging product liability claims brought against us by clinical trial participants, consumers, health care providers, corporate partners or others. We have product liability insurance covering commercial sales of current products and our ongoing clinical trials. Any defects or errors could lead to the filing of product liability claims, which could be costly and time-consuming to defend and result in substantial damages. If we experience a sustained material defect or error, this could result in loss or delay of revenues, delayed market acceptance, damaged reputation, diversion of development resources, legal claims, increased insurance costs or increased service and warranty costs, any of which could

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materially harm our business. We cannot assure you that our product liability insurance would protect our assets from the financial impact of defending a product liability claim. A product liability claim could have a serious adverse effect on our business, financial condition and results of operations.

Adverse results in material litigation matters or governmental inquiries could have a material adverse effect upon our business and financial condition.

We may from time to time become subject in the ordinary course of business to material legal action related to, among other things, intellectual property disputes, professional liability, contractual and employee-related matters, as well as inquiries from governmental agencies and Medicare or Medicaid carriers requesting comment and information on allegations of billing irregularities and other matters that are brought to their attention through billing audits, third parties or other sources. The health care industry is subject to substantial federal and state government regulation and audit. Legal actions could result in substantial monetary damages as well as damage to the Company's reputation with customers, which could have a material adverse effect upon our results of operations and financial position.

Medicare legislation and future legislative or regulatory reform of the health care system may affect our ability to sell our products profitably.

In the U.S., there have been a number of legislative and regulatory initiatives, at both the federal and state government levels, to change the healthcare system in ways that, if approved, could affect our ability to sell our products and provide our laboratory services profitably. While many of the proposed policy changes require congressional approval to implement, we cannot assure you that reimbursement payments under governmental and private third party payor programs will remain at levels comparable to present levels or will be sufficient to cover the costs allocable to patients eligible for reimbursement under these programs. Any changes that lower reimbursement rates under Medicare, Medicaid or private payor programs could negatively affect our business.

Most significantly, on March 23, 2010, President Obama signed into law both the Patient Protection and Affordable Care Act (the "Affordable Care Act") and the reconciliation law known as Health Care and Education Affordability Reconciliation Act (the "Reconciliation Act") and, combined we refer to both Acts as the "2010 Health Care Reform Legislation." The constitutionality of the 2010 Health Care Reform Legislation was confirmed on June 28, 2012 by the Supreme Court of the United States (the "Supreme Court"). Specifically, the Supreme Court upheld the individual mandate and includes changes to extend medical benefits to those who currently lack insurance coverage. Extending coverage to a large population could substantially change the structure of the health insurance system and the methodology for reimbursing medical services, drugs and devices. These structural changes could entail modifications to the existing system of third-party payors and government programs, such as Medicare and Medicaid, the creation of a government-sponsored healthcare insurance source, or some combination of both, as well as other changes. Additionally, restructuring the coverage of medical care in the U.S. could impact the reimbursement for diagnostic tests. If reimbursement for our diagnostic tests is substantially less than we or our clinical laboratory customers expect, or rebate obligations associated with them are substantially increased, our business could be materially and adversely impacted.

Beyond coverage and reimbursement changes, the 2010 Health Care Reform Legislation subjects manufacturers of medical devices to an excise tax of 2.3% on certain U.S. sales of medical devices in January 2013. This excise tax will likely increase our expenses in the future.

Further, the 2010 Health Care Reform Legislation includes the Physician Payments Sunshine Act, which, in conjunction with its implementing regulations, requires manufacturers of certain drugs, biologics, and devices that are covered by Medicare and Medicaid to record all transfers of value to physicians and teaching hospitals starting on August 1, 2013 and to begin reporting the same for public disclosure to the Centers for Medicare and Medicaid Services by March 31, 2014. Several other states and a number of countries worldwide have adopted or are considering the adoption of similar transparency laws. The failure to report appropriate data may result in civil or criminal fines and/or penalties.

Regulations under the 2010 Health Care Reform Legislation are expected to continue being drafted, released and finalized throughout the next several years. Pending the promulgation of these regulations, we are unable to fully evaluate the impact of the 2010 Health Care Reform Legislation.

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RISKS RELATED TO INTERNATIONAL OPERATIONS

Failure to obtain regulatory approval outside the U.S. will prevent us from marketing our product candidates abroad.

We intend to market certain of our existing and future product candidates in non-U.S. markets. In order to market our existing and future product candidates in the European Union and many other non-U.S. jurisdictions, we must obtain separate regulatory approvals. We have had limited interactions with non-U.S. regulatory authorities, the approval procedures vary among countries and can involve additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval or clearance. Approval or clearance by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more non-U.S. regulatory authority does not ensure approval by other regulatory authorities in other countries or by the FDA. The non-U.S. regulatory approval process may include all of the risks associated with obtaining FDA approval or clearance. We may not obtain non-U.S. regulatory approvals on a timely basis, if at all. We may not be able to file for non-U.S. regulatory approvals and may not receive necessary approvals to commercialize our existing and future product candidates in any market, which would have a material adverse effect on our business, results of operations and financial condition.

Non-U.S. governments often impose strict price controls, which may adversely affect our future profitability.

We intend to seek approval to market certain of our existing and future product candidates in both the U.S. and in non-U.S. jurisdictions. If we obtain approval in one or more non-U.S. jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to our product. In some countries, particularly countries of the European Union, each of which has developed its own rules and regulations, pricing is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug or medical device candidate. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our existing and future product candidates to other available products. If reimbursement of our future product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to generate revenues and achieve or sustain profitability, which would have a material adverse effect on our business, results of operations and financial condition.

Potential political, economic and military instability in the State of Israel, where we have office, laboratory and manufacturing operations, may adversely affect our results of operations.

We maintain office, laboratory and manufacturing facilities in the State of Israel. Political, economic and military conditions in Israel may directly affect our ability to conduct business. Since the State of Israel was established in 1948, a number of armed conflicts have occurred between Israel and its neighbors. Any hostilities involving Israel or the interruption or curtailment of trade between Israel and its present trading partners, or a significant downturn in the economic or financial condition of Israel, could affect adversely our operations. Ongoing and revived hostilities or other Israeli political or economic factors could harm our operations and product development and cause our revenues to decrease.

Due to the international scope of our business activities, our results of operations may be significantly affected by currency fluctuations.

We derive a significant portion of our consolidated net revenues from international sales, subjecting us to risks relating to fluctuations in currency exchange rates. Currency variations can adversely affect margins on sales of our products in countries outside of the U.S. and margins on sales of products that include components obtained from suppliers located outside of the U.S. Through our subsidiaries, we operate in a wide variety of jurisdictions. Certain countries in which we operate or may operate have experienced geopolitical instability, economic problems and other uncertainties from time to time. To the extent that world events or economic conditions negatively affect our future sales to customers in these and other regions of the world, or the collectability of receivables, our future results of operations, liquidity and financial condition may be adversely affected. Although we do not speculate in the foreign exchange market, we may manage exposures arising in the normal course of business related to fluctuations in foreign currency exchange rates by entering into offsetting positions through the use of foreign exchange forward contracts. Certain firmly committed transactions are hedged with foreign exchange forward contracts whereby exchange rates change, gains and losses on the exposed transactions are partially offset by gains and losses related to the hedging contracts. However, our subsidiaries receive their income and pay their expenses primarily in their local currencies.

To the extent that transactions of these subsidiaries are settled in their local currencies, a devaluation of those currencies versus the U.S. dollar could reduce the contribution from these subsidiaries to our consolidated results of operations as reported in U.S. dollars. For financial reporting purposes, such depreciation will negatively affect our reported results of operations since earnings denominated in foreign currencies would be converted to U.S. dollars at a decreased value. While we have employed economic cash flow and fair value hedges to minimize the risks associated with these exchange rate fluctuations, the hedging activities may be ineffective or may not offset more than a portion of the adverse financial impact

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resulting from currency variations. Accordingly, we cannot assure you that fluctuations in the values of the currencies of countries in which we operate will not materially adversely affect our future results of operations.

We may be exposed to liabilities under the Foreign Corrupt Practices Act, and any determination that we violated the Foreign Corrupt Practices Act could have a material adverse effect on our business.

We are subject to the Foreign Corrupt Practice Act ("FCPA") and other laws that prohibit U.S. companies or their agents and employees from providing anything of value to a foreign official or political party for the purposes of influencing any act or decision of these individuals in their official capacity to help obtain or retain business, direct business to any person or corporate entity or obtain any unfair advantage. We have operations and agreements with third parties and we generate sales internationally. Our international activities create the risk of unauthorized and illegal payments or offers of payments by our employees, consultants, sales agents or distributors, even though they may not always be subject to our control. We discourage these practices by our employees and agents. However, our existing safeguards and any future improvements may prove to be less than effective, and our employees, consultants, sales agents or distributors may engage in conduct for which we might be held responsible. Any failure by us to adopt appropriate compliance procedures and ensure that our employees and agents comply with the FCPA and applicable laws and regulations in foreign jurisdictions could result in substantial penalties or restrictions on our ability to conduct business in certain foreign jurisdictions.

Violations of the FCPA may result in severe criminal or civil sanctions, and we may be subject to other liabilities, which could negatively affect our business, operating results and financial condition. In addition, the U.S. government may seek to hold our Company liable for successor liability FCPA violations committed by companies in which we invest or that we acquire.

We are subject to risks associated with doing business globally.

Our operations, both within and outside the U.S., are subject to risks inherent in conducting business globally and under the laws, regulations and customs of various jurisdictions and geographies. These risks include fluctuations in currency exchange rates, changes in exchange controls, loss of business in government tenders that are held annually in many cases, nationalization, increasingly complex labor environments, expropriation and other governmental actions, changes in taxation, including legislative changes in U.S. and international taxation of income earned outside of the U.S., importation limitations, export control restrictions, violations of U.S. or local laws, including the FCPA, dependence on a few government entities as customers, pricing restrictions, economic destabilization, political and economic instability, disruption or destruction in a significant geographic region — due to the location of manufacturing facilities, distribution facilities or customers — regardless of cause, including war, terrorism, riot, civil insurrection or social unrest, or natural or man-made disasters, including famine, flood, fire, earthquake, storm or disease. Failure to comply with the laws and regulations that affect our global operations, could have an adverse effect on our business, financial condition or results of operations.

RISKS RELATED TO ACQUISITIONS AND INVESTMENTS

Acquisitions, investments and strategic alliances that we have made or may make in the future may use significant resources, result in disruptions to our business or distractions of our management, may not proceed as planned, and could expose us to unforeseen liabilities. We intend to continue to expand our business through the acquisition of, investments in and strategic alliances with companies, technologies, products, and services. Acquisitions, investments and strategic alliances involve a number of special problems and risks, including, but not limited to:

- difficulty integrating acquired technologies, products, services, operations, and personnel with the existing businesses;
- diversion of management's attention in connection with both negotiating the acquisitions and integrating the businesses;
- strain on managerial and operational resources as management tries to oversee larger operations and investments;
- difficulty implementing and maintaining effective internal control over financial reporting at businesses that we acquire or invest in, particularly if they are not located near our existing operations;
- exposure to unforeseen liabilities of acquired companies or companies in which we invest;
- potential costly and time-consuming litigation, including stockholder lawsuits;
- potential issuance of securities to equity holders of the company being acquired with rights that are superior to the rights of holders of our Common Stock, or which may have a dilutive effect on our stockholders;

- the need to incur additional debt or use cash; and

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- the requirement to record potentially significant additional future operating costs for the amortization of intangible assets.

As a result of these or other problems and risks, businesses we acquire or invest in may not produce the revenues, earnings, or business synergies that we anticipated, and acquired products, services, or technologies might not perform as we expected. As a result, we may incur higher costs and realize lower revenues than we had anticipated. We may not be able to successfully address these problems and we cannot assure you that the acquisitions or investments will be successfully identified and completed or that, if completed, the acquired businesses, investments, products, services, or technologies will generate sufficient revenue to offset the associated costs or other negative effects on our business.

Any of these risks can be greater if an acquisition or investment is large relative to our size. Failure to manage effectively our growth through acquisitions could adversely affect our growth prospects, business, results of operations, financial condition and cash flows.

Funding may not be available for us to continue to make acquisitions, investments and strategic alliances in order to grow our business.

We have made and anticipate that we may continue to make acquisitions, investments and strategic alliances with complementary businesses, technologies, products and services to expand our business. Our growth plans rely, in part, on the successful completion of future acquisitions. At any particular time, we may need to raise substantial additional capital or to issue additional equity to finance such acquisitions, investments, and strategic alliances. There is no assurance that we will be able to secure additional funding on acceptable terms, or at all, or obtain the stockholder approvals necessary to issue additional equity to finance such acquisitions, investments, and strategic alliances. If we are unsuccessful in obtaining the financing, our business would be adversely impacted.

We have a large amount of goodwill and other intangible assets as a result of acquisitions and a significant write-down of goodwill and/or other intangible assets would have a material adverse effect on our reported results of operations and net worth.

We have a large amount of goodwill and other intangible assets and we are required to perform an annual, or in certain situations a more frequent, assessment for possible impairment for accounting purposes. At December 31, 2014, we have goodwill and other intangible assets of $1.1 billion, or approximately 85% of our total assets. If we do not achieve our planned operating results, we may be required to incur a non-cash impairment charge. Any impairment charges in the future will adversely affect our results of operations. A significant write down of goodwill and/or other intangible assets would have a material adverse effect on our reported results of operations and net worth.

RISKS RELATED TO OWNERSHIP OF OUR COMMON STOCK

The market price of our Common Stock may fluctuate significantly.

The market price of our Common Stock may fluctuate significantly in response to numerous factors, some of which are beyond our control, such as:

- the announcement of new products or product enhancements by us or our competitors;
- results of our clinical trials and other development efforts;
- developments concerning intellectual property rights and regulatory approvals;
- variations in our and our competitors' results of operations;
- changes in earnings estimates or recommendations by securities analysts, if our Common Stock is covered by analysts;
- developments in the biotechnology, pharmaceutical, diagnostic, and medical device industry;
- the results of product liability or intellectual property lawsuits;
- future issuances of our Common Stock or other securities, including debt;
- purchases and sales of our Common Stock by our officers, directors or affiliates;
- the addition or departure of key personnel;
- announcements by us or our competitors of acquisitions, investments, or strategic alliances; and
- general market conditions and other factors, including factors unrelated to our operating performance.

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Further, the stock market in general, and the market for biotechnology, pharmaceutical, diagnostic, and medical device companies in particular, has experienced extreme price and volume fluctuations in recent years. Continued market fluctuations could result in extreme volatility in the price of our Common Stock, which could cause a decline in the value of our Common Stock.

Trading of our Common Stock may be limited and restrictions imposed by securities regulation may further reduce our trading, making it difficult for our stockholders to sell shares.

Our Common Stock began trading on the American Stock Exchange, now known as the NYSE MKT, in June 2007. In September 2011, we transferred the listing of our Common Stock from the NYSE MKT to the New York Stock Exchange ("NYSE"). Historically, the liquidity of our Common Stock has been limited. A substantial amount of the outstanding shares of our Common Stock are restricted securities. These factors may result in lower prices for our Common Stock than might otherwise be obtained and could also result in a larger spread between the bid and ask prices for our Common Stock. In addition, without a large float, our Common Stock is less liquid than the stock of companies with broader public ownership and, as a result, the trading prices of our Common Stock may be more volatile. In the absence of an active public trading market, an investor may be unable to liquidate his investment in our Common Stock. Further, the limited liquidity could be an indication that the trading price is not reflective of the actual fair market value of our Common Stock. Trading of a relatively small volume of our Common Stock may have a greater impact on the trading price of our stock than would be the case if our public float were larger.

Future sales of our Common Stock could reduce our stock price.

Some or all of the "restricted" shares of our Common Stock issued to former stockholders of Froptix and Acuity in connection with the acquisition or held by other of our stockholders may be offered from time to time in the open market pursuant to an effective registration statement, or beginning April 2, 2008, pursuant to Rule 144. We have also issued or agreed to issue a substantial number of securities in private placement transactions with two year lockup restrictions which expired in each of December 2009, August 2010, and February 2011. In connection with our Series D Preferred Stock offering, shares were issued with a three year lockup restriction that expired in September 2012. On March 8, 2013, the Company converted each outstanding share of Series D Preferred Stock into ten shares of Common Stock. In January 2013, we also entered into note purchase agreements with various purchasers (collectively, the "Purchasers") for the sale of $175.0 million aggregate principal amount of 2033 Senior Notes. The 2033 Senior Notes will be convertible at any time on or after November 1, 2032, through the second scheduled trading day immediately preceding the maturity date, at the option of the holders. Additionally, holders may convert their 2033 Senior Notes prior to the close of business on the scheduled trading day immediately preceding November 1, 2032, upon the occurrence of specified events. The 2033 Senior Notes will be convertible into cash, shares of the Company's Common Stock, or a combination of cash and shares of Common Stock at an initial conversion rate of 141.4827 shares of Common Stock per $1,000 principal amount of 2033 Senior Notes (equivalent to an initial conversion price of approximately $7.07 per share of Common Stock), and will be subject to adjustment upon the occurrence of certain events. On August 30, 2013, one of the conversion rights in the 2033 Senior Notes was triggered. Holders of the 2033 Senior Notes converted $16.9 million principal amount into 2,396,145 shares of our Common Stock at a rate of 141.48 shares of Common Stock per $1,000 principal amount of 2033 Senior Notes. In June 2014, we also entered into an exchange agreement with a holder of the Company's 2033 Senior Notes pursuant to which such holder exchanged $70.4 million in aggregate principal amount of Notes for 10,974,431 shares of the Company's Common Stock and approximately $0.8 million in cash representing accrued interest through the date of completion of the exchange. As of February 20, 2015, $87.6 million of 2033 Senior Notes remain outstanding. Sales of a substantial number of shares of our Common Stock in the public market pursuant to Rule 144 or the 2033 Senior Notes are converted, or the perception that such sales could occur, could adversely affect the price of our Common Stock.

Directors, executive officers, principal stockholders and affiliated entities own a majority of our capital stock, and they may make decisions that you do not consider to be in the best interests of our stockholders.

As of February 17, 2015, our directors, executive officers, principal stockholders, and affiliated entities beneficially owned, in the aggregate a majority of our outstanding voting securities. Frost Gamma Investments Trust ("Gamma Trust"), of which Phillip Frost, M.D., the Company's Chairman and CEO, is the sole trustee, is deemed to beneficially

own in the aggregate approximately 38.8% of our Common Stock as of February 17, 2015. As a result, Dr. Frost acting with other members of management, would have the ability to control the election of our Board of Directors, the adoption or amendment of provisions in the Company's Certificate of Incorporation, the approval of mergers and other significant corporate transactions, and the outcome of issues requiring approval by our stockholders. This concentration of ownership may also have the effect of delaying or preventing a change in control of our company that may be favored by other stockholders. This could prevent transactions in which stockholders might otherwise recover a premium for their shares over current market prices.

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A significant short position in our stock could have a substantial impact on the trading price of our stock. Historically, there has been a significant "short" position in our common stock. As of February 13, 2015, investors held a short position of approximately 47,799,891 million shares of our common stock which represented approximately 22.97% of our public float. The anticipated downward pressure on our stock price due to actual or anticipated sales of our stock by some institutions or individuals who engage in short sales of our common stock could cause our stock price to decline. Such stock price decrease could encourage further short-sales that could place additional downward pressure on our stock price. This could lead to further increases in the already large short position in our common stock and cause volatility in our stock price. The volatility of our stock may cause the value of a stockholder's investment to decline rapidly. Additionally, if our stock price declines, it may be more difficult for us to raise capital and may have other adverse effects on our business.

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business and operating results. In addition, current and potential stockholders could lose confidence in our financial reporting, which could have a material adverse effect on the price of our Common Stock. Section 404 of the Sarbanes-Oxley Act of 2002 requires annual management assessments of the effectiveness of our internal control over financial reporting and a report by our independent registered public accounting firm on the effectiveness of internal control over financial reporting as of year end. We are required to report, among other things, control deficiencies that constitute material weaknesses or changes in internal control that, or that are reasonably likely to, materially affect internal control over financial reporting. A "material weakness" is a significant deficiency or combination of significant deficiencies that results in more than a remote likelihood that a material misstatement of the annual or interim financial statements will not be prevented or detected. We have identified that we have a material weakness as of December 31, 2013, which related to the Company's financial statement close process at its Chilean subsidiary due to the lack of sufficient controls to assure that inventory and accounts receivable balances are recoded correctly in accordance with U.S. generally accepted accounting principles. As a result, we concluded that our internal control over financial reporting was not effective as of December 31, 2013. Effective internal controls are necessary for us to provide reliable financial reports and effectively prevent fraud. Although we are taking steps to improve the control environment at our Chilean operations, we cannot assure you that we will at all times in the future be able to report that our internal controls are effective. If we cannot provide reliable financial reports or prevent fraud, our results of operation could be harmed. Our failure to maintain the effective internal control over financial reporting could cause the cost related to remediation to increase and could cause our stock price to decline. In addition, we may not be able to accurately report our financial results, may be subject to regulatory sanction, and investors may lose confidence in our financial statements.

Compliance with changing regulations concerning corporate governance and public disclosure may result in additional expenses.

There have been changing laws, regulations, and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, the Dodd-Frank Act, regulations promulgated by the Securities and Exchange Commission and rules promulgated by the NYSE and the other national securities exchanges. These new or changed laws, regulations, and standards are subject to varying interpretations in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. As a result, our efforts to comply with evolving laws, regulations, and standards are likely to continue to result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities. Our board members, Chief Executive Officer, Chief Financial Officer, and Principal Accounting Officer could face an increased risk of personal liability in connection with the performance of their duties. As a result, we may have difficulty attracting and retaining qualified board members and executive officers, which could harm our business. If our efforts to comply with new or changed laws, regulations, and standards differ from the activities intended by regulatory or governing bodies, we could be subject to liability under applicable laws or our reputation may be harmed, which could materially adversely affect our business, results of operations and financial condition.

The exercise of warrants we have issued may result in dilution to the holders of our Common Stock and cause the price of our Common Stock to decline.

As of December 31, 2014, we had outstanding warrants to purchase 21,429,746 shares of our Common Stock. The exercise of warrants has, or may, result in substantial dilution to our existing stockholders and could have a material adverse effect on our stock price. The possibility of the issuance of shares of our Common Stock upon the exercise of warrants could cause our stock price to decline as well.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

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None.

ITEM 2. PROPERTIES.

Our principal corporate office is located at 4400 Biscayne Blvd, Miami, Florida. We lease this space from Frost Real Estate Holdings, LLC ("Frost Real Estate"), an entity which is controlled by Dr. Phillip Frost, our Chairman of the Board and Chief Executive Officer. Pursuant to the lease agreement with Frost Real Estate Holdings, we lease approximately 11,555 square feet, which encompasses space for our corporate offices and administrative services. The lease is for a five-year term, which commenced effective January 1, 2014. We previously leased the premises from Frost Real Estate pursuant to a five-year lease that originally expired in August 2012, but was extended through December 31, 2013 by agreement by the parties. The lease currently requires annual rent of approximately $0.6 million.

We lease office and laboratory space in Jupiter and Miramar, Florida and Nes Ziona, Israel, which is where our molecular diagnostics research and development, oligonucleotide research and development, and CTP research and development operations are based, respectively. We lease office, manufacturing and warehouse space in Woburn, Massachusetts for our point-of-care diagnostics business, and in Nesher, Israel for our API business. We lease laboratory and office space in Nashville, Tennessee, Burlingame, California, and Miramar, Florida for our CLIA-certified laboratory business, and we lease office space in Bannockburn, Illinois and Markham, Ontario for our Renal Division. Our Chilean and Uruguayan operations are located in leased offices and warehouse facilities in Santiago and Montevideo, respectively. Our Mexican operations are based in an owned manufacturing facility and a leased warehouse facility in Guadalajara and in leased offices in Mexico City. Our Spanish operations are based in owned offices in Barcelona, in an owned manufacturing facility in Banyoles and a leased warehouse facility in Palol de Revardit. Our Brazilian operations are located in leased offices in Sao Paulo.

ITEM 3. LEGAL PROCEEDINGS.

On or around October 21, 2014, we received a Civil Investigative Demand ("Demand") from the U.S. Attorney's Office for the Middle District of Tennessee ("Attorney's Office"). The Demand concerns an investigation of allegations that the Company or one of its affiliated entities or other parties submitted false claims for payment related to services provided to government healthcare program beneficiaries in violation of the False Claims Act, 31 U.S.C. Section 3729. We intend to fully cooperate with the investigation and produce documents responsive to the Demand. It is too early to assess the probability of a favorable or unfavorable outcome in this matter or the loss or range of loss, if any.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

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PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

Our Common Stock is traded publicly on the New York Stock Exchange ("NYSE") under the symbol "OPK". Effective in August 2013, our Common stock also began trading on the Tel Aviv Stock Exchange.

The following table sets forth for the periods indicated the high and low sales prices per share of our Common Stock during each of the quarters set forth below as reported on the NYSE:

	High	Low
2014		
First Quarter	$10.25	$7.32
Second Quarter	9.83	7.82
Third Quarter	9.62	8.09
Fourth Quarter	10.16	8.02
2013		
First Quarter	$7.83	$4.83
Second Quarter	7.65	6.14
Third Quarter	10.00	7.13
Fourth Quarter	12.95	8.17

As of February 20, 2015, there were approximately 439 holders of record of our Common Stock.

We have not declared or paid any cash dividends on our Common Stock. No cash dividends have been previously paid on our Common Stock and none are anticipated in fiscal 2015. Prior to March 8, 2013, we had shares of Series D Preferred Stock outstanding that had preferential dividend rights over any dividend payments to holders of Common Stock. On March 1, 2013, our Board of Directors declared a cash dividend to all Series D Preferred stockholders as of March 8, 2013. The total cash dividend was approximately $3.0 million. In addition, on March 1, 2013, our Board of Directors also exercised our option to convert all 1,129,032 shares of our outstanding Series D Preferred Stock into 11,290,320 shares of our Common Stock effective on March 8, 2013. Following the conversion there are no outstanding shares of Series D Preferred Stock.

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Stock Performance Graph

The following graph compares the five-year cumulative total return of our Common Stock with the S&P 500 Index and the NASDAQ Biotechnology Index. The graph assumes $100 invested on December 31, 2009 in our Common Stock and in each of the foregoing indices. The stock price performance reflected in the graph below is not necessarily indicative of future price performance.

	12/31/2009	12/31/2010	12/31/2011	12/31/2012	12/31/2013	12/31/2014
OPKO Health, Inc.	$100.00	$200.55	$267.76	$262.84	$461.20	$545.90
S&P 500	100.00	115.06	117.49	136.30	180.44	205.14
NASDAQ Biotechnology	100.00	106.73	122.40	166.72	286.55	379.71

Recent Sales of Unregistered Securities

None.

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ITEM 6. SELECTED FINANCIAL DATA.

The following selected historical consolidated statement of operations data for the years ended December 31, 2014, 2013, 2012, 2011, and 2010 and the consolidated balance sheet data as of December 31, 2014, 2013, 2012, 2011, and 2010, below are derived from our audited consolidated financial statements and related notes thereto. This data should be read in conjunction with our "Management's Discussion and Analysis of Financial Condition and Results of Operation" and our consolidated financial statements and the related notes thereto.

	For the years ended December 31,				
(In thousands, except share and per share information)	2014	2013	2012	2011	2010
Statement of operations data:					
Revenues	$91,125	$96,530	$47,044	$27,979	$28,494
Costs and expenses:					
Cost of revenues	48,009	48,860	27,878	17,243	13,495
Selling, general and administrative	57,940	55,320	27,795	19,169	18,133
Research and development	83,571	53,902	19,520	11,352	5,949
In-process research and development	12,055	—	—	—	—
Other operating expenses	35,365	18,080	9,120	3,404	2,053
Total costs and expenses	236,940	176,162	84,313	51,168	39,630
Operating loss from continuing operations	(145,815)	(79,632)	(37,269)	(23,189)	(11,136)
Other income and (expense), net	(25,212)	(24,586)	165	(1,044)	(844)
Loss from continuing operations before income taxes and investment losses	(171,027)	(104,218)	(37,104)	(24,233)	(11,980)
Income tax benefit (provision)	(24)	(1,672)	9,626	19,358	18
Loss from continuing operations before investment losses	(171,051)	(105,890)	(27,478)	(4,875)	(11,962)
Loss from investments in investees	(3,587)	(11,456)	(2,062)	(1,589)	(714)
Loss from continuing operations	(174,638)	(117,346)	(29,540)	(6,464)	(12,676)
Income (loss) from discontinued operations, net of tax	—	—	—	5,181	(6,250)
Net loss	(174,638)	(117,346)	(29,540)	(1,283)	(18,926)
Less: Net loss attributable to noncontrolling interests	(2,972)	(2,939)	(492)	—	—
Net loss attributable to common shareholders before preferred stock dividend	(171,666)	(114,407)	(29,048)	(1,283)	(18,926)
Preferred stock dividend	—	(420)	(2,240)	(2,379)	(2,624)
Net loss attributable to common shareholders	$(171,666)	$(114,827)	$(31,288)	$(3,662)	$(21,550)
Loss per share, basic and diluted:					
Loss from continuing operations	$(0.41)	$(0.32)	$(0.11)	$(0.03)	$(0.06)
Income (loss) from discontinued operations	$—	$—	$—	$0.02	$(0.02)
Net loss per share	$(0.41)	$(0.32)	$(0.11)	$(0.01)	$(0.08)
Weighted average number of common shares outstanding basic and diluted:	422,014,039	355,095,701	295,750,077	280,673,122	255,095,586
Balance sheet data:					

Total assets	$1,267,664	$1,391,516	$289,830	$229,489	$77,846
Working capital	$59,758	$150,878	$26,275	$80,804	$29,793
Long-term liabilities	$348,812	$426,687	$34,168	$25,443	$7,908
Series D Preferred Stock	$—	$—	$24,386	$24,386	$26,128
Shareholders' equity attributable to OPKO	$842,144	$876,410	$179,386	$160,882	$23,052
Total shareholders' equity	$835,741	$872,979	$178,894	$160,882	$23,052

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ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

This Annual Report on Form 10-K contains certain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 ("PSLRA"), Section 27A of the Securities Act of 1933, as amended, (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended, (the "Exchange Act"), about our expectations, beliefs, or intentions regarding our product development efforts, business, financial condition, results of operations, strategies, or prospects. You can identify forward-looking statements by the fact that these statements do not relate strictly to historical or current matters. Rather, forward-looking statements relate to anticipated or expected events, activities, trends, or results as of the date they are made. Because forward-looking statements relate to matters that have not yet occurred, these statements are inherently subject to risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements. These factors include those contained in "Item 1A — Risk Factors" of this Annual Report on Form 10-K. We do not undertake any obligation to update forward-looking statements. We intend that all forward-looking statements be subject to the safe harbor provisions of PSLRA. These forward-looking statements are only predictions and reflect our views as of the date they are made with respect to future events and financial performance.

OVERVIEW

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

We own established pharmaceutical platforms in Spain, Chile, Mexico, and Uruguay which are generating revenue and from which we expect to facilitate future market entry for our products currently in development. We also have established pharmaceutical operations in Brazil. We operate a specialty APIs manufacturer in Israel, which we expect will facilitate the development of our pipeline of molecules and compounds for our proprietary products. In the U.S., we own a laboratory certified under the CLIA, with a urologic focus that generates revenue and serves as the commercial platform for the U.S. launch of the 4Kscore.

RECENT DEVELOPMENTS

In December 2014, we entered into an exclusive worldwide agreement with Pfizer for the development and commercialization of our long-acting hGH-CTP for the treatment of GHD in adults and children, as well as for the treatment of growth failure in children born SGA (the "Pfizer Transaction"). hGH-CTP has the potential to reduce the required dosing frequency of human growth hormone to a single weekly injection from the current standard of one injection per day. hGH-CTP is currently in a global phase 3 trial in adults and a global phase 2 trial in children and has orphan drug designation in the U.S. and Europe for both adults and children with GHD.

The Pfizer Transaction closed in January 2015 following the termination of the waiting period under the Hart-Scott-Rodino Act. Under the terms of the Pfizer Transaction, we received non-refundable and non-creditable upfront payments of $295 million and are eligible to receive up to an additional $275 million upon the achievement of certain regulatory milestones. Pfizer received the exclusive license to commercialize hGH-CTP worldwide. In addition, we are eligible to receive initial royalty payments associated with the commercialization of hGH-CTP for Adult GHD. Upon the launch of hGH-CTP for Pediatric GHD, the royalties will transition to a regional, tiered gross profit sharing for both hGH-CTP and Pfizer's Genotropin®.

We will lead the clinical activities and will be responsible for funding the development programs for the key indications, which includes Adult and Pediatric GHD and Pediatric SGA. Pfizer will be responsible for all development costs for additional indications as well as all post-marketing studies. In addition, Pfizer will fund the commercialization activities for all indications and lead the manufacturing activities covered by the global

development plan.

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RESULTS OF OPERATIONS
For The Years Ended December 31, 2014 and December 31, 2013

Revenues. Revenues for the year ended December 31, 2014, were $91.1 million, compared to $96.5 million for the year ended December 31, 2013. The decrease in revenue principally reflects non-recurring, non–cash revenue related to the transfer of technology under the RXi Asset Purchase Agreement of $12.5 million in 2013, which was partially offset by (i) a milestone payment of $5.0 million from TESARO during the year ended December 31, 2014, which we recognized in Revenue from transfer of intellectual property and (ii) a 14% increase in pharmaceutical product revenue principally from FineTech of $6.2 million for the year ended December 31, 2014. In addition, pharmaceutical product revenue from our European and Mexican operations increased by $2.5 million and $1.6 million, respectively, during the year ended December 31, 2014, primarily due to increased sales by OPKO Health Europe and an increase in government tenders in Mexico. Revenue related to OPKO Lab decreased $2.9 million during the year ended December 31, 2014, compared to the year ended December 31, 2013, primarily related to decreased reimbursement rates from government payors and decreased specimen volume, partially offset by revenue from the launch of our 4Kscore test and a price increase to non-government payors initiated in June 2014.
Costs of revenue. Costs of revenue for the year ended December 31, 2014, were $48.0 million, compared to $48.9 million for the year ended December 31, 2013. Costs of revenue for the year ended December 31, 2014 decreased principally due to decreased revenue at OPKO Lab, which has a lower margin than pharmaceutical product sales. In addition, inventory obsolescence charges decreased $0.9 million for the year ended December 31, 2014 compared to 2013. This was partially offset by increased cost of revenue due to increased pharmaceutical product sales.
Selling, general and administrative expenses. Selling, general and administrative expenses for the year ended December 31, 2014 were $57.9 million, compared to $55.3 million for the year ended December 31, 2013. The increase in selling, general and administrative expenses for the year ended December 31, 2014 was a result of increased personnel expenses including equity based compensation as well as sales and marketing activities related to the launch of our 4Kscore test in the U.S. in March 2014 and Europe in September 2014. These increases were partially offset by decreased professional fees as the 2013 period included expenses related to the acquisitions of OPKO Renal and OPKO Biologics. Selling, general and administrative expenses during the years ended December 31, 2014 and 2013, include equity-based compensation expense of $9.7 million and $7.3 million, respectively.
Research and development expenses. Research and development expenses for the year ended December 31, 2014 were $83.6 million, compared to $53.9 million for the year ended December 31, 2013. Research and development costs include external and internal expenses, partially offset by third-party grants and funding arising from collaboration agreements. External expenses include clinical and non-clinical activities performed by contract research organizations, lab services, purchases of drug and diagnostic product materials and manufacturing development costs. We track external research and development expenses by individual program for phase 3 clinical trials for drug approval and PMA’s (pre-market approval) for diagnostics tests, if any. Internal expenses include employee-related expenses including salaries, benefits and stock-based compensation expense. Other unallocated internal research and development expenses are incurred to support overall research and development activities and include expenses related to general overhead and facilities.

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The following table summarizes the components of our research and development expenses:

	For the years ended December 31,	
	2014	2013
External expenses:		
Phase 3 clinical trials	$14,512	$13,078
CMC expense for biological products	18,692	1,765
Earlier-stage programs	9,093	4,599
Research and development employee-related expenses	21,642	17,215
Other unallocated internal research and development expenses	21,982	18,998
Third-party grants and funding from collaboration agreements	(2,350)	(1,753)
Total research and development expenses	$83,571	$53,902

The increase in research and development expenses during the year ended December 31, 2014, as compared to the year ended December 31, 2013, principally resulted from $38.6 million of costs related to OPKO Biologics which we acquired in August 2013 and an increase related to research and development expenses incurred by OPKO Renal related to the external costs of two pivotal phase 3 clinical trials for Rayaldee (CTAP101) which were completed in 2014, and a third open-label phase 3 trial completed in 2015. OPKO Biologics principally incurred development and clinical manufacturing costs ("CMC") related to hGH-CTP, a long acting human growth hormone which was outlicensed to Pfizer in 2015. Research and development expenses for the year ended December 31, 2014 and year ended December 31, 2013 include equity-based compensation expense of $5.0 million and $3.6 million, respectively. Research and development expenses for the year ended December 31, 2013, includes an offset to research and development expenses of $2.7 million related to the correction of an error related to equity awards granted to non-employees with performance based vesting.

Contingent consideration. Contingent consideration expenses for the years ended December 31, 2014 and 2013, were $24.4 million and $6.9 million, respectively. The increase in contingent consideration expense was primarily attributable to an increase in the fair value of our contingent obligations to the former stockholders of OPKO Renal due to changes in assumptions regarding probabilities of successful achievement of future milestones driven by the two successful phase 3 trials of Rayaldee in 2014. The contingent consideration liabilities at December 31, 2014 relate to potential amounts payable to former stockholders of CURNA, OPKO Diagnostics, OPKO Health Europe and OPKO Renal pursuant to our acquisition agreements in January 2011, October 2011, August 2012 and March 2013, respectively.

Amortization of intangible assets. Amortization of intangible assets was $10.9 million and $11.1 million, respectively, for the years ended December 31, 2014 and 2013. Amortization expense reflects the amortization of acquired intangible assets with defined useful lives. The acquisitions of OPKO Renal and OPKO Biologics resulted in principally acquiring IPR&D assets which will not be amortized until the underlying development programs are completed. Upon obtaining regulatory approval by the FDA, the IPR&D asset will then be accounted for as a finite-lived intangible asset and amortized on a straight-line basis over its estimated useful life.

In-Process Research and Development. In May 2014, we acquired Inspiro, a privately held company that is developing the Inspiromatic, a "smart" easy-to-use dry powder inhaler with several advantages over existing devices. We recorded the transaction as an asset acquisition and recorded the assets and liabilities at fair value. As the asset had no alternative future use, we recorded $10.1 million of acquired in-process research and development expense. In addition, pursuant to our agreement with Schering Plough Corporation, now Merck & Co. ("Merck"), we were required to make a $2.0 million payment upon the achievement of a milestone for rolapitant which was achieved in the fourth quarter of 2014. The agreement was accounted for as an asset acquisition and the entire $2.0 million milestone payment was allocated to in-process research and development expense. We did not have any such activity during the year ended December 31, 2013.

We record expense for in-process research and development projects accounted for as asset acquisitions which have not reached technological feasibility and which have no alternative future use. Inspiromatic and rolapitant have not reached a stage of technological feasibility and have no alternative future use.

Other income and (expense), net. Other income and (expense), net for the years ended December 31, 2014 and 2013 was $(25.2) million and $(24.6) million, respectively. During the year ended December 31, 2014, we recorded $12.2 million non-cash other charge, net, related to the changes in the fair value of the embedded derivatives in the 2033 Senior Notes, and a $2.7 million gain as the result of the exchange of $70.4 million principal of 2033 Senior Notes in June 2014. Other income and (expense), net, for the year ended December 31, 2014, also included $12.3 million of interest expense principally related to

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interest incurred on the 2033 Senior Notes and the amortization of related deferred financing costs. Other income and (expense), net for the year ended December 31, 2014, includes a $1.4 million other-than-temporary impairment charge to write our investment in ARNO Therapeutics, Inc. down to its fair value of $0.6 million as of December 31, 2014. For the year ended December 31, 2013, we recorded a $52.7 million non-cash charge, net, related to the changes in the fair value of the embedded derivatives in the 2033 Senior Notes, partially offset by a $1.0 million gain on early partial conversion of the 2033 Senior Notes, income of $6.5 million related to changes in the fair value of the Pharmsynthez Note Receivable, a certain Pharmsynthez purchase option, warrants and options received in connection with our investment in Neovasc and ARNO, and by a gain of $29.9 million on the sale of certain of our strategic investments. Other income and (expense), net, for the year ended December 31, 2013, also included $13.8 million of interest expense primarily related to the 2033 Senior Notes and the amortization of related deferred financing costs. The decrease in interest expense for the year ended December 31, 2014 compared to the same period in 2013 is due the exchange of $70.4 million principal of 2033 Senior Notes in June 2014, which was partially offset by a non-cash write-off of deferred financing costs of $1.5 million as interest expense related to exchange of the 2033 Senior Notes in June 2014.

Loss from investments in investees. We have made investments in other early stage companies that we perceive to have valuable proprietary technology and significant potential to create value for us as a shareholder. We account for these investments under the equity method of accounting, resulting in the recording of our proportionate share of their losses until our share of their loss exceeds our investment. Until the investees' technologies are commercialized, if ever, we anticipate they will continue to report a net loss. Loss from investments in investees was $3.6 million and $11.5 million for the years ended December 31, 2014 and 2013, respectively. The decrease in loss from investments in investees is primarily due to decreased losses at RXi Pharmaceuticals Corporation and Cocrystal Pharma, Inc. During the third quarter of 2014, we discontinued applying the equity method of accounting for RXi and account for our investment in RXi as an available for sale investment.

Income taxes. Our income tax provision reflects the projected income tax payable in Israel, Chile, Spain, Mexico, Canada and SciVac Ltd ("SciVac"), a consolidated variable interest entity. We have recorded a full valuation allowance against our deferred tax assets in the U.S.

For The Years Ended December 31, 2013 and December 31, 2012

Revenues. Revenues for the year ended December 31, 2013, were $96.5 million, compared to $47.0 million for the year ended December 31, 2012. The increase principally reflected revenues related to the December 2012 acquisition of OPKO Lab, the October 2012 acquisition of SciVac, and the August 2012 acquisition of OPKO Health Europe, which contributed $10.8 million, $1.7 million and $18.8 million of revenue, respectively, during the year ended December 31, 2013, as compared with revenues from those units of $0.4 million, $0.6 million and $6.1 million, respectively, during the year ended December 31, 2012. Revenue from our Chilean operations increased $5.1 million during the year ended December 31, 2013, primarily due to increased sales to government agencies. Revenue from FineTech increased $4.6 million during the year ended December 31, 2013, primarily related to increased sales to new and existing customers. Revenues for the year ended December 31, 2013 also reflects the one-time, non–cash revenue of $12.5 million related to the transfer of substantially all of our assets in the field of RNA interference to RXi (the "RXi Revenue"). Revenue related to our molecular diagnostics collaboration agreements and license agreements, excluding the RXi Revenue, increased $3.7 million during the year ended December 31, 2013, compared to the year ended December 31, 2012, primarily related to revenue recorded in connection to the Pharmsynthez Collaboration Agreements.

Cost of revenues. Costs of revenues for the year ended December 31, 2013, were $48.9 million, compared to $27.9 million for the year ended December 31, 2012. Costs of revenues for the year ended December 31, 2013, increased principally as a result of costs of revenue recorded by OPKO Lab, SciVac and OPKO Health Europe of $10.0 million, $3.6 million and $4.3 million, respectively. Costs of revenue recorded by FineTech, our Chilean and Mexican operations increased $1.1 million, $1.9 million and $0.5 million, respectively, during the year ended December 31, 2013, primarily related to higher revenue levels recorded by those businesses.

Selling, general and administrative expenses. Selling, general and administrative expenses for the year ended December 31, 2013, were $55.3 million, compared to $27.8 million for the year ended December 31, 2012. The

increase in selling, general and administrative expenses principally resulted from $15.0 million of such expenses recorded during the year ended December 31, 2013, by OPKO Health Europe, SciVac, OPKO Lab, OPKO Renal, the January 2013 acquisition of OPKO Brazil, and the August 2013 acquisition of OPKO Biologics (collectively, the "Acquired Businesses"). Excluding the selling, general and administrative expenses of the Acquired Businesses, selling, general and administrative expenses increased by $10.4 million during the year ended December 31, 2013, principally as a result of increased personnel expenses and professional fees associated with our increased operations. Selling, general and administrative expenses during the year ended December 31, 2013 and 2012, include equity-based compensation expense of $7.3 million and $3.1 million, respectively.

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Research and development expenses. Research and development expenses for the years ended December 31, 2013 and 2012, were $53.9 million and $19.5 million, respectively. Research and development expenses include external and internal expenses, partially offset by third-party grants and funding arising from collaboration agreements. External expenses include clinical and non-clinical activities performed by contract research organizations, lab services, purchases of drug and diagnostic product materials and manufacturing development costs. We track external research and development expenses by individual program, with phase 3 clinical trials for drug approval and/or PMAs, if any. Research and development employee-related expenses include salaries, benefits and stock-based compensation expense. Other unallocated internal research and development expenses are incurred to support overall research and development activities and include expenses related to general overhead and facilities.

The following table summarizes the components of our research and development expenses:

	For the years ended December 31,	
	2013	2012
External expenses:		
Phase 3 clinical trials	$13,078	$—
Earlier-stage programs	6,364	—
Research and development employee-related expenses	17,215	8,315
Other unallocated internal research and development expenses	18,998	11,497
Third-party grants and funding from collaboration agreements	(1,753)	(292)
Total research and development expenses	$53,902	$19,520

The increase in research and development expenses during the year ended December 31, 2013 as compared with the year ended December 31, 2012, principally resulted from an increase of $28.3 million related to research and development expenses incurred by OPKO Renal, which business was acquired in March 2013, and OPKO Biologics, including $13.1 million related to the costs of ongoing phase 3 clinical trials for Rayaldee (CTAP101) and hGH-CTP. Research and development expenses for the years ended December 31, 2013 and 2012, include equity-based compensation expense of $3.6 million and $2.0 million, respectively. The increase in equity-based compensation expense during the year ended December 31, 2013, principally reflects the mark to market impact of Common Stock options granted to non-employees and the associated increase in the trading price of our Common Stock during the year ended December 31, 2013. Research and development expenses for the year ended December 31, 2013, includes an offset to research and development expenses of $2.7 million related to the correction of an error related to equity awards granted to non-employees with performance based vesting.

Contingent consideration. Contingent consideration expenses for the years ended December 31, 2013 and 2012, were $6.9 million and $0.8 million, respectively. The increase in contingent consideration expense resulted from changes in the fair value of the contingent consideration liabilities due to the time value of money and the impact of changes in the underlying assumptions, if any, during the period. The contingent consideration liabilities relate to potential amounts payable to former stockholders of CURNA, OPKO Diagnostics, FineTech, OPKO Health Europe and OPKO Renal pursuant to our acquisition agreements in January 2011, October 2011, December 2011, August 2012 and March 2013, respectively.

Amortization of intangible assets. Amortization of intangible assets was $11.1 million and $8.3 million for the years ended December 31, 2013 and 2012, respectively. Amortization expense increased due to the acquisitions of OPKO Health Europe, OPKO Lab and OPKO Renal in August 2012, December 2012 and March 2013, respectively.

Other income and (expense), net. Other income and (expense), net for the years ended December 31, 2013 and 2012, was ($24.6) million and $0.2 million, respectively. During the year ended December 31, 2013, we recorded a $52.7 million non-cash charge, net, related to the changes in the fair value of the embedded derivatives in the 2033 Senior Notes, partially offset by a $1.0 million gain on early partial conversion of the 2033 Senior Notes, income of $6.5 million related to changes in the fair value of the Pharmsynthez Note Receivable, a certain Pharmsynthez purchase option, and warrants and options received in connection with our investment in Neovasc and ARNO, and by a gain of $29.9 million on the sale of certain of our strategic investments. Other income and (expense), net, for the year ended December 31, 2013, also included $13.8 million of interest expense primarily related to interest incurred on the 2033 Senior Notes and by the amortization of related deferred financing costs related to the 2033 Senior Notes. For the year

ended December 31, 2012, other income net, included $1.5 million of other income recognized from the change in fair value of the warrants received in connection with our investment in Biozone Pharmaceuticals, Inc. (“BZNE”), partially offset by other expense recognized for the decrease in fair value of warrants and options received in connections with our investment in Neovasc and the interest expense incurred on our lines of credit at OPKO Chile and OPKO Health Europe.

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Loss from investments in investees. We have made investments in other early stage companies that we perceive to have valuable proprietary technology and significant potential to create value for us as a shareholder. We account for eight of these investments under the equity method of accounting, resulting in our recording of our proportionate share of their losses until our share of their loss exceeds our investment. Until the investees' technologies are commercialized, if ever, we anticipate they will continue to report a net loss. Loss from investments in investees was $11.5 million and $2.1 million for the years ended December 31, 2013 and 2012, respectively. The increase in loss from investments in investees is primarily due to the result of increased research and development activities at our investees as well as the impact of including the activities of our recent investments in RXi, Pharmsynthez and Zebra.
Income taxes. Our income tax provision reflects the projected income tax payable in Israel, Chile, Spain, Mexico and Canada. We have recorded a full valuation allowance against our deferred tax assets in the U.S.

LIQUIDITY AND CAPITAL RESOURCES

At December 31, 2014, we had cash and cash equivalents of approximately $96.9 million. Cash used in operations during 2014 principally reflects expenses related to selling, general and administrative activities related to our corporate operations, research and development activities and our operations at OPKO Biologics, OPKO Renal and OPKO Diagnostics, partially offset by cash provided from our operations at FineTech and OPKO Health Europe. Cash used in investing activities includes net cash used in business combinations of $1.7 million, capital expenditures of $4.7 million and investments in investees of $0.6 million, which was partially offset by proceeds from the sale of equity securities of $1.3 million. Cash provided by financing activities primarily reflects $12.9 million received from Common Stock option and Common Stock warrant exercises, which was partially offset by $6.4 million of deferred and contingent consideration payments related to our acquisitions of OPKO Health Europe and FineTech. In addition to cash contingent consideration payments made during the year ended December 31, 2014, we also satisfied a $20.0 million contingent payment to the former owners of OPKO Renal through the issuance of 2,236,210 shares of our common stock in September 2014. Since our inception, we have not generated gross margins sufficient to offset our operating and other expenses and our primary source of cash has been from the public and private placement of stock and credit facilities available to us.

In December 2014, we entered into an exclusive worldwide agreement with Pfizer for the development and commercialization of our long-acting hGH-CTP for the treatment of GHD in adults and children, as well as for the treatment of growth failure in children born SGA.

The agreements with Pfizer closed in January 2015 following the termination of the waiting period under the Hart-Scott-Rodino Act. Under the terms of the agreements with Pfizer, we received non-refundable and non-creditable upfront payments of $295 million and are eligible to receive up to an additional $275 million upon the achievement of certain regulatory milestones. Pfizer received the exclusive license to commercialize hGH-CTP worldwide. In addition, we are eligible to receive initial royalty payments associated with the commercialization of hGH-CTP for Adult GHD. Upon the launch of hGH-CTP for Pediatric GHD, the royalties will transition to a regional, tiered gross profit sharing for both hGH-CTP and Pfizer's Genotropin®.

We will lead the clinical activities and will be responsible for funding the development programs for the key indications, which includes Adult and Pediatric GHD and Pediatric SGA. Pfizer will be responsible for all development costs for additional indications as well as all post-marketing studies. In addition, Pfizer will fund the commercialization activities for all indications and lead the manufacturing activities covered by the global development plan.

In the first quarter of 2015, we expect to make a payment of $25.6 million to the Office of the Chief Scientist of the Israeli Ministry of Economy ("OCS") in connection with repayment obligations resulting from grants previously made by the OCS to OPKO Biologics to support development of hGH-CTP and from the outlicense of the technology outside of Israel.

In September 2014, our licensee, TESARO, submitted a NDA to the FDA for approval of oral rolapitant, an investigational neurokinin-1 receptor antagonist in development for the prevention of chemotherapy-induced nausea and vomiting. Under the terms of our agreement with TESARO, TESARO paid us a milestone payment of $5.0 million upon acceptance by the FDA of a NDA in the fourth quarter of 2014 of which we are required to pay $2.0 million to Merck. We will also receive double digit tiered-royalties on sales of rolapitant. In addition, TESARO and

OPKO will share future profits from the commercialization of rolapitant in Japan, and we will have an option to market the products in Latin America. Under the terms of our agreement with Merck, we are required to pay up to an additional $25.0 million upon the achievement of certain development milestones for rolapitant.

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In May 2014, we acquired Inspiro, an Israeli medical device company developing a new platform to deliver small molecule drugs such as corticosteroids and beta agonists and larger molecules to treat respiratory diseases. In connection with the transaction, we paid an aggregate of $10.1 million, of which $1.5 million was paid in cash and $8.6 million was paid in 999,556 shares of the Company's Common Stock based on the closing price per share of our Common Stock as reported by the NYSE on the actual closing date of the acquisition, or $8.57 per share. The number of shares issued was based upon our trading price as reported by the NYSE for the ten trading days immediately preceding the execution date of the purchase agreement, or $9.00 per share.

In April 2013, we invested $9.6 million in exchange for approximately 13.6 million shares of Pharmsynthez common stock. Concurrent with our investment, Pharmsynthez also agreed, at its option, to issue approximately 12.0 million shares of its common stock or pay us Russian Rubles ("RUR") 265.0 million (approximately $8.1 million as of December 31, 2013) on or before December 31, 2013. We had a right to purchase additional shares in Pharmsynthez at a fixed price if Pharmsynthez paid us in cash rather than the 12.0 million shares of Pharmsynthez common stock. Pharmsynthez delivered approximately 12.0 million shares of its common stock to us in January 2014.

2033 Senior Notes. In January 2013, we issued $175.0 million of the 2033 Senior Notes. The 2033 Senior Notes were sold in a private placement in reliance on exemptions from registration under the Securities Act. A $4.5 million discount was granted to the placement agent and an additional $0.4 million in deferred charges were recorded for professional fees related to the issuance. Net cash proceeds from the offering totaled $170.2 million. Interest on the 2033 Senior Notes is payable semiannually on February 1 and August 1, beginning August 1, 2013. Holders of the 2033 Senior Notes may require us to repurchase the 2033 Senior Notes for 100% of their principal amount, plus accrued and unpaid interest, on February 1, 2019, February 1, 2023 and February 1, 2028, or following the occurrence of a fundamental change as defined in the indenture governing the 2033 Senior Notes.

On August 30, 2013, one of the conversion rights in the 2033 Senior Notes was triggered. Holders of the 2033 Senior Notes converted $16.9 million principal amount into 2,396,145 shares of our Common Stock at a rate of 141.48 shares of Common Stock per $1,000 principal amount of 2033 Senior Notes. We recorded a $1.0 million non-cash gain related to the exchange. The gain on exchange is included within Other income (expense), net on our Consolidated Statement of Operations.

In June 2014, we entered into an exchange agreement with a holder of the Company's 2033 Senior Notes pursuant to which such holder exchanged $70.4 million in aggregate principal amount of Notes for 10,974,431 shares of the Company's Common stock, par value $0.01 per share and approximately $0.8 million in cash representing accrued interest through the date of completion of the exchange. We recorded a $2.7 million non-cash gain related to the exchange. The gain on exchange is included within Other income (expense), net on our Consolidated Statement of Operations.

In August 2012, we entered into a stock purchase agreement pursuant to which we acquired all of the outstanding stock of OPKO Health Europe (previously Farmadiet Group Holding, S.L.), a Spanish company engaged in the development, manufacture, marketing, and sale of pharmaceutical, nutraceutical, and veterinary products in Europe (the "OPKO Health Europe Transaction"). In connection with the OPKO Health Europe Transaction, we agreed to pay an aggregate purchase price of €13.5 million (approximately $16.0 million), of which (i) 50% ($8.4 million) was paid in cash at closing, and (ii) 50% (the "Deferred Payments") was paid, at our option, in cash or shares of our Common Stock as follows: (x) 25% to be paid on the first anniversary of the closing date; and (y) 25% to be paid 18 months after the closing date. In the event we elected to pay the Deferred Payments in shares of our Common Stock, the number of shares issuable shall be calculated using the average closing price per share of our Common Stock as reported on the NYSE for the 10 trading days immediately preceding the applicable payment date. On August 2, 2013, we issued 585,703 shares of our Common Stock, in accordance with the first Deferred Payment. The number of shares issued was based on the average closing price per share of our Common Stock as reported on the NYSE for the 10 trading days up to and including August 1, 2013, or $7.61 per share. On February 14, 2014, we delivered approximately €3.4 million in cash in accordance with the second Deferred Payment.

In connection with our acquisitions of CURNA, OPKO Diagnostics, FineTech and OPKO Renal, we agreed to pay future consideration to the sellers upon the achievement of certain events, including minimum cash payments of $2.7 million and $3.2 million, paid in March 2013 and 2014, respectively, to the former stockholder of FineTech upon the

achievement of certain sales milestones; up to an additional $19.1 million in shares of our Common Stock to the former stockholders of OPKO Diagnostics upon and subject to the achievement of certain milestones; and up to an additional $190.0 million in either shares of our Common Stock or cash, at our option subject to the achievement of certain milestones, to the former shareholders of OPKO Renal. In September 2014, we satisfied a $20.0 million contingent payment to the former owners of OPKO Renal through the issuance of 2,236,210 shares of our common stock.

As of December 31, 2014, we have outstanding lines of credit in the aggregate amount of $7.7 million with 10 financial institutions in Chile and Spain, of which $5.5 million is unused. The weighted average interest rate on these lines of credit is

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approximately 6.1%. These lines of credit are short-term and are generally due within three months. These lines of credit are used primarily as a source of working capital for inventory purchases. The highest balance at any time during the years ended December 31, 2014, was $8.8 million. We intend to continue to enter into these lines of credit as needed. There is no assurance that these lines of credit or other funding sources will be available to us on acceptable terms, or at all, in the future.

We expect to incur losses from operations for the foreseeable future. We expect to incur substantial research and development expenses, including expenses related to the hiring of personnel and additional clinical trials. We expect that selling, general and administrative expenses will also increase as we expand our sales, marketing and administrative staff and add infrastructure.

We believe that the cash and cash equivalents on hand at December 31, 2014, the proceeds we received under our agreements with Pfizer and the amounts available to be borrowed under our lines of credit are sufficient to meet our anticipated cash requirements for operations and debt service beyond the next 12 months. We based this estimate on assumptions that may prove to be wrong or are subject to change, and we may be required to use our available cash resources sooner than we currently expect. If we acquire additional assets or companies, accelerate our product development programs or initiate additional clinical trials, we will need additional funds. Our future cash requirements will depend on a number of factors, including our relationship with Pfizer, possible acquisitions, the continued progress of research and development of our product candidates, the timing and outcome of clinical trials and regulatory approvals, the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing patent claims and other intellectual property rights, the status of competitive products, the availability of financing, and our success in developing markets for our product candidates. If we are not able to secure additional funding when needed, we may have to delay, reduce the scope of, or eliminate one or more of our clinical trials or research and development programs or possible acquisitions.

The following table provides information as of December 31, 2014, with respect to the amounts and timing of our known contractual obligation payments due by period.

Contractual obligations (In thousands)	2015	2016	2017	2018	2019	Thereafter	Total
Open purchase orders	$14,653	$—	$—	$—	$—	$—	$14,653
Operating leases	2,744	2,290	1,478	1,149	653	3,256	11,570
2033 Senior Notes	—	—	—	—	87,642	—	87,642
Mortgages and other debts payable [1]	613	332	298	247	240	1,313	3,043
Lines of credit	7,658	—	—	—	—	—	7,658
Interest commitments	2,779	2,710	2,699	2,688	489	55	11,420
Total	$28,447	$5,332	$4,475	$4,084	$89,024	$4,624	$135,986

[1] Excludes $5.2 million of consolidated liabilities related to SciVac, as to which there is no recourse against us.

The preceding table does not include information where the amounts of the obligations are not currently determinable, including the following:

- Contractual obligations in connection with clinical trials, which span over two years, and that depend on patient enrollment. The total amount of expenditures is dependent on the actual number of patients enrolled and as such, the contracts do not specify the maximum amount we may owe.
- Product license agreements effective during the lesser of 15 years or patent expiration whereby payments and amounts are determined by applying a royalty rate on uncapped future sales.
- Contingent consideration that includes payments upon achievement of certain milestones including meeting development milestones such as the completion of successful clinical trials, NDA approvals by the FDA and revenue milestones upon the achievement of certain revenue targets all of which are anticipated to be paid within the next 7 years and are payable in either shares of our Common Stock or cash, at our option, and that may aggregate up to $238.5 million.

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CRITICAL ACCOUNTING POLICIES AND ESTIMATES

Accounting estimates. The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of sales and expenses during the reporting period. Actual results could differ from those estimates.

Goodwill and Intangible Assets. Goodwill and other intangible assets, including IPR&D, acquired in business combinations, licensing and other transactions was $1.1 billion at both December 31, 2014 and 2013, representing approximately 85% and 79% of total assets, respectively.

Assets acquired and liabilities assumed in business combinations, licensing and other transactions are recognized at the date of acquisition at their respective fair values. Any excess of the purchase price over the estimated fair values of the net assets acquired is recognized as goodwill. We determined the fair value of intangible assets, including IPR&D, using the "income method." This method starts with a forecast of net cash flows, risk adjusted for estimated probabilities of technical and regulatory success (for IPR&D) and adjusted to present value using an appropriate discount rate that reflects the risk associated with the cash flow streams. All assets are valued from a market participant view which might be different than our specific views. The valuation process is very complex and requires significant input and judgment using internal and external sources. Although the valuations are required to be finalized within a one-year period, it must consider all and only those facts and evidence which existed at the acquisition date. The most complex and judgmental matters applicable to the valuation process are summarized below:

- Unit of account – Most intangible assets are valued as single global assets rather than multiple assets for each jurisdiction or indication after considering the development stage, expected levels of incremental costs to obtain additional approvals, risks associated with further development, amount and timing of benefits expected to be derived in the future, expected patent lives in various jurisdictions and the intention to promote the asset as a global brand.
- Estimated useful life – The asset life expected to contribute meaningful cash flows is determined after considering all pertinent matters associated with the asset, including expected regulatory approval dates (if unapproved), exclusivity periods and other legal, regulatory or contractual provisions as well as the effects of any obsolescence, demand, competition, and other economic factors, including barriers to entry.
- Probability of Technical and Regulatory Success ("PTRS") Rate – PTRS rates are determined based upon industry averages considering the respective programs development stage and disease indication and adjusted for specific information or data known at the acquisition date. Subsequent clinical results or other internal or external data obtained could alter the PTRS rate and materially impact the estimated fair value of the intangible asset in subsequent periods leading to impairment charges.
- Projections – Future revenues are estimated after considering many factors such as initial market opportunity, pricing, sales trajectories to peak sales levels, competitive environment and product evolution. Future costs and expenses are estimated after considering historical market trends, market participant synergies and the timing and level of additional development costs to obtain the initial or additional regulatory approvals, maintain or further enhance the product. We generally assume initial positive cash flows to commence shortly after the receipt of expected regulatory approvals which typically may not occur for a number of years. Actual cash flows attributed to the project are likely to be different than those assumed since projections are subjected to multiple factors including trial results and regulatory matters which could materially change the ultimate commercial success of the asset as well as significantly alter the costs to develop the respective asset into commercially viable products.
- Tax rates – The expected future income is tax effected using a market participant tax rate. Our recent valuations typically use a U.S. tax rate (and applicable state taxes) after considering the jurisdiction in which the intellectual property is held and location of research and manufacturing infrastructure. We also considered that any repatriation of earnings would likely have U.S. tax consequences.
- Discount rate – Discount rates are selected after considering the risks inherent in the future cash flows; the assessment of the asset's life cycle and the competitive trends impacting the asset, including consideration of any technical, legal, regulatory, or economic barriers to entry, as well as expected changes in standards of practice for indications addressed by the asset.

Goodwill was $224.3 million and $226.4 million, respectively, at December 31, 2014 and 2013. The decrease in goodwill from December 31, 2013 to 2014 is due to foreign exchange translation adjustments recognized in 2014. Goodwill is tested at least annually for impairment or when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable, on an enterprise level by assessing qualitative factors or performing a quantitative analysis in determining

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whether it is more likely than not that its fair value exceeds the carrying value. Examples of qualitative factors include our share price, our financial performance compared to budgets, long-term financial plans, macroeconomic, industry and market conditions as well as the substantial excess of fair value over the carrying value of net assets from the annual impairment test performed in the prior year. No goodwill impairment was recorded for the years ended December 31, 2014 and 2013 as a result of our testing.

The estimated fair value of the reporting unit is highly sensitive to changes in projections and assumptions; therefore, in some instances changes in these assumptions could potentially lead to impairment. We perform sensitivity analyses around our assumptions in order to assess the reasonableness of the assumptions and the results of our testing. Ultimately, future potential changes in these assumptions may impact the estimated fair value of a reporting unit and cause the fair value of the reporting unit to be below its carrying value. We believe that our estimates are consistent with assumptions that marketplace participants would use in their estimates of fair value. However, if actual results are not consistent with our estimates and assumptions, we may be exposed to an impairment charge that could be material.

Intangible assets were $855.8 million and $867.9 million, including IPR&D of $793.2 million and $793.3 million, respectively, at December 31, 2014 and 2013. Intangible assets are tested for impairment whenever events or changes in circumstances warrant a review, although IPR&D is required to be tested at least annually until the project is completed or abandoned. Upon obtaining regulatory approval, the IPR&D asset is then accounted for as a finite-lived intangible asset and amortized on a straight-line basis over its estimated useful life. If the project is abandoned, the IPR&D asset is charged to expense.

Intangible assets are highly vulnerable to impairment charges, particularly newly acquired assets for recently launched products or IPR&D. These assets are initially measured at fair value and therefore any reduction in expectations used in the valuations could potentially lead to impairment. Some of the more common potential risks leading to impairment include competition, earlier than expected loss of exclusivity, pricing pressures, adverse regulatory changes or clinical trial results, delay or failure to obtain regulatory approval and additional development costs, inability to achieve expected synergies, higher operating costs, changes in tax laws and other macro-economic changes. The complexity in estimating the fair value of intangible assets in connection with an impairment test is similar to the initial valuation.

Considering the high risk nature of research and development and the industry’s success rate of bringing developmental compounds to market, IPR&D impairment charges are likely to occur in future periods. IPR&D is closely monitored and assessed each period for impairment.

Contingent consideration. Each period we revalue the contingent consideration obligations associated with certain acquisitions to their fair value and record increases in the fair value as contingent consideration expense and decreases in the fair value as contingent consideration income. Changes in contingent consideration result from changes in the assumptions regarding probabilities of successful achievement of related milestones, the estimated timing in which the milestones are achieved and the discount rate used to estimate the fair value of the liability. Contingent consideration may change significantly as our development programs progress, revenue estimates evolve and additional data is obtained, impacting our assumptions. The assumptions used in estimating fair value require significant judgment. The use of different assumptions and judgments could result in a materially different estimate of fair value which may have a material impact on our results from operations and financial position.

Equity-based compensation. We recognize equity based compensation as an expense in our financial statements and that cost is measured at the fair value of the awards and expensed over their vesting period. Equity-based compensation arrangements to non-employees are recorded at their fair value on the measurement date. We estimate the grant-date fair value of our stock option grants using a valuation model known as the Black-Scholes-Merton formula or the “Black-Scholes Model” and allocate the resulting compensation expense over the corresponding requisite service period associated with each grant. The Black-Scholes Model requires the use of several variables to estimate the grant-date fair value of stock options including expected term, expected volatility, expected dividends and risk-free interest rate. We perform analyses to calculate and select the appropriate variable assumptions used in the Black-Scholes Model and to estimate forfeitures of equity-based awards. We are required to adjust our forfeiture estimates on at least an annual basis based on the number of share-based awards that ultimately vest. The selection of

assumptions and estimated forfeiture rates is subject to significant judgment and future changes to our assumptions and estimates which may have a material impact on our Consolidated Financial Statements.

Allowance for doubtful accounts and revenue recognition. Generally, we recognize revenue from product sales when goods are shipped and title and risk of loss transfer to our customers. Our estimates for sales returns are based upon the historical patterns of products returned matched against the sales from which they originated, and management's evaluation of specific factors that may increase or decrease the risk of product returns. Revenue for services is recognized on the accrual basis at the time test results are reported, which approximates when services are provided. Services are provided to certain

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patients covered by various third-party payer programs including various managed care organizations, as well as the Medicare and Medicaid programs. Billings for services under third-party payer programs are included in sales net of allowances for contractual discounts and allowances for differences between the amounts billed and estimated program payment amounts. Adjustments to the estimated payment amounts based on final settlement with the programs are recorded upon settlement as an adjustment to revenue. We analyze accounts receivable and historical bad debt levels, customer credit worthiness and current economic trends when evaluating the adequacy of the allowance for doubtful accounts using the specific identification method. Our reported net loss is directly affected by management's estimate of the collectability of accounts receivable. The allowance for doubtful accounts recognized in our Consolidated Balance Sheets at December 31, 2014 and 2013 was $1.9 million and $1.9 million, respectively.

Inventories. Inventories are valued at the lower of cost or market (net realizable value). Cost is determined by the first-in, first-out method. We consider such factors as the amount of inventory on hand, estimated time required to sell such inventories, remaining shelf-life, and current market conditions to determine whether inventories are stated at the lower of cost or market.

Pre-launch inventories. We may accumulate commercial quantities of certain product candidates prior to the date we anticipate that such products will receive final U.S. FDA approval. The accumulation of such pre-launch inventories involves the risk that such products may not be approved for marketing by the FDA on a timely basis, or ever. This risk notwithstanding, we may accumulate pre-launch inventories of certain products when such action is appropriate in relation to the commercial value of the product launch opportunity. In accordance with our policy, this pre-launch inventory is expensed.

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RECENT ACCOUNTING PRONOUNCEMENTS

In July 2013, the FASB issued an Accounting Standards Update ("ASU"), ASU 2013-11, Presentation of an Unrecognized Tax Benefit When a Net Operating Loss Carryforward, a Similar Tax Loss, or a Tax Credit Carryforward Exists. ASU 2013-11 is intended to eliminate inconsistent practices regarding the presentation of an unrecognized tax benefit when a net operating loss carryforward, a similar tax loss, or a tax credit carryforward is available to reduce the taxable income or tax payable that would result from the disallowance of a tax position. ASU 2013-11 is effective for our fiscal year beginning January 1, 2014 and subsequent interim periods. The adoption of ASU 2013-11 does not have a material effect on our Consolidated Financial Statements.

In May 2014, the FASB issued ASU No. 2014-09, "Revenue from Contracts with Customers." ASU No. 2014-09 clarifies the principles for recognizing revenue and develops a common revenue standard for GAAP and International Financial Reporting Standards that removes inconsistencies and weaknesses in revenue requirements, provides a more robust framework for addressing revenue issues, improves comparability of revenue recognition practices across entities, industries, jurisdictions, and capital markets, provides more useful information to users of financial statements through improved disclosure requirements and simplifies the preparation of financial statements by reducing the number of requirements to which an entity must refer. ASU No. 2014-09 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016. Companies can choose to apply the ASU using either the full retrospective approach or a modified retrospective approach. We are currently evaluating both methods of adoption and the impact that the adoption of this ASU will have on our Consolidated Financial Statements.

In June 2014, the FASB issued ASU No. 2014-12, "Accounting for Share-Based Payments When the Terms of an Award Provide That a Performance Target Could Be Achieved after the Requisite Service Period (a consensus of the FASB Emerging Issues Task Force)." ASU No. 2014-12 requires that a performance target that affects vesting and that could be achieved after the requisite service period be treated as a performance condition. ASU No. 2014-12 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2015. Earlier adoption is permitted. The amendments can be applied either prospectively to all awards granted or modified after the effective date or retrospectively to all awards with performance targets that are outstanding as of the beginning of the earliest annual period presented in the financial statements and to all new or modified awards. We expect to apply the ASU prospectively and do not expect the adoption to have an impact on our Consolidated Financial Statements as our existing share-based payment awards do not fall within the scope of this ASU.

In August 2014, the FASB issued ASU No. 2014-15, "Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern," to provide guidance on management's responsibility in evaluating whether there is substantial doubt about a company's ability to continue as a going concern and to provide related footnote disclosures. ASU 2014-15 is effective for annual periods ending after December 15, 2016 with early adoption permitted. We do not believe the impact of our pending adoption of ASU 2014-15 on our Consolidated Financial Statements will be material.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

In the normal course of doing business, we are exposed to the risks associated with foreign currency exchange rates and changes in interest rates.

Foreign Currency Exchange Rate Risk – We operate globally and, as such, we are subject to foreign exchange risk in our commercial operations as a significant portion of our revenues are exposed to changes in foreign currency exchange rates, primarily the Chilean peso, the Mexican peso, the euro and the New Israeli shekel.

Although we do not speculate in the foreign exchange market, we may from time to time manage exposures that arise in the normal course of business related to fluctuations in foreign currency exchange rates by entering into offsetting positions through the use of foreign exchange forward contracts. Certain firmly committed transactions are hedged with foreign exchange forward contracts. As exchange rates change, gains and losses on the exposed transactions are partially offset by gains and losses related to the hedging contracts. Both the exposed transactions and the hedging contracts are translated at current spot rates, with gains and losses included in earnings.

Our derivative activities, which consist of foreign exchange forward contracts, are initiated to hedge forecasted cash flows that are exposed to foreign currency risk. The foreign exchange forward contracts generally require us to exchange local currencies for foreign currencies based on pre-established exchange rates at the contracts' maturity

dates. As exchange rates change, gains and losses on these contracts are generated based on the change in the exchange rates that are recognized in the Consolidated Statement of Operations and offset the impact of the change in exchange rates on the foreign currency cash flows that are hedged. If the counterparties to the exchange contracts do not fulfill their obligations to deliver the contracted currencies, we could be at risk for currency related fluctuations. We had $0.9 million in foreign exchange forward contracts outstanding at December 31, 2014, primarily to hedge Chilean-based operating cash flows against U.S. dollars. If Chilean

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pesos were to strengthen or weaken in relation to the U.S. dollar, our loss or gain on hedged foreign currency cash-flows would be offset by the derivative contracts, with a net effect of zero.

We do not engage in trading market risk sensitive instruments or purchasing hedging instruments or "other than trading" instruments that are likely to expose us to significant market risk, whether interest rate, foreign currency exchange, commodity price, or equity price risk.

Interest Rate Risk – Our exposure to market risk relates to our cash and investments and to our borrowings. We maintain an investment portfolio of money market funds. The securities in our investment portfolio are not leveraged, and are, due to their very short-term nature, subject to minimal interest rate risk. We currently do not hedge interest rate exposure. Because of the short-term maturities of our investments, we do not believe that a change in market interest rates would have a significant negative impact on the value of our investment portfolio except for reduced income in a low interest rate environment.

At December 31, 2014, we had cash and cash equivalents and marketable securities of $96.9 million. The weighted average interest rate related to our cash and cash equivalents for the years ended December 31, 2014 was 0%. As of December 31, 2014, the principal value of our credit lines was $7.7 million at a weighted average interest rate of approximately 6.1%.

Our $87.6 million aggregate principal amount of our 2033 Senior Notes has a fixed interest rate, and therefore is not subject to fluctuations in market interest rates.

The primary objective of our investment activities is to preserve principal while at the same time maximizing yields without significantly increasing risk. To achieve this objective, we invest our excess cash in debt instruments of the U.S. Government and its agencies, bank obligations, repurchase agreements and high-quality corporate issuers, and money market funds that invest in such debt instruments, and, by policy, restrict our exposure to any single corporate issuer by imposing concentration limits. To minimize the exposure due to adverse shifts in interest rates, we maintain investments at an average maturity of generally less than three months.

Equity Price Risk – We are subject to equity price risk related to the (i) rights to convert into shares of our Common Stock, including upon a fundamental change; and (ii) a coupon make-whole payment in the event of a conversion by the holders of the 2033 Senior Notes on or after February 1, 2017 but prior to February 1, 2019. These terms are considered to be embedded derivatives. On a quarterly basis, we are required to record these embedded derivatives at fair value with the changes being recorded in our Consolidated Statement of Operations. Accordingly, our results of operations are subject to exposure associated with increases or decreases in the estimated fair value of our embedded derivatives.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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Report of Independent Registered Public Accounting Firm
The Board of Directors and Shareholders of OPKO Health, Inc. and subsidiaries

We have audited the accompanying consolidated balance sheets of OPKO Health, Inc. and subsidiaries as of December 31, 2014 and 2013, and the related consolidated statements of operations, comprehensive loss, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of OPKO Health, Inc. and subsidiaries at December 31, 2014 and 2013, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), OPKO Health, Inc. and subsidiaries' internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 27, 2015 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP
Certified Public Accountants
Miami, Florida
February 27, 2015

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Report of Independent Registered Public Accounting Firm
The Board of Directors and Shareholders of OPKO Health, Inc. and subsidiaries

We have audited OPKO Health, Inc. and subsidiaries' internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the "COSO criteria"). OPKO Health, Inc. and subsidiaries' management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

As indicated in the accompanying Management's Annual Report on Internal Control Over Financial, management's assessment of and conclusion on the effectiveness of internal control over financial reporting did not include the internal controls of SciVac Ltd, which is included in the December 31, 2014 consolidated financial statements of OPKO Health, Inc. and subsidiaries and constituted $7.6 million and $(4.5) million of total and net assets, respectively, as of December 31, 2014 and $2.8 million and $(2.6) million of revenues and net loss attributable to common shareholders, respectively, for the year then ended. Our audit of internal control over financial reporting of OPKO Health, Inc. and subsidiaries also did not include an evaluation of the internal control over financial reporting of SciVac Ltd.

In our opinion, OPKO Health, Inc. and subsidiaries maintained, in all material respects, effective internal control over financial reporting as of December 31, 2014, based on the COSO criteria.

/s/ Ernst & Young LLP
Certified Public Accountants

Miami, Florida
February 27, 2015

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OPKO Health, Inc. and Subsidiaries
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	December 31, 2014[1]	2013[1]
ASSETS		
Current assets:		
Cash and cash equivalents	$96,907	$185,798
Accounts receivable, net	19,969	19,767
Inventory, net	16,604	18,079
Prepaid expenses and other current assets	9,389	19,084
Total current assets	142,869	242,728
Property, plant, equipment, and investment properties, net	16,411	17,027
Intangible assets, net	62,649	74,533
In-process research and development	793,152	793,341
Goodwill	224,292	226,373
Investments, net	22,453	30,653
Other assets	5,838	6,861
Total assets	$1,267,664	$1,391,516
LIABILITIES AND EQUITY		
Current liabilities:		
Accounts payable	$8,744	$13,414
Accrued expenses	60,912	65,874
Current portion of lines of credit and notes payable	13,455	12,562
Total current liabilities	83,111	91,850
2033 Senior Notes, net of discount and estimated fair value of embedded derivatives	131,454	211,912
Other long-term liabilities, principally contingent consideration and deferred tax liabilities	217,358	214,775
Total long-term liabilities	348,812	426,687
Total liabilities	431,923	518,537
Equity:		
Common Stock - $0.01 par value, 750,000,000 shares authorized; 433,421,677 and 414,818,195 shares issued at December 31, 2014 and 2013, respectively	4,334	4,148
Treasury Stock - 1,245,367 and 2,264,063 shares at December 31, 2014 and 2013, respectively	(4,051)	(7,362)
Additional paid-in capital	1,529,096	1,379,383
Accumulated other comprehensive income (loss)	(12,392)	3,418
Accumulated deficit	(674,843)	(503,177)
Total shareholders' equity attributable to OPKO	842,144	876,410
Noncontrolling interests	(6,403)	(3,431)
Total shareholders' equity	835,741	872,979
Total liabilities and equity	$1,267,664	$1,391,516

(1) As of December 31, 2014 and December 31, 2013, total assets include $7.6 million and $6.7 million, respectively, and total liabilities include $12.1 million and $10.4 million, respectively, related to SciVac, previously known as SciGen (I.L.) Ltd, a consolidated variable interest entity. SciVac's consolidated assets are owned by SciVac and SciVac's consolidated liabilities have no recourse against us. Refer to Note 4.

The accompanying Notes to Consolidated Financial Statements are an integral part of these statements.
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OPKO Health, Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share data)

	For the years ended December 31,		
	2014	2013	2012
Revenues:			
Products	$76,983	$68,161	$45,295
Revenue from services	8,666	11,658	1,749
Revenue from transfer of intellectual property	5,476	16,711	—
Total revenues	91,125	96,530	47,044
Costs and expenses:			
Costs of revenues	48,009	48,860	27,878
Selling, general and administrative	57,940	55,320	27,795
Research and development	83,571	53,902	19,520
In-process research and development	12,055	—	—
Contingent consideration	24,446	6,947	785
Amortization of intangible assets	10,919	11,133	8,335
Total costs and expenses	236,940	176,162	84,313
Operating loss	(145,815)	(79,632)	(37,269)
Other income and (expense), net:			
Interest income	771	376	188
Interest expense	(12,263)	(13,802)	(1,405)
Fair value changes of derivative instruments, net	(10,632)	(45,942)	1,218
Other income (expense), net	(3,088)	34,782	164
Other income and (expense), net	(25,212)	(24,586)	165
Loss before income taxes and investment losses	(171,027)	(104,218)	(37,104)
Income tax benefit (provision)	(24)	(1,672)	9,626
Loss before investment losses	(171,051)	(105,890)	(27,478)
Loss from investments in investees	(3,587)	(11,456)	(2,062)
Net loss	(174,638)	(117,346)	(29,540)
Less: Net loss attributable to noncontrolling interests	(2,972)	(2,939)	(492)
Net loss attributable to common shareholders before preferred stock dividend	(171,666)	(114,407)	(29,048)
Preferred stock dividend	—	(420)	(2,240)
Net loss attributable to common shareholders	$(171,666)	$(114,827)	$(31,288)
Loss per share, basic and diluted:			
Net loss per share	$(0.41)	$(0.32)	$(0.11)
Weighted average number of common shares outstanding, basic and diluted	422,014,039	355,095,701	295,750,077

The accompanying Notes to Consolidated Financial Statements are an integral part of these statements.
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OPKO Health, Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	For the years ended December 31,		
	2014	2013	2012
Net loss	$(174,638)	$(117,346)	$(29,540)
Other comprehensive income (loss), net of tax:			
Change in foreign currency translation and other comprehensive income (loss) from equity investments	(8,088)	(1,825)	2,289
Available for sale investments:			
Change in other unrealized gain (loss), net	(8,044)	2,467	4,160
Less: reclassification adjustments for (gains) losses included in net loss, net of tax	322	(4,580)	—
Comprehensive loss	(190,448)	(121,284)	(23,091)
Less: Comprehensive loss attributable to noncontrolling interest	(2,972)	(2,939)	(492)
Comprehensive loss attributable to common shareholders before preferred stock dividend	(187,476)	(118,345)	(22,599)
Preferred stock dividend	—	(420)	(2,240)
Comprehensive loss attributable to common shareholders	$(187,476)	$(118,765)	$(24,839)

The accompanying Notes to Consolidated Financial Statements are an integral part of these statements.
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OPKO Health, Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF EQUITY
(In thousands, except share and per share data)
For the years ended December 31, 2014, 2013, 2012

	Common Stock		Treasury		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Noncontrolling Interests	Total
	Shares	Dollars	Shares	Dollars					
Balance at December 31, 2011	297,503,033	$2,975	(2,488,477)	$(8,092)	$524,814	$907	$(359,722)	$—	$160,882
Equity-based compensation expense	—	—	—	—	5,131	—	—	—	5,131
Exercise of Common Stock options	1,019,967	10	—	—	2,224	—	—	—	2,234
Exercise of Common Stock warrants	65,015	1	—	—	44	—	—	—	45
Adjustment of Common Stock	(100,000)	(1)	—	—	1	—	—	—	—
Issuance of Common Stock from Treasury in connection with OPKO Health Europe acquisition at $4.12 per share	—	—	195,421	635	170	—	—	—	805
Issuance of Common Stock in connection with OPKO Lab acquisition at $4.65 per share	7,072,748	71	—	—	32,817	—	—	—	32,888
Net loss attributable to common shareholders before preferred stock dividend	—	—	—	—	—	—	(29,048)	—	(29,048)
Net loss attributable to noncontrolling interests	—	—	—	—	—	—	—	(492)	(492)

Other comprehensive income	—	—	—	—	—	6,449	—	—	6,449
Balance at December 31, 2012	305,560,763	$3,056	(2,293,056)	$(7,457)	$565,201	$7,356	$(388,770)	$(492)	$178,894

The accompanying Notes to Consolidated Financial Statements are an integral part of these statements.

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OPKO Health, Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF EQUITY
(In thousands, except share and per share data)
For the years ended December 31, 2014, 2013, 2012 (continued)

	Common Stock		Treasury		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Noncontrolling Interests	Total
	Shares	Dollars	Shares	Dollars					
Balance at December 31, 2012	305,560,763	$3,056	(2,293,056)	$(7,457)	$565,201	$7,356	$(388,770)	$(492)	$178,894
Equity-based compensation expense	—	—	—	—	10,983	—	—	—	10,983
Exercise of Common Stock options	9,244,971	92	—	—	22,704	—	—	—	22,796
Exercise of Common Stock warrants	1,487,774	15	—	—	613	—	—	—	628
Series D Preferred Stock dividend	—	—	—	—	(3,015)	—	—	—	(3,015)
Conversion of Series D Preferred Stock	11,290,320	113	—	—	24,273	—	—	—	24,386
Conversion of 2033 Senior Notes	2,396,145	24	—	—	20,815	—	—	—	20,839
Issuance of Common Stock in connection with OPKO Brazil acquisition at $6.73 per share	64,684	1	—	—	434	—	—	—	435
Issuance of Common Stock in connection with OPKO Renal acquisition at $7.16 per share	20,517,030	205	—	—	146,697	—	—	—	146,902
Issuance of Common Stock	63,670,805	637	—	—	586,006	—	—	—	586,643

in connection with OPKO Biologics acquisition at $8.49 per share and fair value of stock options and warrants exchanged									
Issuance of Common Stock in connection with OPKO Health	585,703	5	—	—	4,430	—	—	—	4,435
Europe's first Deferred Payment at $7.52 per share									
Issuance of Treasury Stock in connection with OPKO Health			28,993	95	242				337
Europe's Contingent Consideration at $11.60 per share									
Net loss attributable to common shareholders before preferred stock dividend	—	—	—	—	—	—	(114,407)	—	(114,407)
Net loss attributable to noncontrolling interests	—	—	—	—	—	—	—	(2,939)	(2,939)
Other comprehensive loss	—	—		—	—	(3,938)	—	—	(3,938)
Balance at December 31, 2013	414,818,195	$4,148	(2,264,063)	$(7,362)	$1,379,383	$3,418	$(503,177)	$(3,431)	$872,979

The accompanying Notes to Consolidated Financial Statements are an integral part of these statements.
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OPKO Health, Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF EQUITY
(In thousands, except share and per share data)
For the years ended December 31, 2014, 2013, 2012 (continued)

	Common Stock		Treasury		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Noncontrolling Interests	Total
	Shares	Dollars	Shares	Dollars					
Balance at December 31, 2013	414,818,195	$4,148	(2,264,063)	$(7,362)	$1,379,383	$3,418	$(503,177)	$(3,431)	$872,979
Equity-based compensation expense	—	—	—	—	14,737	—	—	—	14,737
Exercise of Common Stock options	2,328,947	23	—	—	5,892	—	—	—	5,915
Exercise of Common Stock warrants	3,063,894	31	—	—	6,982	—	—	—	7,013
Issuance of Common Stock for OPKO Uruguay Ltda.	—	—	19,140	61	98	—	—	—	159
Issuance of Common Stock upon exchange of 2033 Senior Notes	10,974,431	110	—	—	95,555	—	—	—	95,665
Issuance of Common Stock for Inspiro at 8.57	—	—	999,556	3,250	5,316	—	—	—	8,566
Issuance of Common Stock for OPKO Renal earnout	2,236,210	22	—	—	21,133	—	—	—	21,155
Net loss attributable to common shareholders	—	—	—	—	—	—	(171,666)	—	(171,666)
Net loss attributable to noncontrolling interests	—	—	—	—	—	—	—	(2,972)	(2,972)

Other comprehensive income	—	—	—	—	—	(15,810)	—	—	(15,810)
Balance at December 31, 2014	433,421,677	$4,334	(1,245,367)	$(4,051)	$1,529,096	$(12,392)	$(674,843)	$(6,403)	$835,741

The accompanying Notes to Consolidated Financial Statements are an integral part of these statements.

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OPKO Health, Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	For the years ended December 31,		
	2014	2013	2012
Cash flows from operating activities:			
Net loss	$(174,638)	$(117,346)	$(29,540)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	14,927	15,216	10,160
Non-cash interest on 2033 Senior Notes	5,662	5,980	—
Amortization of deferred financing costs	2,007	1,170	—
Losses from investments in investees	3,587	11,456	2,062
Equity-based compensation – employees and non-employees	14,779	10,983	5,131
(Recovery of) provision for bad debts	646	979	(95)
Provision for inventory obsolescence	1,082	2,015	2,688
Revenue from receipt of equity	(240)	(12,740)	(159)
Realized gain on sale of equity securities	167	(29,881)	—
Gain on conversion of 3.00% convertible senior notes	(2,668)	(972)	—
Loss on sale of property, plant and equipment	—	60	—
Change in fair value of derivative instruments	10,632	45,942	(1,218)
In-process research and development	12,055	—	—
Change in fair value of contingent consideration	24,446	6,947	785
Deferred income tax (benefit) expense	1,017	599	(9,958)
Changes in assets and liabilities, net of the effects of acquisitions:			
Accounts receivable	(3,919)	754	763
Inventory	(1,752)	1,892	(5,807)
Prepaid expenses and other current assets	3,182	(1,131)	(2,877)
Other assets	(3,378)	(544)	(361)
Accounts payable	(3,852)	1,829	1,247
Foreign currency measurement	945	(2,386)	86
Accrued expenses	4,934	3,525	1,678
Net cash used in operating activities	(90,379)	(55,653)	(25,415)
Cash flows from investing activities:			
Investments in investees	(589)	(17,441)	(3,396)
Proceeds from sale of equity securities	1,331	30,556	—
Acquisition of businesses, net of cash	(1,683)	20,528	(19,092)
Purchase of marketable securities	—	(50,027)	(25,806)
Maturities of short-term marketable securities	—	50,027	24,997
Proceeds from the sale of property, plant and equipment	—	636	—
Capital expenditures	(4,734)	(3,962)	(1,472)
Net cash provided by (used in) investing activities	(5,675)	30,317	(24,769)
Cash flows from financing activities:			
Issuance of 2033 Senior Notes, net, including related parties	—	170,184	—
Payment of Series D dividends, including related parties	—	(3,015)	—
Proceeds from the exercise of Common Stock options and warrants	12,928	23,425	2,279
Cash from non-controlling interest	2,696	—	—
Contingent consideration payments	(6,435)	(2,539)	—

Borrowings on lines of credit	26,443	34,577	36,506
Repayments of lines of credit	(28,369)	(38,997)	(32,754)
Net cash provided by financing activities	7,263	183,635	6,031
Effect of exchange rate on cash and cash equivalents	(100)	138	(2)
Net (decrease) increase in cash and cash equivalents	(88,891)	158,437	(44,155)
Cash and cash equivalents at beginning of period	185,798	27,361	71,516
Cash and cash equivalents at end of period	$96,907	$185,798	$27,361
SUPPLEMENTAL INFORMATION:			
Interest paid	$6,276	$3,407	$945
Income taxes paid, net	$954	$1,321	$575
RXi common stock received	$—	$12,500	$—
Pharmsynthez common stock received	$6,264	$—	$—
Non-cash financing:			
Shares issued upon the conversion of:			
Series D Preferred Stock	$—	$24,386	$—
2033 Senior Notes	$95,665	$20,839	$—
Common Stock options and warrants, surrendered in net exercise	$3,494	$815	$7
Issuance of capital stock to acquire:			
OPKO Biologics	$—	$586,643	$—
OPKO Renal	$21,155	$146,902	$—
OPKO Brazil	$—	$436	$—
OPKO Health Europe	$—	$4,404	$805
OPKO Lab	$—	$—	$32,888
OPKO Uruguay Ltda.	$159	$—	$—
Inspiro	$8,566	$—	$—

The accompanying Notes to Consolidated Financial Statements are an integral part of these statements.

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OPKO Health, Inc. and Subsidiaries
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (unaudited)

Note 1 Business and Organization

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

We own established pharmaceutical platforms in Chile, Spain, Mexico, and Uruguay, which are generating revenue and which we expect to facilitate future market entry for our products currently in development. In addition, we have established a global supply chain operation and holding company in Ireland and pharmaceutical operations in Brazil. We own a specialty active pharmaceutical ingredients ("APIs") manufacturer in Israel, which we expect will facilitate the development of our pipeline of molecules and compounds for our proprietary molecular diagnostic and therapeutic products. In the U.S., we own a laboratory certified under the Clinical Laboratory Improvement Amendments of 1988, as amended ("CLIA"), with a urologic focus that generates revenue and serves as the commercial platform for the U.S. launch of our next generation prostate cancer test to improve cancer risk stratification of patient candidates prior to prostate biopsy.

We are incorporated in Delaware and our principal executive offices are located in leased offices in Miami, Florida. We lease office and lab space in Jupiter and Miramar, Florida, and Nes Ziona, Israel, which is where our molecular diagnostics research and development, oligonucleotide research and development and CTP research and development operations are based, respectively. We lease office, manufacturing and warehouse space in Woburn, Massachusetts for our point-of-care diagnostics business, and in Nesher, Israel for our API business. We lease laboratory and office space in Nashville, Tennessee, Burlingame, California, and Miramar, Florida for our CLIA-certified laboratory business, and we lease office space in Bannockburn, Illinois, and Markham, Ontario for our pharmaceutical business directed to chronic kidney disease ("CKD"). Our Chilean and Uruguayan operations are located in leased offices and warehouse facilities in Santiago and Montevideo, respectively. Our Mexican operations are based in owned offices, an owned manufacturing facility and a leased warehouse facility in Guadalajara and in leased offices in Mexico City. Our Spanish operations are based in owned offices in Barcelona, in an owned manufacturing facility in Banyoles and a leased warehouse facility in Palol de Revardit. Our Brazilian operations are located in leased offices in Sao Paulo. Our Irish operations are located in leased offices in Dublin.

Note 2 Summary of Significant Accounting Policies

Basis of presentation. The accompanying Consolidated Financial Statements have been prepared in accordance with accounting principles generally accepted in the U.S. and with the instructions to Form 10-K and of Regulation S-X.

Reclassifications and correction of immaterial errors. During 2013 and the first quarter of 2014, we reported payments for contingent consideration and some deferred payments as cash outflows from operating activities. Amounts paid pertaining to the initial purchase accounting contingent liabilities should have been classified as cash outflows from financing activities. Amounts paid in excess of the initial purchase accounting contingent liabilities have been classified as cash outflows from operating activities. We have corrected the amounts previously reported in our Form 10-K for the year ended December 31, 2013 in conjunction with the filing of this Form 10-K and the year ended December 31, 2014 by reducing cash outflows from operating activities and increasing cash outflows from financing activities by $2.5 million and $6.4 million for 2013 and 2014, respectively.

During the year ended December 31, 2013, we reported an $8.7 million loss on early conversion of our 2033 Senior Notes (defined in Note 6) in Other income (expense), net and expense of $43.1 million for the change in the fair value of the 2033 Senior Notes' embedded derivative in Fair value changes of derivative instruments, net in our Consolidated Statement of Operations. The loss on early conversion was overstated by $9.7 million while the change in the fair value of the embedded derivative was understated by the same amount. We have corrected the amounts previously reported in our Consolidated Statement of Operations in our Form 10-K for the year ended December 31, 2013 in conjunction with the filing of this Form 10-K by increasing the expense related to the embedded derivative in the 2033

Senior Notes in Fair value changes of derivative instruments, net and reducing the early conversion of the 2033 Senior Notes in Other income (expense), net by $9.7 million. This adjustment also increased Change in fair value of derivative instruments and reduced Gain on conversion of 3.00% convertible senior notes by $9.7 million in our Consolidated Statement of Cash Flows. The adjustment only affects the components of Other income and expense in our Consolidated Statement of Operations and the components of Cash flows from

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operating activities in our Consolidated Statement of Cash Flows and does not affect Net loss, Net loss per share, net cash flows or income taxes for the period. See further discussion of the 2033 Senior Notes in Note 6.

Certain insignificant reclassifications have been made to the prior periods' Consolidated Statements of Operations and Consolidated Statements of Cash Flows to conform to the current period's presentation.

Principles of consolidation. The accompanying Consolidated Financial Statements include the accounts of OPKO Health, Inc. and of our wholly-owned subsidiaries and variable interest entities in which we are deemed to be the primary beneficiary. All intercompany accounts and transactions are eliminated in consolidation.

Use of estimates. The preparation of financial statements in conformity with accounting principles generally accepted in the U.S. requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Cash and cash equivalents. Cash and cash equivalents include short-term, interest-bearing instruments with original maturities of 90 days or less at the date of purchase. We also consider all highly liquid investments with original maturities at the date of purchase of 90 days or less as cash equivalents. These investments include money markets, bank deposits, certificates of deposit and U.S. treasury securities.

Inventories. Inventories are valued at the lower of cost or market (net realizable value). Cost is determined by the first-in, first-out method. We consider such factors as the amount of inventory on hand, estimated time required to sell such inventories, remaining shelf-life, and current market conditions to determine whether inventories are stated at the lower of cost or market.

Pre-launch inventories. We may accumulate commercial quantities of certain product candidates prior to the date we anticipate that such products will receive final FDA approval. The accumulation of such pre-launch inventories involves the risk that such products may not be approved for marketing by the FDA on a timely basis, or ever. This risk notwithstanding, we may accumulate pre-launch inventories of certain products when such action is appropriate in relation to the commercial value of the product launch opportunity. In accordance with our policy, this pre-launch inventory is expensed. At December 31, 2014 and 2013, there were no pre-launch inventories recognized.

Goodwill and intangible assets. Goodwill represents the difference between the purchase price and the estimated fair value of the net assets acquired when accounted for by the purchase method of accounting and arose from our acquisitions of Pharma Genexx, S.A. ("OPKO Chile"), Pharmacos Exakta S.A. de C.V. ("OPKO Mexico"), CURNA, Inc. ("CURNA"), Claros Diagnostics, Inc. ("OPKO Diagnostics"), FineTech Pharmaceuticals, Ltd. ("FineTech"), ALS Distribuidora Limitada ("ALS"), Farmadiet Group Holding, S.L. ("OPKO Health Europe"), previously known as OPKO Spain, Prost-Data, Inc. ("OPKO Lab"), Cytochroma Inc. ("OPKO Renal"), Silcon Comércio, Importacao E Exportacao de Produtos Farmaceuticos e Cosmeticos Ltda. ("OPKO Brazil") and PROLOR Biotech, Inc. ("OPKO Biologics"). Goodwill, in-process research and development ("IPR&D") and other intangible assets acquired in business combinations, licensing and other transactions at December 31, 2014 and 2013, were $1.1 billion and $1.1 billion, respectively.

Assets acquired and liabilities assumed in business combinations, licensing and other transactions are recognized at the date of acquisition at their respective fair values. Any excess of the purchase price over the estimated fair values of the net assets acquired is recognized as goodwill. We determined the fair value of intangible assets, including IPR&D, using the "income method."

Goodwill is tested at least annually for impairment, or when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable, by assessing qualitative factors or performing a quantitative analysis in determining whether it is more likely than not that its fair value exceeds the carrying value.

Intangible assets are tested for impairment whenever events or changes in circumstances warrant a review, although IPR&D is required to be tested at least annually until the project is completed or abandoned. Upon obtaining regulatory approval, the IPR&D asset is then accounted for as a finite-lived intangible asset and amortized on a straight-line basis over its estimated useful life. If the project is abandoned, the IPR&D asset is charged to expense.

We amortize intangible assets with definite lives on a straight-line basis over their estimated useful lives, currently ranging from 3 to 10 years, and review for impairment at least annually, or when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. We use the straight-line method of amortization as there is no reliably determinable pattern in which the economic benefits of our intangible assets are

consumed or otherwise used up. Amortization expense was $10.9 million, $11.1 million and $8.3 million for the years ended December 31, 2014, 2013 and

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2012, respectively. Amortization expense from operations for our intangible assets is expected to be $10.9 million, $9.7 million, $9.0 million, $6.9 million and $6.3 million for the years ended December 2015, 2016, 2017, 2018 and 2019, respectively.

Fair value measurements. The carrying amounts of our cash and cash equivalents, accounts receivable and accounts payable approximate their fair value due to the short-term maturities of these instruments. Investments that are considered available for sale as of December 31, 2014 are carried at fair value.

Short-term investments, which we invest in from time to time, include bank deposits, corporate notes, U.S. treasury securities and U.S. government agency securities with original maturities of greater than 90 days and remaining maturities of less than one year. Long-term investments include corporate notes, U.S. treasury securities and U.S. government agency securities with maturities greater than one year.

In evaluating the fair value information, considerable judgment is required to interpret the market data used to develop the estimates. The use of different market assumptions and/or different valuation techniques may have a material effect on the estimated fair value amounts. Accordingly, the estimates of fair value presented herein may not be indicative of the amounts that could be realized in a current market exchange. Refer to Note 17.

Contingent consideration. Each period we revalue the contingent consideration obligations associated with certain acquisitions to their fair value and record increases in the fair value as contingent consideration expense and decreases in the fair value as contingent consideration income. Changes in contingent consideration result from changes in the assumptions regarding probabilities of successful achievement of related milestones, the estimated timing in which the milestones are achieved and the discount rate used to estimate the fair value of the liability. Contingent consideration may change significantly as our development programs progress, revenue estimates evolve and additional data is obtained, impacting our assumptions. The assumptions used in estimating fair value require significant judgment. The use of different assumptions and judgments could result in a materially different estimate of fair value which may have a material impact on our results from operations and financial position.

Derivative financial instruments. We record derivative financial instruments on our Consolidated Balance Sheet at their fair value and recognize the changes in the fair value in our Consolidated Statement of Operations when they occur, the only exception being derivatives that qualify as hedges. For the derivative instrument to qualify as a hedge, we are required to meet strict hedge effectiveness and contemporaneous documentation requirements at the initiation of the hedge and assess the hedge effectiveness on an ongoing basis over the life of the hedge. At December 31, 2014 and 2013, our forward contracts for inventory purchases did not meet the documentation requirements to be designated as hedges. Accordingly, we recognize all changes in the fair values of our derivatives instruments, net, in our Consolidated Statement of Operations. Refer to Note 18.

Property, Plant, Equipment and Investment Properties. Property, plant, equipment and investment properties are recorded at cost. Depreciation is provided using the straight-line method over the estimated useful lives of the assets, generally five to ten years and includes amortization expense for assets capitalized under capital leases. The estimated useful lives by asset class are as follows: software - 3 years, machinery and equipment - 5-8 years, furniture and fixtures - 5-10 years, leasehold improvements - the lesser of their useful life or the lease term, buildings and improvements - 10-40 years. Expenditures for repairs and maintenance are charged to expense as incurred. Depreciation expense was $4.0 million, $4.1 million and $1.8 million for the years ended December 31, 2014, 2013 and 2012, respectively.

Impairment of Long-Lived Assets. Long-lived assets, such as property and equipment, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, then an impairment charge is recognized for the amount by which the carrying amount of the asset exceeds the fair value, or carrying amount for cost basis assets, of the asset.

Income Taxes. Income taxes are accounted for under the asset-and-liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and the respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the

years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in operations in the period that includes the enactment date. We periodically evaluate the realizability of our net deferred tax assets. Our tax accruals are analyzed periodically and adjustments are made as events occur to warrant such adjustment.

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Revenue recognition. Generally, we recognize revenue from product sales when goods are shipped and title and risk of loss transfer to our customers. Our estimates for sales returns and allowances are based upon the historical patterns of product returns and allowances taken, matched against the sales from which they originated, and management's evaluation of specific factors that may increase or decrease the risk of product returns.

Revenue for laboratory services is recognized on the accrual basis at the time test results are reported, which approximates when services are provided. Services are provided to certain patients covered by various third-party payer programs including various managed care organizations, as well as the Medicare and Medicaid programs. Billings for services under third-party payer programs are included in sales net of allowances for contractual discounts and allowances for differences between the amounts billed and estimated program payment amounts. Adjustments to the estimated payment amounts based on final settlement with the programs are recorded upon settlement as an adjustment to revenue.

For the years ended December 31, 2014, 2013 and 2012, revenue from services also includes $0.8 million, $0.8 million and $1.4 million, respectively, of revenue related to our consulting agreement with Neovasc and to revenue related to molecular diagnostics collaboration agreements. We recognize this revenue on a straight-line basis over the contractual term of the agreements.

Revenue from transfer of intellectual property includes revenue related to the sale, license or transfer of intellectual property such as upfront license payments, license fees and milestone payments received through our license, collaboration and commercialization agreements. We analyze our multiple-element arrangements to determine whether the elements can be separated and accounted for individually as separate units of accounting.

Non-refundable license fees for the out-license of our technology are recognized depending on the provisions of each agreement. We recognize non-refundable upfront license payments as revenue upon receipt if the license has standalone value and qualifies for treatment as a separate unit of accounting under Accounting Standards Codification, or ASC, 605-25, Multiple-Element Arrangements. License fees with ongoing involvement or performance obligations that do not have standalone value are recorded as deferred revenue, included in Accrued expenses or Other long-term liabilities, when received and generally are recognized ratably over the period of such performance obligation only after both the license period has commenced and we have delivered the technology.

The assessment of our obligations and related performance periods requires significant management judgment. If an agreement contains research and development obligations, the relevant time period for the research and development phase is based on management estimates and could vary depending on the outcome of clinical trials and the regulatory approval process. Such changes could materially impact the revenue recognized, and as a result, management reviews the estimates related to the relevant time period of research and development on a quarterly basis. For the year ended December 31, 2014, 2013 and 2012 we recorded $5.5 million, $16.7 million and $0 of revenue from the transfer of intellectual property, respectively. For the year ended December 31, 2014, $5.0 million related to a milestone payment that TESARO, Inc. ("TESARO") paid us under our license agreement with TESARO. For the year ended December 31, 2013, $12.5 million related to the sale of substantially all of our assets in the field of RNA interference to RXi Pharmaceuticals Corporation ("RXi") and $3.8 million related to the rights granted to OAO Pharmsynthez ("Pharmsynthez") for certain technologies. Refer to Note 4.

Revenue from milestone payments related to arrangements under which we have continuing performance obligations are recognized as Revenue from transfer of intellectual property upon achievement of the milestone only if all of the following conditions are met: the milestone payments are non-refundable; there was substantive uncertainty at the date of entering into the arrangement that the milestone would be achieved; the milestone is commensurate with either the vendor's performance to achieve the milestone or the enhancement of the value of the delivered item by the vendor; the milestone relates solely to past performance; and the amount of the milestone is reasonable in relation to the effort expended or the risk associated with the achievement of the milestone. If any of these conditions are not met, the milestone payments are not considered to be substantive and are, therefore, deferred and recognized as Revenue from transfer of intellectual property over the term of the arrangement as we complete our performance obligations.

Total deferred revenue included in Accrued expenses and Other long-term liabilities was $6.7 million and $8.3 million at December 31, 2014 and 2013, respectively.

Allowance for doubtful accounts. We analyze accounts receivable balances by considering factors such as historical experience, customer credit worthiness, the age of the accounts receivable balances and current economic conditions and trends that may affect a customer's ability to pay. The allowance for doubtful accounts is based on our assessment of the collectability of customer accounts. Our reported net loss is directly affected by our estimate of the collectability of accounts receivable. The amount of the allowance for doubtful accounts was $1.9 million and $1.9 million at December 31, 2014 and 2013, respectively.

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Equity-based compensation. We measure the cost of employee services received in exchange for an award of equity instruments based on the grant-date fair value of the award. That cost is recognized in the Consolidated Statement of Operations over the period during which an employee is required to provide service in exchange for the award. We record excess tax benefits, realized from the exercise of stock options as a financing cash inflow rather than as a reduction of taxes paid in cash flow from operations. Equity-based compensation arrangements to non-employees are recorded at their fair value on the measurement date. The measurement of equity-based compensation to non-employees is subject to periodic adjustment as the underlying equity instruments vest. During the years ended December 31, 2014, 2013 and 2012, we recorded $14.8 million, $11.0 million and $5.1 million, respectively, of equity-based compensation expense.

Research and development expenses. Research and development expenses include external and internal expenses, partially offset by third-party grants and fundings arising from collaboration agreements. External expenses include clinical and non-clinical activities performed by contract research organizations, lab services, purchases of drug and diagnostic product materials and manufacturing development costs. Research and development employee-related expenses include salaries, benefits and stock-based compensation expense. Other unallocated internal research and development expenses are incurred to support overall research and development activities and include expenses related to general overhead and facilities. We expense these costs in the period in which they are incurred. We estimate our liabilities for research and development expenses in order to match the recognition of expenses to the period in which the actual services are received. As such, accrued liabilities related to third party research and development activities are recognized based upon our estimate of services received and degree of completion of the services in accordance with the specific third party contract.

We record expense for in-process research and development projects acquired as asset acquisitions which have not reached technological feasibility and which have no alternative future use. For in-process research and development projects acquired in business combinations, the in-process research and development project is capitalized and evaluated for impairment until the development process has been completed. Once the development process has been completed the asset will be amortized over its remaining useful life.

Segment reporting. Our chief operating decision-maker (“CODM”) is Phillip Frost, M.D., our Chairman and Chief Executive Officer. Our CODM reviews our operating results and operating plans and makes resource allocation decisions on a Company-wide or aggregate basis. We currently manage our operations in two reportable segments, pharmaceuticals and diagnostics. The pharmaceutical segment consists of two operating segments, our (i) pharmaceutical research and development segment which is focused on the research and development of pharmaceutical products, and vaccines, and (ii) the pharmaceutical operations we acquired in Chile, Mexico, Israel, Spain, Uruguay and Brazil. The diagnostics segment consists of two operating segments, our (i) pathology operations we acquired through the acquisition of OPKO Lab and (ii) point-of-care and molecular diagnostics operations. There are no significant inter-segment sales. We evaluate the performance of each segment based on operating profit or loss. There is no inter-segment allocation of interest expense and income taxes.

Shipping and Handling Costs. We do not charge customers for shipping and handling costs. Shipping and handling costs are classified as Cost of revenues in the Consolidated Statements of Operations.

Variable interest entities. The consolidation of variable interest entities (“VIE”) is required when an enterprise has a controlling financial interest. A controlling financial interest in a VIE will have both of the following characteristics: (a) the power to direct the activities of a VIE that most significantly impact the VIE’s economic performance and (b) the obligation to absorb losses of the VIE that could potentially be significant to the VIE. Refer to Note 4.

Investments. We have made strategic investments in development stage and emerging companies. We record these investments as equity method investments or investments available for sale based on our percentage of ownership and whether we have significant influence over the operations of the investees. For investments classified under the equity method of accounting, we record our proportionate share of their losses in Losses from investments in investees in our Consolidated Statement of Operations. Refer to Note 4. For investments classified as available for sale, we record changes in their fair value as unrealized gain or loss in Other comprehensive income (loss) based on their closing price per share at the end of each reporting period. Refer to Note 4.

Recent accounting pronouncements. In July 2013, the FASB issued an Accounting Standards Update (“ASU”), ASU 2013-11, Presentation of an Unrecognized Tax Benefit When a Net Operating Loss Carryforward, a Similar Tax Loss, or a Tax Credit Carryforward Exists. ASU 2013-11 is intended to eliminate inconsistent practices regarding the presentation of an unrecognized tax benefit when a net operating loss carryforward, a similar tax loss, or a tax credit carryforward is available to reduce the taxable income or tax payable that would result from the disallowance of a tax position. ASU 2013-11 is effective for our fiscal year beginning January 1, 2014 and subsequent interim periods. The adoption of ASU 2013-11 does not have a material effect on our Consolidated Financial Statements.

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In May 2014, the FASB issued ASU No. 2014-09, “Revenue from Contracts with Customers.” ASU No. 2014-09 clarifies the principles for recognizing revenue and develops a common revenue standard for GAAP and International Financial Reporting Standards that removes inconsistencies and weaknesses in revenue requirements, provides a more robust framework for addressing revenue issues, improves comparability of revenue recognition practices across entities, industries, jurisdictions, and capital markets, provides more useful information to users of financial statements through improved disclosure requirements and simplifies the preparation of financial statements by reducing the number of requirements to which an entity must refer. ASU No. 2014-09 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016. Companies can choose to apply the ASU using either the full retrospective approach or a modified retrospective approach. We are currently evaluating both methods of adoption and the impact that the adoption of this ASU will have on our Consolidated Financial Statements.

In June 2014, the FASB issued ASU No. 2014-12, “Accounting for Share-Based Payments When the Terms of an Award Provide That a Performance Target Could Be Achieved after the Requisite Service Period (a consensus of the FASB Emerging Issues Task Force).” ASU No. 2014-12 requires that a performance target that affects vesting and that could be achieved after the requisite service period be treated as a performance condition. ASU No. 2014-12 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2015. Earlier adoption is permitted. The amendments can be applied either prospectively to all awards granted or modified after the effective date or retrospectively to all awards with performance targets that are outstanding as of the beginning of the earliest annual period presented in the financial statements and to all new or modified awards. We expect to apply the ASU prospectively and do not expect the adoption to have an impact on our Consolidated Financial Statements as our existing share-based payment awards do not fall within the scope of this ASU.

In August 2014, the FASB issued ASU No. 2014-15, “Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern,” to provide guidance on management’s responsibility in evaluating whether there is substantial doubt about a company’s ability to continue as a going concern and to provide related footnote disclosures. ASU 2014-15 is effective for annual periods ending after December 15, 2016 with early adoption permitted. We do not believe the impact of our pending adoption of ASU 2014-15 on our Consolidated Financial Statements will be material.

NOTE 3 LOSS PER SHARE

Basic loss per share is computed by dividing our net loss by the weighted average number of shares outstanding during the period. Diluted loss per share is computed by dividing our net loss increased by dividends on preferred stock by the weighted average number of shares outstanding and the impact of all dilutive potential common shares, primarily stock options. The dilutive impact of stock options and warrants is determined by applying the “treasury stock” method. In the periods in which their effect would be antidilutive, no effect has been given to outstanding options, warrants or convertible Preferred Stock in the diluted computation. Potentially dilutive shares issuable pursuant to the 2033 Senior Notes (defined in Note 6) were not included in the computation of net loss per share for the year ended December 31, 2014, because their inclusion would be antidilutive.

A total of 28,456,149, 32,105,859 and 26,695,436 potential shares of Common Stock have been excluded from the calculation of diluted net loss per share for the years ended December 31, 2014, 2013 and 2012, respectively, because their inclusion would be antidilutive.

During the year ended December 31, 2014, 5,787,983 Common Stock options and Common Stock warrants to purchase shares of our Common Stock were exercised, resulting in the issuance of 5,392,741 shares of Common Stock. Of the 5,787,983 Common Stock options and Common Stock warrants exercised, 426 shares of Common Stock were surrendered in lieu of a cash payment via the net exercise feature of the agreements.

During the year ended December 31, 2013, 10,881,570 Common Stock options and Common Stock warrants to purchase shares of our Common Stock were exercised, resulting in the issuance of 10,732,745 shares of Common Stock. Of the 10,881,570 Common Stock options and Common Stock warrants exercised, 148,825 shares of Common Stock were surrendered in lieu of a cash payment via the net exercise feature of the agreements.

During the year ended December 31, 2012, 1,086,361 Common Stock options and Common Stock warrants to purchase shares of our Common Stock were exercised, resulting in the issuance of 1,084,982 shares of Common Stock. Of the 1,086,361 Common Stock options and Common Stock warrants exercised, 1,379 shares of Common

Stock were surrendered in lieu of a cash payment via the net exercise feature of the agreements.

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Note 4 Acquisitions, Investments and Licenses

Inspiro Medical Ltd. acquisition

On April 17, 2014, we entered into a stock purchase agreement to acquire 100% of the issued and outstanding share capital of Inspiro Medical Ltd. ("Inspiro"), an Israeli medical device company developing a new platform to deliver small molecule drugs such as corticosteroids and beta agonists and larger molecules to treat respiratory diseases.

In connection with the transaction, we paid $1.5 million in cash and delivered 999,556 shares of our Common Stock valued at $8.6 million based on the closing price per share of our Common Stock as reported by the NYSE on the actual closing date of the acquisition, or $8.57 per share. The transaction closed on May 22, 2014. The number of shares issued was based upon our trading price as reported by the NYSE for the ten trading days immediately preceding the execution date of the purchase agreement, or $9.00 per share.

Inspiro's Inspiromatic is a "smart" easy-to-use dry powder inhaler with several advantages over existing devices. We anticipate that this innovative device will play a valuable role in the improvement of therapy for asthma, chronic obstructive pulmonary disease, cystic fibrosis and other respiratory diseases. We recorded the transaction as an asset acquisition and recorded the assets and liabilities at fair value. As the asset had no alternative future use, we recorded $10.1 million of acquired in-process research and development expenses.

We record expense for in-process research and development projects accounted for as asset acquisitions which have not reached technological feasibility and which have no alternative future use.

OPKO Biologics acquisition

In August 2013, we acquired OPKO Biologics (formerly PROLOR) pursuant to an agreement and plan of merger dated April 23, 2013 (the "Merger Agreement") in an all-stock transaction. OPKO Biologics is an Israeli-based biopharmaceutical company focused on developing and commercializing longer-acting proprietary versions of already approved therapeutic proteins.

Under the terms of the Merger Agreement, holders of PROLOR common stock received 0.9951 shares of our Common Stock for each share of PROLOR common stock. At closing, we delivered 63,670,805 shares of our Common Stock valued at $540.6 million based on the closing price per share of our Common Stock as reported by the NYSE on the closing date of the acquisition, or $8.49 per share. In addition, each outstanding option and warrant to purchase shares of PROLOR common stock that was outstanding and unexercised immediately prior to the closing date, whether vested or not vested, was converted into 7,889,265 options and warrants to purchase OPKO Common Stock at a fair value of $46.1 million.

Until completion of the acquisition, Dr. Phillip Frost, our Chairman and Chief Executive Officer, was PROLOR's Chairman of the Board and owned greater than 5% of its stock. Dr. Jane H. Hsiao, our Vice Chairman and Chief Technology Officer, and Mr. Steven Rubin, our Executive Vice President, Administration, were both directors of PROLOR and owned less than 5% of its stock.

OPKO Renal acquisition

In March 2013, we acquired OPKO Renal, formerly Cytochroma, Inc., whose lead products, both in Phase 3 development, are Rayaldee (CTAP101), a vitamin D prohormone to treat secondary hyperparathyroidism in patients with stage 3 or 4 CKD and vitamin D insufficiency, and Alpharen (Fermagate Tablets), a non-absorbed phosphate binder to treat hyperphosphatemia in dialysis patients (the "OPKO Renal Acquisition").

In connection with the OPKO Renal Acquisition, we delivered 20,517,030 shares of our Common Stock valued at $146.9 million based on the closing price per share of our Common Stock as reported by the NYSE on the actual closing date of the acquisition, or $7.16 per share. The number of shares issued was based on the volume-weighted average price per share of our Common Stock as reported on the NYSE for the 10 trading days immediately preceding the date of the purchase agreement for the OPKO Renal Acquisition, or $4.87 per share.

In addition, the OPKO Renal Acquisition requires payments of up to an additional $190.0 million in cash or additional shares of our Common Stock, at our election, upon the achievement of certain milestones relating to development and annual revenue. As a result, we recorded $47.7 million as contingent consideration at acquisition. We evaluate the contingent consideration on an ongoing basis and the changes in the fair value are recognized in earnings until the milestones are achieved. Refer to Note 17.

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Upon the achievement of a development milestone in September 2014, we delivered 2,236,210 shares of our Common Stock valued at $21.2 million based on the $9.46 closing price per share of our Common Stock on August 8, 2014, the date the milestone was achieved.

The following table summarizes the purchase price allocation and the fair value of the net assets acquired and liabilities assumed in the acquisitions of OPKO Renal and OPKO Biologics:

(In thousands)	OPKO Renal	OPKO Biologics
Current assets [1]	$1,224	$21,500
Intangible assets:		
In-process research and development	191,530	590,200
Patents	210	—
Total intangible assets	191,740	590,200
Goodwill	2,411	139,784
Property, plant and equipment	306	1,057
Other assets	—	371
Accounts payable and accrued expenses	(1,069)	(9,866)
Deferred tax liability	—	(156,403)
Total purchase price	$194,612	$586,643

(1) Current assets include cash of $0.4 million and $20.5 million related to the OPKO Renal and OPKO Biologics acquisitions, respectively.

Goodwill from the acquisition of OPKO Biologics principally relates to the deferred tax liability generated as a result of this being a stock transaction and the assembled workforce. Goodwill from the acquisition of OPKO Renal principally relates to the assembled workforce. Goodwill is not tax deductible for income tax purposes.

Pro forma disclosure for acquisitions

The following table includes the pro forma results for the years ended December 31, 2013 and 2012 of the combined companies as though the acquisition of OPKO Biologics and OPKO Renal had been completed as of the beginning of the period presented.

	For the years ended December 31,	
(In thousands)	2013	2012
Revenues	$96,530	$53,595
Loss from continuing operations	—	(63,479)
Net loss	(147,546)	(55,663)
Net loss attributable to common shareholders	(145,027)	(57,411)
Basic and diluted loss per share	$(0.37)	$(0.15)

The unaudited pro forma financial information is presented for information purposes only. The unaudited pro forma financial information may not necessarily reflect our future results of operations or what the results of operations would have been had we owned and operated each company as of the beginning of the period presented.

OPKO Brazil asset acquisition

In February 2013, we acquired the assets of OPKO Brazil, a Brazilian pharmaceutical company, pursuant to a purchase agreement entered into in December 2012. Pursuant to the purchase agreement, we paid $0.3 million in cash and delivered 64,684 shares of our Common Stock at closing valued at $0.4 million based on the closing price per share of our Common Stock as reported by the NYSE on the actual closing date of the acquisition, or $6.73 per share. The number of shares issued was based on the average closing price per share of Common Stock as reported on the NYSE for the 10 trading days immediately preceding the execution of the purchase agreement, or $4.64 per share. We accounted for this acquisition as an asset acquisition rather than a business combination. As a result, we recorded the assets at fair value, with most of the value being allocated to the most significant asset, its pharmaceutical business licenses.

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Investments

The following table reflects the accounting method, carrying value and underlying equity in net assets of our unconsolidated investments as of December 31, 2014:

(in thousands)

Investment type	Investment Carrying Value	Underlying Equity in Net Assets
Equity method investments	$9,400	$30,787
Variable interest entity, equity method	981	—
Available for sale investments	5,758	
Warrants and options	6,314	
Total carrying value of investments	$22,453	

Equity Method Investments

Our equity method investments consist of investments in Pharmsynthez (ownership 17%), Cocrystal Pharma, Inc. ("CPI") (8%), Sevion Therapeutics, Inc. ("Sevion") (4%), Non-Invasive Monitoring Systems, Inc. (1%) and Neovasc Inc. (6%). The total assets, liabilities, and net losses of our equity method investees for the year ended December 31, 2014 were $466.7 million, $91.5 million, and $55.9 million, respectively. We have determined that we and/or our related parties can significantly influence the success of our equity method investments through our board representation and voting power. Accordingly, we account for our investment in these entities under the equity method. For investments classified under the equity method of accounting, we record our proportionate share of their losses in Loss from investments in investees in our Consolidated Statement of Operations. The aggregate value of our equity method investments based on the quoted market price of their common stock and the number of shares held by us as of December 31, 2014 is $49.2 million. See further discussion of our investment in Pharmsynthez below.

Available for Sale Investments

Our available for sale investments consist of investments in RXi Pharmaceuticals Corporation ("RXi") (ownership 11%), ChromaDex Corporation (2%) and ARNO Therapeutics, Inc. ("ARNO") (4%). We have determined that our ownership, along with that of our related parties, does not provide us with significant influence over the operations of our available for sale investments. Accordingly, we account for our investment in these entities as available for sale, and we record changes in these investments as an unrealized gain or loss in Other comprehensive income (loss) each reporting period.

Based on our evaluation of the value of our investment in ARNO, including ARNO's decreasing stock price during the year ended December 31, 2014, we determined that the decline in fair value of our ARNO common shares was other-than-temporary and recorded an impairment charge of $1.4 million in Other income (expense), net in our Consolidated Statement of Operations for the year ended December 31, 2014 to write our investment in ARNO common shares down to its fair value of $0.6 million as of December 31, 2014. See further discussion of the Company's available for sale investments in Note 17.

Sales of Investments

Gains (losses) included in earnings from sales of our investments for the years ended December 31, 2014, 2013 and 2012 were $1.3 million, $29.9 million and $0.0 million, respectively, and were recorded in Other income (expense), net in our Consolidated Statement of Operations. The cost of securities sold is based on the specific identification method.

Warrants and Options

In addition to our equity method investments and available for sale investments, we hold options to purchase 1.0 million additional shares of Neovasc, which are fully vested as of December 31, 2014, and 1.0 million, 1.7 million and 0.1 million warrants to purchase additional shares of CPI, ARNO and Sevion, respectively. We recorded the changes in the fair value of the options and warrants in Fair value changes of derivative instruments, net in our Consolidated Statements of Operations. We record the fair value of the options and warrants in Investments, net in our Consolidated Balance Sheets. See further discussion of the Company's options and warrants in Note 17 and Note 18.

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Pharmsynthez

In April 2013, we entered into a series of concurrent transactions with Pharmsynthez, a Russian pharmaceutical company traded on the Moscow Stock Exchange. The transactions consisted of:

- We delivered approximately $9.6 million to Pharmsynthez.
- Pharmsynthez issued to us approximately 13.6 million of its common shares.
- Pharmsynthez agreed, at its option, to issue approximately 12.0 million common shares to us or to pay us cash in Russian Rubles ("RUR") 265.0 million (approximately $8.1 million as of December 31, 2013) on or before December 31, 2013 (the "Pharmsynthez Note Receivable"). In January 2014, Pharmsynthez delivered to us approximately 12.0 million shares of its common stock in satisfaction of the Pharmsynthez Notes Receivable.
- We had a right to purchase additional shares in Pharmsynthez at a fixed price if Pharmsynthez pays us in cash rather than delivering to us the 12.0 million Pharmsynthez common shares (the "Purchase Option"), however in connection with the settlement of the Pharmsynthez Note Receivable in January 2014, this right terminated.
- We granted rights to certain technologies in the Russian Federation, Ukraine, Belarus, Azerbaijan and Kazakhstan (the "Territories") to Pharmsynthez.
- We will receive from Pharmsynthez royalties on net sales of products incorporating the technologies in the Territories, as well as a percentage of any sublicense income from third parties for the technologies in the Territories.
- Pharmsynthez paid us $9.5 million under the various collaboration and funding agreements for the grant of rights and development of the technologies (the "Collaboration Payments").

We recorded the shares received in Pharmsynthez as an equity method investment. We initially recorded the Pharmsynthez Note Receivable, and the Purchase Option, as financial instruments and elected the fair value option for subsequent measurement. Changes in the fair value of the Pharmsynthez Note Receivable and the Purchase Option were recorded in Fair value changes of derivative instruments, net in our Consolidated Statements of Operations. Upon settlement in January 2014, we recorded the additional shares at fair value as an equity method investment.

We have accounted for the license and development activities as a multi-element arrangement, and allocated the total arrangement consideration based on the relative selling prices of the elements. We record the allocated consideration for development activities as an offset to Research and development expenses over the three-year term of the Collaboration Payments. We recorded revenue in connection with the grant of rights to the technologies proportionately as the payments were received.

During the years ended December 31, 2014 and 2013, we received $1.4 million and $8.2 million, respectively, related to the Collaboration Payments of which we recorded $0.5 million and $3.8 million in Revenue from transfer of intellectual property and $1.6 million and $1.1 million as an offset to Research and development expenses in 2014 and 2013, respectively.

Investments in variable interest entities

We have determined that we hold variable interests in SciVac Ltd ("SciVac") and Zebra Biologics, Inc. ("Zebra"). We made this determination as a result of our assessment that they do not have sufficient resources to carry out their principal activities without additional financial support.

We acquired 840,000 shares of Zebra Series A-2 Preferred Stock and 900,000 shares of Zebra restricted common stock (ownership 28% at December 31, 2014). Zebra is a privately held biotechnology company focused on the discovery and development of biosuperior antibody therapeutics and complex drugs. Dr. Richard Lerner, M.D., a member of our Board of Directors, is a founder of Zebra and, along with Dr. Frost, serves as a member of Zebra's Board of Directors.

In order to determine the primary beneficiary of Zebra, we evaluated our investment and our related parties' investment, as well as our investment combined with the related party group's investment to identify if we had the power to direct the activities that most significantly impact the economic performance of Zebra. We determined that we do not have the power to direct the activities that most significantly impact Zebra's economic performance. Based on the capital structure, governing documents and overall business operations of Zebra, we determined that, while a VIE, we do not have the power to direct the activities that most significantly impact Zebra's economic performance. We did determine, however, that we can significantly influence the success of Zebra through our board representation and voting power. Accordingly, as we have the ability to exercise significant influence over Zebra's operations, we

account for our investment in Zebra under the equity method.

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Consolidated variable interest entities

In June 2012, we acquired a 50% stock ownership in SciVac (45% as of December 31, 2014) from FDS Pharma LLP ("FDS"). SciVac is a privately-held Israeli company that produces a third-generation hepatitis B-vaccine. From November 2012 until December 31, 2014, we loaned to SciVac a combined $5.7 million for working capital purposes. We have determined that we hold variable interests in SciVac based on our assessment that SciVac does not have sufficient resources to carry out its principal activities without financial support. In order to determine the fair market value of our investment in SciVac, we have utilized a business enterprise valuation approach.

In order to determine the primary beneficiary of SciVac, we evaluated our investment to identify if we had the power to direct the activities that most significantly impact the economic performance of SciVac. We have determined that the power to direct the activities that most significantly impact the economic performance of SciVac is conveyed through SciVac's board of directors. SciVac's board of directors appoint and oversee SciVac's management team who carry out the activities that most significantly impact the economic performance of SciVac. As part of the share and debt purchase agreement, SciVac's board of directors is constituted by 5 members, of which 3 members will be appointed by us, representing 60% of SciVac's board. Based on this analysis, we determined that we have the power to direct the activities of SciVac and as such we are the primary beneficiary. As a result of this conclusion, we have consolidated the results of operations and financial position of SciVac and recorded a reduction of equity for the portion of SciVac we do not own.

The following table represents the consolidated assets and non-recourse liabilities related to SciVac as of December 31, 2014 and December 31, 2013. These assets are owned by, and these liabilities are obligations of, SciVac, not us.

(In thousands)	December 31, 2014	December 31, 2013
Assets		
Current assets:		
Cash and cash equivalents	$393	$2
Accounts receivable, net	316	283
Inventories, net	1,649	1,696
Prepaid expenses and other current assets	718	218
Total current assets	3,076	2,199
Property, plant and equipment, net	1,725	1,374
Intangible assets, net	875	1,111
Goodwill	1,553	1,821
Other assets	384	261
Total assets	$7,613	$6,766
Liabilities		
Current liabilities:		
Accounts payable	$445	$1,136
Accrued expenses	4,446	6,498
Notes payable	5,189	1,537
Total current liabilities	10,080	9,171
Other long-term liabilities	2,042	1,240
Total liabilities	$12,122	$10,411

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Note 5 Composition of Certain Financial Statement Captions

	For the years ended December 31,	
(In thousands)	2014	2013
Accounts receivable, net		
Accounts receivable	$21,875	$21,651
Less: allowance for doubtful accounts	(1,906)	(1,884)
	$19,969	$19,767
Inventories, net		
Finished products	$12,116	$13,374
Work in-process	1,011	1,350
Raw materials	4,116	4,132
Less: inventory reserve	(639)	(777)
	$16,604	$18,079
Prepaid expenses and other current assets		
Prepaid supplies	$1,123	$945
Prepaid insurance	968	892
Pharmsynthez notes receivable	—	6,151
Other receivables	669	1,985
Taxes recoverable	2,417	3,458
Other	4,212	5,653
	$9,389	$19,084
Property, plant, equipment and investment properties, net:		
Machinery and equipment	$13,710	$11,656
Building	3,171	3,615
Land	2,391	2,666
Furniture and fixtures	2,148	2,051
Software	1,695	807
Leasehold improvements	3,592	3,107
Construction in process	225	489
Less: accumulated depreciation	(10,521)	(7,364)
	$16,411	$17,027
Intangible assets, net:		
Technologies	$52,508	$51,660
Customer relationships	22,108	22,725
Product registrations	8,763	9,692
Trade names	3,483	3,669
Covenants not to compete	8,639	8,671
Other	1,079	2,519
Less: accumulated amortization	(33,931)	(24,403)
	$62,649	$74,533
Accrued expenses:		
Taxes payable	$77	$702
Deferred revenue	4,185	7,639
Clinical trials	8,643	3,342
Professional fees	1,860	402
Employee benefits	4,127	4,399
Deferred acquisition payments, net of discount	15	5,465

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	For the years ended December 31,	
Contingent consideration	27,352	28,047
Other	14,653	15,878
	$60,912	$65,874

Other long-term liabilities:		
Contingent consideration – OPKO Renal	$36,529	$34,401
Contingent consideration – OPKO Health Europe	254	504
Contingent consideration – OPKO Diagnostics	6,992	8,340
Contingent consideration – CURNA	440	316
Mortgages and other debts payable	2,434	3,270
Deferred tax liabilities	167,153	166,435
Other, including deferred revenue	3,556	1,509
	$217,358	$214,775

The following table summarizes the fair values assigned to our major intangible asset classes upon each acquisition:

(In thousands)	Technology	In-process research and development	Customer relationships	Product registrations	Covenants not to compete	Tradename	Other	Total identified intangible assets	Goodwill
OPKO Chile[1]	$—	$ —	$ 3,945	$ 5,829	$—	$ 1,032	$—	$10,806	$5,441
OPKO Mexico	—	—	121	77	70	77	—	345	21
CURNA	—	10,000	—	—	—	—	290	10,290	4,827
OPKO Diagnostics	44,400	—	—	—	—	—	—	44,400	17,977
FineTech	2,700	—	14,200	—	1,500	400	—	18,800	11,623
OPKO Health Europe	3,017	1,459	436	2,930	187	349	—	8,378	8,062
OPKO Lab	1,370	—	3,860	—	6,900	1,830	70	14,030	29,629
SciVac	1,090	—	40	—	—	—	—	1,130	760
OPKO Brazil	—	—	—	—	—	—	686	686	—
OPKO Renal	—	191,530	—	—	—	—	210	191,740	2,411
OPKO Biologics	—	590,200	—	—	—	—	—	590,200	139,784
OPKO Uruguay Ltda.	—	—	—	—	—	—	347	347	—
Weighted average amortization period	9 years	Indefinite	6 years	9 years	5 years	4 years	4 years		Indefinite

[1] Includes intangible assets and goodwill related to ALS acquisition.

All of the intangible assets and goodwill acquired relate to our acquisitions of OPKO Chile, including the intangible assets and goodwill related to the ALS acquisition, OPKO Mexico, CURNA, OPKO Diagnostics, FineTech, OPKO Health Europe, OPKO Lab, OPKO Brazil, OPKO Renal, OPKO Biologics, OPKO Uruguay Ltda. and SciVac, a consolidated VIE. The pharmaceutical, nutraceutical and veterinary products from ALS and OPKO Health Europe do

not require ongoing product renewals. We do not anticipate capitalizing the cost of product registration renewals, rather we expect to expense these costs, as incurred. Our goodwill is not tax deductible for income tax purposes in the U.S., Chile, Canada, Mexico, Spain, or Israel.

At December 31, 2014, the changes in value of the intangible assets and goodwill are primarily due to foreign currency fluctuations between the Chilean and Mexican pesos, the Euro and the Shekel against the U.S. dollar. At December 31, 2013, the changes in value of the intangible assets and goodwill are primarily due to the acquisitions of OPKO Brazil, Cytochroma and PROLOR, as well as the foreign currency fluctuations between the Chilean and Mexican pesos, the Brazilian reals, the euro and the shekel against the U.S. dollar.

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The following table reflects the changes in the allowance for doubtful accounts, provision for inventory reserve and tax valuation allowance accounts:

(In thousands)	Beginning balance	Charged to expense	Written-off	Charged to other	Ending balance
2014					
Allowance for doubtful accounts	$(1,884)	(646)	321	303	$(1,906)
Inventory reserve	$(777)	(1,082)	1,028	192	$(639)
Tax valuation allowance	$(85,370)	—	—	(46,561)	$(131,931)
2013					
Allowance for doubtful accounts	$(474)	(979)	28	(459)	$(1,884)
Inventory reserve	$(1,313)	(2,015)	2,188	363	$(777)
Tax valuation allowance	$(59,145)	(1,148)	—	(25,077)	$(85,370)

The following table summarizes the changes in Goodwill during the years ended December 31, 2014.

	2014				2013			
(In thousands)	Balance at January 1st	Acquisitions	Foreign exchange	Balance at December 31st	Balance at January 1	Acquisitions	Foreign exchange, other	Balance at December 31
Pharmaceuticals								
CURNA	$4,827	$—	$—	$4,827	$4,827	$—	$—	$4,827
OPKO Mexico	114	—	(14)	100	114	—	—	114
OPKO Chile	6,102	—	(819)	5,283	6,697	—	(595)	6,102
OPKO Health Europe	9,075	—	(1,062)	8,013	8,712	—	363	9,075
FineTech	11,698	—	—	11,698	11,698	—	—	11,698
SciVac	1,739	—	(186)	1,553	796	—	943	1,739
OPKO Renal	2,069	—	—	2,069	—	2,411	(342)	2,069
OPKO Biologics	139,784	—	—	139,784	—	139,784	—	139,784
Diagnostics								
OPKO Diagnostics	17,977	—	—	17,977	17,977	—	—	17,977
OPKO Lab	32,988	—	—	32,988	29,629	—	3,359	32,988
	$226,373	$—	$(2,081)	$224,292	$80,450	$142,195	$3,728	$226,373

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Note 6 Debt

In January 2013, we entered into note purchase agreements (the "2033 Senior Notes") with qualified institutional buyers and accredited investors (collectively, the "Purchaser") in a private placement in reliance on exemptions from registration under the Securities Act of 1933, (the "Securities Act"). The Purchasers of the 2033 Senior Notes include Frost Gamma Investments Trust, a trust affiliated with Dr. Frost, and Hsu Gamma Investment, L.P., an entity affiliated with Dr. Hsiao. The 2033 Senior Notes were issued on January 30, 2013. The 2033 Senior Notes, which total $175.0 million, bear interest at the rate of 3.00% per year, payable semiannually on February 1 and August 1 of each year, beginning August 1, 2013. The 2033 Senior Notes will mature on February 1, 2033, unless earlier repurchased, redeemed or converted. Upon a fundamental change as defined in the instruments governing the 2033 Senior Notes, subject to certain exceptions, the holders may require us to repurchase all or any portion of their 2033 Senior Notes for cash at a repurchase price equal to 100% of the principal amount of the 2033 Senior Notes being repurchased, plus any accrued and unpaid interest to but not including the fundamental change repurchase date.

The following table sets forth information related to the 2033 Senior Notes which is included our Consolidated Balance Sheets as of December 31, 2014:

(In thousands)	Embedded conversion option	2033 Senior Notes	Discount	Total
Balance at December 31, 2013	$101,087	$158,064	$(47,239)	$211,912
Amortization of debt discount	—	—	5,662	5,662
Change in fair value of embedded derivative	12,213	—	—	12,213
Conversion	(47,353)	(70,422)	19,442	(98,333)
Balance at December 31, 2014	$65,947	$87,642	$(22,135)	$131,454

The following table sets forth information related to the 2033 Senior Notes which is included our Consolidated Balance Sheets as of December 31, 2013:

(In thousands)	Embedded conversion option	2033 Senior Notes	Discount	Total
Balance at December 31, 2012	$—	$—	$—	$—
Issuance of 3.00% convertible notes	59,204	175,000	(59,204)	175,000
Amortization of debt discount	—	—	6,596	6,596
Change in fair value of embedded derivative	52,742	—	—	52,742
Conversion	(10,859)	(16,936)	5,369	(22,426)
Balance at December 31, 2013	$101,087	$158,064	$(47,239)	$211,912

The 2033 Senior Notes will be convertible at any time on or after November 1, 2032, through the second scheduled trading day immediately preceding the maturity date, at the option of the holders. Additionally, holders may convert their 2033 Senior Notes prior to the close of business on the scheduled trading day immediately preceding November 1, 2032, under the following circumstances: (1) conversion based upon satisfaction of the trading price condition relating to the 2033 Senior Notes; (2) conversion based on the Common Stock price; (3) conversion based upon the occurrence of specified corporate events; or (4) if we call the 2033 Senior Notes for redemption. The 2033 Senior Notes will be convertible into cash, shares of our Common Stock, or a combination of cash and shares of Common Stock, at our election unless we have made an irrevocable election of net share settlement. The initial conversion rate for the 2033 Senior Notes will be 141.48 shares of Common Stock per $1,000 principal amount of 2033 Senior Notes (equivalent to an initial conversion price of approximately $7.07 per share of Common Stock), and will be subject to adjustment upon the occurrence of certain events. In addition, we will, in certain circumstances, increase the conversion rate for holders who convert their 2033 Senior Notes in connection with a make-whole fundamental change (as defined in the Indenture) and holders who convert upon the occurrence of certain specific events prior to February 1, 2017 (other than in connection with a make-whole fundamental change). Holders of the 2033 Senior Notes may require us to repurchase the 2033 Senior Notes for 100% of their principal amount, plus accrued and unpaid interest, on February 1, 2019, February 1, 2023 and February 1, 2028, or following the occurrence

of a fundamental change as defined in the indenture governing the 2033 Senior Notes.

We may not redeem the 2033 Senior Notes prior to February 1, 2017. On or after February 1, 2017 and before February 1, 2019, we may redeem for cash any or all of the 2033 Senior Notes but only if the last reported sale price of our

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Common Stock exceeds 130% of the applicable conversion price for at least 20 trading days during the 30 consecutive trading day period ending on the trading day immediately prior to the date on which we deliver the redemption notice. The redemption price will equal 100% of the principal amount of the 2033 Senior Notes to be redeemed, plus any accrued and unpaid interest to but not including the redemption date. On or after February 1, 2019, we may redeem for cash any or all of the 2033 Senior Notes at a redemption price of 100% of the principal amount of the 2033 Senior Notes to be redeemed, plus any accrued and unpaid interest up to but not including the redemption date.

The terms of the 2033 Senior Notes, include, among others: (i) rights to convert into shares of our Common Stock, including upon a fundamental change; and (ii) a coupon make-whole payment in the event of a conversion by the holders of the 2033 Senior Notes on or after February 1, 2017 but prior to February 1, 2019. We have determined that these specific terms are considered to be embedded derivatives. As a result, embedded derivatives are required to be separated from the host contract, the 2033 Senior Notes, and carried at fair value when: (a) the embedded derivative possesses economic characteristics that are not clearly and closely related to the economic characteristics of the host contract; and (b) a separate, stand-alone instrument with the same terms would qualify as a derivative instrument. We have concluded that the embedded derivatives within the 2033 Senior Notes meet these criteria and, as such, must be valued separate and apart from the 2033 Senior Notes and recorded at fair value each reporting period.

For accounting and financial reporting purposes, we combine these embedded derivatives and value them together as one unit of accounting. At each reporting period, we record these embedded derivatives at fair value which is included as a component of the 2033 Senior Notes on our Consolidated Balance Sheets.

On August 30, 2013, one of the conversion rights in the 2033 Senior Notes was triggered. Holders of the 2033 Senior Notes converted $16.9 million principal amount into 2,396,145 shares of our Common Stock at a rate of 141.48 shares of Common Stock per $1,000 principal amount of 2033 Senior Notes. We recorded a $1.0 million non-cash gain related to the conversion. The gain on exchange is included within Other income (expense) on our Consolidated Statement of Operations.

In June 2014, we entered into an exchange agreement with a holder of the Company’s Notes pursuant to which such holder exchanged $70.4 million in aggregate principal amount of Notes for 10,974,431 shares of the Company’s Common Stock and approximately $0.8 million in cash representing accrued interest through the date of completion of the exchange. We recorded a $2.7 million non-cash gain related to the exchange. The gain on exchange is included within Other income (expense) on our Consolidated Statement of Operations.

We used a binomial lattice model in order to estimate the fair value of the embedded derivative in the 2033 Senior Notes. A binomial lattice model generates two probable outcomes — one up and another down —arising at each point in time, starting from the date of valuation until the maturity date. A lattice model was initially used to determine if the 2033 Senior Notes would be converted, called or held at each decision point. Within the lattice model, the following assumptions are made: (i) the 2033 Senior Notes will be converted early if the conversion value is greater than the holding value; or (ii) the 2033 Senior Notes will be called if the holding value is greater than both (a) the redemption price (as defined in the Indenture) and (b) the conversion value plus the coupon make-whole payment at the time. If the 2033 Senior Notes are called, then the holder will maximize their value by finding the optimal decision between (1) redeeming at the redemption price and (2) converting the 2033 Senior Notes.

Using this lattice model, we valued the embedded derivatives using the “with-and-without method,” where the value of the 2033 Senior Notes including the embedded derivatives is defined as the “with,” and the value of the 2033 Senior Notes excluding the embedded derivatives is defined as the “without.” This method estimates the value of the embedded derivatives by looking at the difference in the values between the 2033 Senior Notes with the embedded derivatives and the value of the 2033 Senior Notes without the embedded derivatives.

The lattice model requires the following inputs: (i) price of our Common Stock; (ii) Conversion Rate (as defined in the Indenture); (iii) Conversion Price (as defined in the Indenture); (iv) maturity date; (v) risk-free interest rate; (vi) estimated stock volatility; and (vii) estimated credit spread for the Company.

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The following table sets forth the inputs to the lattice model used to value the embedded derivative:

	December 31, 2014	December 31, 2013	Issuance Date
Stock price	$9.99	$8.44	$6.20
Conversion Rate	141.4827	141.4827	141.4827
Conversion Price	$7.07	$7.07	$7.07
Maturity date	February 1, 2033	February 1, 2033	February 1, 2033
Risk-free interest rate	1.40%	1.78%	1.12%
Estimated stock volatility	39%	55%	40%
Estimated credit spread	1,081 basis points	828 basis points	944 basis points

The following table sets forth the fair value of the 2033 Senior Notes with and without the embedded derivatives, and the fair value of the embedded derivatives at December 31, 2014, December 31, 2013, and January 30, 2013. At December 31, 2014, December 31, 2013, and January 30, 2013, the principal amount of the 2033 Senior Notes was $87.6 million, $158.1 million and $175.0 million, respectively:

(In thousands)	December 31, 2014	December 31, 2013	Issuance Date
Fair value of 2033 Senior Notes:			
With the embedded derivatives	$129,009	$218,081	$175,000
Without the embedded derivatives	$63,062	$116,994	$115,796
Estimated fair value of the embedded derivatives	$65,947	$101,087	$59,204

Changes in certain inputs into the lattice model can have a significant impact on changes in the estimated fair value of the embedded derivatives. For example, a decrease in our estimated credit spread results in an increase in the estimated value of the embedded derivatives. Conversely, a decrease in the price of our Common Stock results in a decrease in the estimated fair value of the embedded derivatives. For the years ended December 31, 2014 and 2013, we observed an increase in the market price of our Common Stock which primarily resulted in a $12.2 million and $52.7 million increase, respectively, in the estimated fair value of our embedded derivatives recorded in Fair value changes of derivative instruments, net in our Consolidated Statements of Operations.

We have line of credit agreements with ten financial institutions as of December 31, 2014 and twelve financial institutions as of December 31, 2013 in Chile and Spain. These lines of credit are used primarily as a source of working capital for inventory purchases.

The following table summarizes the amounts outstanding under the Chilean and Spanish lines of credit:

(Dollars in thousands)			Balance Outstanding	
Lender	Interest rate on borrowings at December 31, 2014	Credit line capacity	December 31, 2014	December 31, 2013
Itau Bank	6.52%	$1,800	965	$1,999
Bank of Chile	6.34%	2,250	1,410	2,079
BICE Bank	6.16%	1,700	1,249	516
Corp Banca	—%	—	—	(47)
BBVA Bank	5.00%	2,000	795	523
Penta Bank	7.34%	1,200	1,008	946
Security Bank	6.16%	640	361	1,075
BCI	—%	—	—	198
Estado Bank	5.30%	2,800	1,870	1,772
Sabadell Bank	4.50%	182	—	—
BBVA Bank	4.75%	304	—	—
Santander Bank	4.50%	243	—	—
Total		$13,119	$7,658	$9,061

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At December 31, 2014 and 2013, the weighted average interest rate on our lines of credit was approximately 6.1% and 7.7%, respectively.

At December 31, 2014 and 2013, we had mortgage notes and other debt related to OPKO Health Europe as follows:

(In thousands)	December 31, 2014	December 31, 2013
Current portion of notes payable	$608	$1,964
Other long-term liabilities	2,435	3,270
Total mortgage notes and other debt	$3,043	$5,234

The mortgages and other debts mature at various dates ranging from 2015 through 2024 bearing variable interest rates from 2.7% up to 6.3%. The weighted average interest rate on the mortgage notes and other debt at December 31, 2014 and 2013, was 3.4% and 3.9%, respectively. The mortgages are secured by our office space in Barcelona.

Note 7 Shareholders' Equity

Our authorized capital stock consists of 750,000,000 shares of Common Stock, par value $0.01 per share, and 10,000,000 shares of Preferred Stock, par value $0.01 per share.

Common Stock

Subject to the rights of the holders of any shares of Preferred Stock currently outstanding or which may be issued in the future, the holders of the Common Stock are entitled to receive dividends from our funds legally available when, as and if declared by our Board of Directors, and are entitled to share ratably in all of our assets available for distribution to holders of Common Stock upon the liquidation, dissolution or winding-up of our affairs subject to the liquidation preference, if any, of any then outstanding shares of Preferred Stock. Holders of our Common Stock do not have any preemptive, subscription, redemption or conversion rights. Holders of our Common Stock are entitled to one vote per share on all matters which they are entitled to vote upon at meetings of stockholders or upon actions taken by written consent pursuant to Delaware corporate law. The holders of our Common Stock do not have cumulative voting rights, which means that the holders of a plurality of the outstanding shares can elect all of our directors. All of the shares of our Common Stock currently issued and outstanding are fully-paid and nonassessable. No dividends have been paid to holders of our Common Stock since our incorporation, and no cash dividends are anticipated to be declared or paid on our Common Stock in the reasonably foreseeable future.

In addition to our equity-based compensation plans, we have issued warrants to purchase our Common Stock. Refer to Note 9 for additional information on our share-based compensation plans. The table below provides additional information for warrants outstanding as of December 31, 2014.

Warrants	Number of warrants	Weighted average exercise price	Expiration date
Outstanding at December 31, 2013	24,496,664	$0.94	Various from September 2014 through March 2017
Issued	—	—	
Exercised	(3,064,317)	2.29	
Expired	(2,601)	0.01	
Outstanding and Exercisable at December 31, 2014	21,429,746	$0.75	Various from July 2015 through March 2017

Of the 3,064,317 Common Stock warrants exercised, 426 shares were surrendered in lieu of a cash payment via the net exercise feature of the warrant agreements.

Preferred Stock

Under our certificate of incorporation, our Board of Directors has the authority, without further action by stockholders, to designate up to 10 million shares of Preferred Stock in one or more series and to fix or alter, from time to time, the designations, powers and rights of each series of Preferred Stock and the qualifications, limitations or restrictions of any series of Preferred Stock, including dividend rights, dividend rate, conversion rights, voting rights,

rights and terms of redemption (including sinking fund provisions), redemption price or prices, and the liquidation preference of any wholly issued series of

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Preferred Stock, any or all of which may be greater than the rights of the Common Stock, and to establish the number of shares constituting any such series.

Of the authorized Preferred Stock, 4,000,000 shares and 500,000 shares were designated Series A Preferred Stock and Series C Preferred Stock, respectively. As of December 31, 2014 and 2013, there were no shares of Series A Preferred Stock or Series C Preferred Stock issued or outstanding.

8% Series D Cumulative Convertible Preferred Stock

Of the authorized Preferred Stock, 2,000,000 shares were designated 8% Series D Cumulative Convertible Preferred Stock ("Series D Preferred Stock"). On March 1, 2013, our Board of Directors declared a cash dividend to all Series D Preferred Stockholders as of March 8, 2013. The total cash dividend paid was approximately $3.0 million. In addition, the Company also exercised its option to convert all 1,129,032 shares of our outstanding Series D Preferred Stock into 11,290,320 shares of our Common Stock effective of March 8, 2013. Following the conversion there are no outstanding shares of Series D Preferred Stock. As of December 31, 2014 and 2013, there were no shares of Series D Preferred Stock issued or outstanding.

The 2012 cash dividend to Series D Preferred Stockholders was approximately $3.0 million. As of December 31, 2012 we had approximately $2.30 per Series D Preferred Share, or $2.6 million, of Series D Preferred Stock dividends in arrears.

Note 8 Accumulated Other Comprehensive Income

For the year ended December 31, 2014, changes in Accumulated other comprehensive income (loss), net of tax, were as follows:

(In thousands)	Foreign currency	Unrealized gain (loss) in Accumulated OCI	Total
Balance at December 31, 2013	$1,371	$2,047	$3,418
Other comprehensive income before reclassifications, net of tax [1]	(8,088)	(8,044)	(16,132)
Amounts reclassified from accumulated other comprehensive income, net of tax [1]	—	322	322
Net other comprehensive loss	(8,088)	(7,722)	(15,810)
Balance at December 31, 2014	$(6,717)	$(5,675)	$(12,392)

[1] Effective tax rate of 40.13%.

Amounts reclassified from Accumulated other comprehensive income (loss) for the year ended December 31, 2014 includes $1.3 million realized gain on the sales of certain of our investments available for sale. Of the $1.3 million gain on the sales of our investments available for sale, a $0.9 million gain was reclassified from unrealized gains in Accumulated other comprehensive income (loss) to Other income (expense), net for the year ended December 31, 2014. Amounts reclassified from Accumulated other comprehensive income (loss) also includes an other-than-temporary impairment charge on our investment in ARNO as discussed in Note 4. Amounts reclassified for our available for sale investments were based on the specific identification method.

For the year ended December 31, 2013, changes in Accumulated other comprehensive income, net of tax, were as follows:

(In thousands)	Foreign currency	Unrealized gain (loss) in Accumulated OCI	Total
Balance at December 31, 2012	$3,196	$4,160	$7,356
Other comprehensive income before reclassifications, net of tax (1)	(1,825)	2,467	642
Amounts reclassified from accumulated other comprehensive income, net of tax (1)	—	(4,580)	(4,580)
Net other comprehensive loss	(1,825)	(2,113)	(3,938)
Balance at December 31, 2013	$1,371	$2,047	$3,418

(1) Effective tax rate of 38.47%.

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Amounts reclassified from Accumulated other comprehensive income for the year ended December 31, 2013, related to $10.8 million realized gain on the sales of certain of our investments available for sale. Of the $10.8 million gain on the sales of our investments available for sale, a $7.5 million gain was reclassified from unrealized gains in Accumulated other comprehensive income to Other income (expense), net for the year ended December 31, 2013.

Note 9 Equity-Based Compensation

We maintain five equity-based incentive compensation plans, the Acuity Pharmaceuticals, Inc. 2003 Equity Incentive Plan, 2007 Equity Incentive Plan, the 2000 Stock Option Plan, the Modigene Inc. 2005 Stock Incentive Plan and the Modigene Inc. 2007 Equity Incentive Plan that provide for grants of stock options and restricted stock to our directors, officers, key employees and certain outside consultants. Equity awards granted under our 2007 Equity Incentive Plan are exercisable for a period of either 7 years or 10 years from the date of grant. Equity awards granted under our 2000 Stock Option Plan, 2003 Equity Incentive Plan and the two Modigene Plans are exercisable for a period of up to 10 years from date of grant. Vesting periods range from immediate to 5 years.

We classify the cash flows resulting from the tax benefit that arises when the tax deductions exceed the compensation cost recognized for those equity awards (excess tax benefits) as financing cash inflows. There were no excess tax benefits for the years ended December 31, 2014, 2013, and 2012.

Equity-based compensation arrangements to non-employees are accounted for at their fair value on the measurement date. The measurement of equity-based compensation to non-employees is subject to periodic adjustment over the vesting period of the equity instruments.

Valuation and Expense Information

We recorded equity based compensation expense of $14.8 million, $11.0 million and $5.1 million for the years ended December 31, 2014, 2013, and 2012, respectively, all of which were reflected as operating expenses. Of the $14.8 million of equity based compensation expense recorded in the year ended December 31, 2014, $9.7 million was recorded as selling, general and administrative expenses, $5.0 million was recorded as research and development expenses and $0.1 million was recorded as a cost of revenue. Of the $11.0 million of equity based compensation expense recorded in the year ended December 31, 2013, $7.3 million was recorded as selling, general and administrative expense and $3.6 million was recorded as research and development expenses. Of the $5.1 million of equity based compensation expense recorded in the year ended December 31, 2012, $3.1 million was recorded as selling, general and administrative expense and $2.0 million was recorded as research and development expenses.

We estimate forfeitures of stock options and recognize compensation cost only for those awards expected to vest. Forfeiture rates are determined for all employees and non-employee directors based on historical experience and our estimate of future vesting. Estimated forfeiture rates are adjusted from time to time based on actual forfeiture experience.

As of December 31, 2014, there was $41.5 million of unrecognized compensation cost related to the stock options granted under our equity-based incentive compensation plans. Such cost is expected to be recognized over a weighted-average period of approximately 3.0 years.

Stock Options

We estimate the fair value of each stock option on the date of grant using the Black-Scholes-Merton Model option-pricing formula and amortize the fair value to expense over the stock option’s vesting period using the straight-line attribution approach for employees and non-employee directors, and for awards issued to non-employees we recognize compensation expense on a graded basis, with most of the compensation expense being recorded during the initial periods of vesting. We apply the following assumptions in our Black-Scholes-Merton Model option-pricing formula:

	Year Ended December 31, 2014	Year Ended December 31, 2013	Year Ended December 31, 2012
Expected term (in years)	1.0 - 10.0	1.0 - 7.0	1.0 - 7.0
Risk-free interest rate	.10% - 2.65%	0.15% - 2.45%	0.09% - 2.61%
Expected volatility	31% - 72%	0.31% - 83%	69%
Expected dividend yield	0%	0%	0%

Expected Term: The expected term of the stock options granted to employees and non-employee directors was calculated using the shortcut method. We believe this method is appropriate as our equity shares have been publicly-traded for a limited

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period of time and as such we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term. The expected term of stock options issued to non-employee consultants is the remaining contractual life of the options issued.

Risk-Free Interest Rate: The risk-free interest rate is based on the rates paid on securities issued by the U.S. Treasury with a term approximating the expected life of the option.

Expected Volatility: The expected volatility for stock options with an expected life of 7 years or less was based on the historical volatility of our stock. The expected volatility for stock options with an expected life of 8 years or greater was based on an average of the volatility of a peer group of publicly-traded entities and the historical volatility of our stock, which we believe will be representative of the volatility over the expected term of the options. We believe the use of peer group's historical volatility is appropriate as our equity shares have not been publicly-traded for 8 years.

Expected Dividend Yield: We do not intend to pay dividends on Common Stock for the foreseeable future. Accordingly, we used a dividend yield of zero in the assumptions.

We maintain incentive stock plans that provide for the grants of stock options to our directors, officers, employees and non-employee consultants. As of December 31, 2014, there were 16,736,892 shares of Common Stock reserved for issuance under our 2007 Incentive Plan. We intend to issue new shares upon the exercise of stock options. Stock options granted under these plans have been granted at an option price equal to the closing market value of the stock on the date of the grant. Stock options granted under these plans to employees typically become exercisable over four years in equal annual installments after the date of grant, and stock options granted to non-employee directors become exercisable in full one-year after the grant date, subject to, in each case, continuous service with us during the applicable vesting period. We assumed stock options to grant Common Stock as part of the mergers with Acuity Pharmaceuticals, Inc., Froptix, Inc. and OPKO Biologics, which reflected various vesting schedules, including monthly vesting to employees and non-employee consultants.

A summary of option activity under our stock option plans as of December 31, 2014, and the changes during the year is presented below:

Options	Number of options	Weighted average exercise price	Weighted average remaining contractual term (years)	Aggregate intrinsic value (in thousands)
Outstanding at December 31, 2013	21,350,597	$4.47	4.8	$85,186
Granted	5,437,500	$8.47		
Exercised	(2,723,666)	$3.45		
Forfeited	(727,126)	$5.65		
Expired	(37,386)	$0.71		
Outstanding at December 31, 2014	23,299,919	$5.50	5.37	$104,797
Vested and expected to vest at December 31, 2014	21,943,140	$5.35	5.25	$101,859
Exercisable at December 31, 2014	11,876,035	$3.89	4.09	$72,481

The total intrinsic value of stock options exercised for the years ended December 31, 2014, 2013, and 2012 was $14.6 million, $59.5 million and $2.4 million, respectively.

The weighted average grant date fair value of stock options granted for the years ended December 31, 2014, 2013, and 2012 was $4.64, $4.00, and $2.44, respectively. The total fair value of stock options vested during the years ended December 31, 2014, 2013, and 2012 was $10.9 million, $5.9 million and $3.4 million, respectively.

Restricted Stock

In 2009, we issued 30,000 shares of restricted Common Stock to one of our independent board members. The restricted stock was granted under our 2007 Equity Incentive Plan with a term of 7 years and vesting occurring 5 years after the grant date with certain events which would accelerate the vesting of the award. The restricted stock was valued using the grant date fair value which was equivalent to the closing price of our Common Stock on the grant date. We record the cost of restricted stock over the vesting period.

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Note 10 Income Taxes

We operate and are required to file tax returns in the U.S. and various foreign jurisdictions.

The (expense) benefit for incomes taxes consists of the following:

	For the years ended December 31,		
(In thousands)	2014	2013	2012
Current			
Federal	$225	$—	$—
State	247	—	—
Foreign	(1,514)	(1,073)	(332)
	(1,042)	(1,073)	(332)
Deferred			
Federal	—	(1,161)	8,191
State	(167)	(104)	1,038
Foreign	1,185	666	729
	1,018	(599)	9,958
Total, net	$(24)	$(1,672)	$9,626

Deferred income tax assets and liabilities as of December 31, 2014 and 2013 are comprised of the following:

(In thousands)	December 31, 2014	December 31, 2013
Deferred income tax assets:		
Federal net operating loss	$63,004	$43,869
State net operating loss	12,050	6,987
Foreign net operating loss	25,825	20,545
Research and development expense	9,244	4,746
Research and development tax credit	6,077	4,876
Stock options	18,422	13,981
Accruals	1,764	1,936
Equity investments	8,038	4,756
Other	4,702	2,904
Deferred income tax assets	149,126	104,600
Deferred income tax liabilities:		
Intangible assets	(177,074)	(179,414)
Other	(4,305)	(4,996)
Deferred income tax liabilities	(181,379)	(184,410)
Net deferred income tax assets	(32,253)	(79,810)
Valuation allowance	(131,931)	(85,370)
Net deferred income tax liabilities	$(164,184)	$(165,180)

The changes in deferred income tax assets, liabilities and valuation allowances at December 31, 2014 reflect the acquisition of various legal entities, including the tax attributes. Certain deferred tax assets and liabilities have been changed to properly reflect their classification. The acquisitions were accounted for under U.S. GAAP as stock acquisitions and business combinations. As of December 31, 2014, we have federal, state and foreign net operating loss carryforwards of approximately $294.9 million, $262.6 million and $97.1 million, respectively, that expire at various dates through 2034. Included in the foreign net operating losses is $74.0 million related to OPKO Biologics. As of December 31, 2014, we have research and development tax credit carryforwards of approximately $6.1 million that expire in varying amounts through 2034. We have determined a full valuation allowance is required against all of our net deferred tax assets that we do not expect to be utilized by the turning of deferred income tax liabilities.

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As a result of certain realization requirements of ASC 718, Compensation - Stock Compensation, the table of deferred tax assets and liabilities shown above does not include certain deferred tax assets as of December 31, 2014, and December 31, 2013, that arose directly from (or the use of which was postponed by) tax deductions related to equity compensation that are greater than the compensation recognized for financial reporting. Equity will be increased by $16.4 million if and when such deferred tax assets are ultimately realized. The Company uses ASC 740 ordering when determining when excess tax benefits have been realized.

Under Section 382 of the Internal Revenue Code of 1986, as amended, certain significant changes in ownership may restrict the future utilization of our income tax loss carryforwards and income tax credit carryforwards in the U.S. The annual limitation is equal to the value of our stock immediately before the ownership change, multiplied by the long-term tax-exempt rate (i.e., the highest of the adjusted Federal long-term rates in effect for any month in the three-calendar-month period ending with the calendar month in which the change date occurs). This limitation may be increased under the IRC§ 338 Approach (IRS approved methodology for determining recognized Built-In Gain). As a result, federal net operating losses and tax credits may expire before we are able to fully utilize them.

During 2008, we conducted a study to determine the impact of the various ownership changes that occurred during 2007 and 2008. As a result, we have concluded that the annual utilization of our net operating loss carryforwards ("NOLs") and tax credits is subject to a limitation pursuant to Internal Revenue Code section 382. Under the tax law, such NOLs and tax credits are subject to expiration from 15 to 20 years after they were generated. As a result of the annual limitation that may be imposed on such tax attributes and the statutory expiration period, some of these tax attributes may expire prior to our being able to use them. As we have established a valuation allowance against all of our net deferred tax assets, including such NOLs and tax credits, there is no current impact on these financial statements as a result of the annual limitation. This study did not conclude as to whether eXegenics' pre-merger NOLs were limited under Section 382. As such, of the $294.9 million of federal net operating loss carryforwards, at least approximately $37.2 million may not be able to be utilized.

Uncertain Income Tax Positions

We file federal income tax returns in the U.S. and various foreign jurisdictions, as well as with various U.S. states and the Ontario and Quebec provinces in Canada. We are subject to routine tax audits in all jurisdictions for which we file tax returns. Tax audits by their very nature are often complex and can require several years to complete. For the period ended December 31, 2014, $3.2 million of accrued uncertain tax benefits were reversed as a result of settlements with foreign tax authorities. It is reasonably possible that some audits will close within the next twelve months, which we do not believe would result in a material change to our accrued uncertain tax positions.

U.S. Federal: Under the tax statute of limitations applicable to the Internal Revenue Code, we are no longer subject to U.S. federal income tax examinations by the Internal Revenue Service for years before 2011. However, because we are carrying forward income tax attributes, such as net operating losses and tax credits from 2011 and earlier tax years, these attributes can still be audited when utilized on returns filed in the future.

State: Under the statutes of limitation applicable to most state income tax laws, we are no longer subject to state income tax examinations by tax authorities for years before 2011 in states in which we have filed income tax returns. Certain states may take the position that we are subject to income tax in such states even though we have not filed income tax returns in such states and, depending on the varying state income tax statutes and administrative practices, the statute of limitations in such states may extend to years before 2011.

Foreign: Under the statutes of limitations applicable to our foreign operations, we are generally no longer subject to tax examination for years before 2009 in jurisdictions where we have filed income tax returns.

Unrecognized Tax Benefits

As of December 31, 2014, 2013, and 2012, the total amount of gross unrecognized tax benefits was approximately $5.9 million, $9.2 million, and $9.2 million, respectively. As of December 31, 2014, the total gross unrecognized tax benefit of $5.9 million consisted of increases of $0.7 million as a result of current year activity, and decreases of $4.1 million as a result of the lapse of statutes of limitations and audit settlements. As of December 31, 2014, the total amount of unrecognized tax benefits that, if recognized, would affect our effective income tax rate was $0.9 million. As of December 31, 2013, $0.2 million of the unrecognized tax benefits, if recognized, would have affected our effective income tax rate and none as of December 31, 2012. We believe it is reasonably possible that approximately

$0.9 million of unrecognized tax benefits may be recognized within the next twelve months.

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The following summarizes the changes in our gross unrecognized income tax benefits.

	For the years ended December 31,		
(In thousands)	2014	2013	2012
Unrecognized tax benefits at beginning of period	$9,231	$9,245	$5,250
Gross increases – tax positions in prior period	717	575	4,467
Gross decreases – tax positions in prior period	(396)	(589)	(472)
Lapse of Statute of Limitations	(472)		
Settlements	(3,190)		
Unrecognized tax benefits at end of period	$5,890	$9,231	$9,245

Other Income Tax Disclosures

The significant elements contributing to the difference between the federal statutory tax rate and the effective tax rate are as follows:

	For the years ended December 31,		
	2014	2013	2012
Federal statutory rate	35.0%	35.0%	35.0%
State income taxes, net of federal benefit	2.5%	2.4%	3.1%
Foreign income tax	(10.3)%	(7.9)%	(0.9)%
Research and development tax credits	1.1%	1.0%	(0.3)%
Non-Deductible components of Convertible Debt	(3.8)%	(16.7)%	—%
Valuation allowance	(25.3)%	(11.4)%	(11.4)%
Other	0.8%	(3.9)%	(0.7)%
Total	—%	(1.5)%	24.8%

The following table reconciles our losses before income taxes between U.S. and foreign jurisdictions:

	For the years ended December 31,		
(In thousands)	2014	2013	2012
Pre-tax loss:			
U.S.	$(84,075)	$(74,861)	$(34,058)
Foreign	(87,567)	(37,874)	(4,725)
Total	$(171,642)	$(112,735)	$(38,783)

The following table reconciles our long-lived assets between U.S. and foreign jurisdictions:

(In thousands)	December 31, 2014	December 31, 2013
Long-lived assets:		
U.S.	$4,286	$4,582
Foreign	12,125	12,445
Total	$16,411	$17,027

No additional provision has been made for U.S. or foreign income taxes on the undistributed earnings of subsidiaries or for unrecognized deferred tax liabilities for temporary differences related to investments in subsidiaries, as such earnings are expected to be permanently reinvested, the investments are essentially permanent in duration, or the Company has concluded that no additional tax liability will arise as a result of distribution of such earnings. A liability could arise if amounts are distributed by such subsidiaries or if such subsidiaries are ultimately disposed. It is not practicable to estimate the additional income taxes related to permanently reinvested earnings or the basis differences related to investments in subsidiaries.

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Note 11 Related Party Transactions

In February 2014, Dr. Frost, our Chairman and Chief Executive Officer, paid a filing fee of $280,000 to the Federal Trade Commission (the "FTC") under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 ("HSR Act") in connection with filings made by us and Dr. Frost. We reimbursed Dr. Frost for the HSR filing fee.

In October, 2013, we paid the $170,000 filing fee to the FTC in connection with filings made by us and Dr. Hsiao, our Vice Chairman of the Board and Chief Technical Officer, under the HSR Act.

In October 2013, we entered into an agreement with ARNO pursuant to which we invested $2.0 million as part of an approximate $30 million financing. In exchange for our investment, we received 833,333 shares of ARNO common stock, one-year warrants to purchase 833,333 shares of ARNO common stock, for $2.40 a share and five-year warrants to purchase an additional 833,333 shares of ARNO common stock for $4.00 a share. Other investors participating in the private financing included Frost Gamma Investments Trust, a trust affiliated with Dr. Frost (the "Gamma Trust"), Hsu Gamma Investment, L.P., an entity affiliated with Dr. Hsiao (the "Hsu Gamma"), and other members of our board of directors and management. In connection with the transaction, ARNO agreed that for so long as we continue to hold at least 3% of the total number of outstanding shares of ARNO's common stock on a fully-diluted basis, we will have the right to appoint a non-voting observer to attend all meetings of ARNO's board of directors and we shall have a right of first negotiation that provides us with exclusive rights to negotiate with ARNO for a 45-day period regarding any potential strategic transactions that ARNO's board of directors elects to pursue.

In October 2013, we made an investment in Zebra pursuant to which we acquired 840,000 shares of Zebra's Series A-2 Preferred stock for $2.0 million. Zebra is a privately held biotechnology company focused on the discovery and development of biosuperior antibody therapeutics and complex drugs. Zebra's patented platform is an advanced version of a core technology developed at The Scripps Research Institute ("TSRI") by Dr. Lerner (the "TSRI Technology"). Zebra acquired the license to the TSRI Technology from a third party who had licensed such rights from TSRI. In connection with its acquisition of rights to the TSRI Technology, Zebra agreed to make certain research funding payments to Dr. Lerner's laboratory at TSRI to further support development of the TSRI Technology. Dr. Lerner also participated in the Series A-2 Preferred Stock financing on the same financial terms as the Company. Each of Drs. Frost and Lerner serve as members of the board of directors and scientific consultants to Zebra. After the closing, we owned 23.5% of the Series A-2 Preferred stock issued and outstanding by Zebra. Each of Drs. Frost and Lerner received 900,000 restricted shares of Zebra common stock in connection with their roles as founders and scientific consultants to Zebra. Dr. Frost gifted his 900,000 shares of Zebra restricted common stock to OPKO.

Effective May 1, 2013, we entered into an agreement with Dr. Hsiao pursuant to which we have the right to utilize approximately 5,000 square feet of laboratory space in Taiwan, inclusive of any and all utility costs, taxes and building maintenance fees. In addition, Dr. Hsiao provides certain other services to us relating to government grant work in Taiwan, as well as the coordination of work flow between our U.S. and Taiwanese operations. The term of the agreement is for five years and obligates us to pay Dr. Hsiao approximately $60,000 annually.

In August 2013, we acquired OPKO Biologics (formerly PROLOR) pursuant to an Agreement and Plan of Merger dated as of April 23, 2013 in an all-stock transaction. Until completion of the acquisition, Dr. Frost was PROLOR's Chairman of the Board and a greater than 5% stockholder of PROLOR. Dr. Hsiao and Mr. Rubin were also directors and less than 5% stockholders of PROLOR.

In January 2013, we sold $175.0 million aggregate principal amount of 2033 Senior Notes in a private placement in reliance on exemptions from registration under the Securities Act. The Purchasers of the 2033 Senior Notes include the Gamma Trust and Hsu Gamma. The 2033 Senior Notes were issued on January 30, 2013.

In December 2012, we entered into a five-year lease agreement with AVI Properties, LLC ("AVI"), an entity affiliated with Dr. Jonathan Oppenheimer, who previously served as OPKO Lab's Chief Executive Officer. The lease is for approximately 44,000 square feet of laboratory and office space in Nashville, Tennessee, where OPKO Lab is based. The lease provides for payments of approximately $18 thousand per month in the first year, increasing annually if the consumer price index exceeds 5%, plus applicable sales tax. In addition to the rent, we pay a portion of operating expenses, property taxes and parking.

During the years ended December 31, 2014, 2013 and 2012, FineTech recorded revenue of $0.3 million, $0.3 million and $0.2 million, respectively, for the sale of APIs to Teva Pharmaceutical Industries, Limited ("Teva"). Dr. Frost

previously served as the Chairman of the Board of Directors of Teva until 2015.

In February 2012, we entered into a cooperative research funding and option agreement with TSRI to support research for the development of novel oligomeric compounds relating to our molecular diagnostics technology (the “Research Agreement”).

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Pursuant to the Research Agreement, we agreed to provide funding of approximately $0.9 million annually over a five year period. OPKO has notified TSRI of its intent to terminate this Agreement effective July 2015. In conjunction with entering into the Research Agreement, we also entered into a license agreement with TSRI for technology relating to libraries of peptide tertiary amides. In addition, we entered into a second license with TSRI for technology relating to highly selective inhibitors of c-Jun-N-Terminal Kinases that may be useful for the treatment of various diseases, including Parkinson's disease. We also entered into a research funding and option agreement to provide funding of approximately $0.2 million annually over three years to support further development of the technology. Dr. Frost served as a Trustee for TSRI until November 2012 and Dr. Lerner, a member of our Board of Directors, served as its President until December 2011.

In February 2012, we made a $1.0 million investment in ChromaDex. Other investors participating in the private financing included the Gamma Trust, Hsu Gamma, and Dr. Lerner. Following our investment, we owned 1.5% of ChromaDex, the Gamma Trust owned approximately 16% of ChromaDex; Hsu Gamma owned approximately 1%; and certain of our directors owned less than 1% of ChromaDex.

In 2012, we made a $1.7 million investment in Biozone. Effective January 2, 2014, Biozone completed a merger with Cocrystal, another entity in which we have an equity investment, to which Cocrystal was the surviving entity, and the name of the issuer was changed to Cocrystal Pharma, Inc. ("CPI"). Dr. Frost previously invested in both Biozone and Cocrystal. Effective January 16, 2014, we invested an additional $0.5 million in the company as part of a $2.75 million private placement and received 1.0 million shares of common stock and 1.0 million 10-year warrants exercisable at $0.50 per share. At December 31, 2014, we hold an 8% ownership interest in CPI.

In August 2011, we made an investment in Neovasc. Dr. Frost and other members of our management are shareholders of Neovasc. Prior to the investment, Dr. Frost beneficially owned approximately 36% of Neovasc, Dr. Hsiao owned approximately 6%, and Mr. Rubin owned less than 1%. Dr. Hsiao and Mr. Rubin also serve on the board of directors of Neovasc.

In November 2010, we made an investment in Fabrus and on May 16, 2014, Senesco Technologies, Inc. acquired Fabrus pursuant to an agreement and plan of merger. On September 29, 2014, Senesco changed its name to Sevion Therapeutics, Inc. Dr. Frost and Steven Rubin serve on the Sevion board of directors. At December 31, 2014, we hold an 4% ownership interest in Sevion.

In June 2010, we entered into a cooperative research and development agreement with Academia Sinica, Taipei, Taiwan ("Academia Sinica"), for pre-clinical work for a compound against various forms of cancer. Dr. Alice Yu, a member of our Board of Directors, previously served as a Distinguished Research Fellow and Associate Director at the Genomics Research Center, Academia Sinica ("Genomics Research Center"). In connection with the Academia Sinica Agreement, we are required to pay Academia Sinica approximately $0.2 million over the term of the agreement.

In June 2009, we entered into a stock purchase agreement with Sorrento, pursuant to which we invested $2.3 million in Sorrento Therapeutics, Inc. ("Sorrento"). In exchange for the investment, we acquired approximately one-third of the outstanding common shares of Sorrento and received a fully-paid, exclusive license to the Sorrento antibody library for the discovery and development of therapeutic antibodies in the field of ophthalmology. On September 21, 2009, Sorrento entered into a merger transaction with Quikbyte Software, Inc. ("Quikbyte"). Prior to the merger transaction, certain investors, including Dr. Frost and other members of our management group, made an investment in Quikbyte. Dr. Lerner serves as a consultant and scientific advisory board member to Sorrento and owns less than one percent of its shares. In December 2013, we completed the sale of our stake in Sorrento and recorded a gain on the sale of $17.2 million and other income of $2.7 million related to an early termination fee under a license agreement with Sorrento.

In November 2007, we entered into an office lease with Frost Real Estate Holdings, LLC ("Frost Holdings"), an entity affiliated with Dr. Frost. The lease was for approximately 8,300 square feet of space in an office building in Miami, Florida, where our principal executive offices are located. The lease provided for payments of approximately $18 thousand per month in the first year increasing annually to $24 thousand per month in the fifth year, plus applicable sales tax. The rent was inclusive of operating expenses, property taxes and parking. The rent for the first year was reduced to reflect a $30 thousand credit for the costs of tenant improvements. In August 2012, we entered into a six-month extension on the same terms as the 2007 expiring lease and in February 2013, we agreed to extend the lease

on a month-to-month basis. Effective January 1, 2014, we entered into a new lease agreement with Frost Holdings. The lease, as amended on July 28, 2014, was for approximately 22,000 square feet of space. The lease provides for payments of approximately $57 thousand per month in the first year increasing annually to $65 thousand per month in the fifth year, plus applicable sales tax. As in the original lease, the rent is inclusive of operating expenses, property taxes and parking. The rent will be reduced by $216 thousand for the cost of tenant improvements, of which approximately $113 thousand and $103 thousand will be credited against rent payments in 2014 and 2015, respectively.

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We reimburse Dr. Frost for Company-related use by Dr. Frost and our other executives of an airplane owned by a company that is beneficially owned by Dr. Frost. We reimburse Dr. Frost in an amount equal to the cost of a first class airline ticket between the travel cities for each executive, including Dr. Frost, traveling on the airplane for Company-related business. We do not reimburse Dr. Frost for personal use of the airplane by Dr. Frost or any other executive; nor do we pay for any other fixed or variable operating costs of the airplane. For the years ended December 31, 2014, 2013, and 2012, we reimbursed Dr. Frost approximately $175 thousand, $93 thousand, and $203 thousand, respectively, for Company-related travel by Dr. Frost and other OPKO executives.

Note 12 Employee Benefit Plans

Effective January 1, 2007, the OPKO Health Savings and Retirement Plan (the "Plan") permits employees to contribute up to 50% of qualified pre-tax annual compensation up to annual statutory limitations. The discretionary company match for employee contributions to the Plan is 100% up to the first 4% of the participant's earnings contributed to the Plan. Our matching contributions to the Plan were approximately $0.6 million, $0.5 million and $0.3 million for the years ended December 31, 2014, 2013, and 2012 respectively.

Note 13 Commitments and Contingencies

In connection with our acquisitions of CURNA, OPKO Diagnostics, OPKO Health Europe and OPKO Renal, we agreed to pay future consideration to the sellers upon the achievement of certain events. As a result, as of December 31, 2014, we recorded $71.6 million as contingent consideration, with $27.4 million recorded within Accrued expenses and $44.2 million recorded within Other long-term liabilities in the accompanying Consolidated Balance Sheets. Refer to Note 5. In addition, in connection with our asset purchase agreement with Schering Plough Corporation, now Merck & Co. ("Merck"), we are required to pay up to an additional $25.0 million upon the achievement of certain development milestones. Future payments to be made under the agreement with Merck will be recognized when the milestones are achieved and consideration is issued or becomes issuable. Refer to Note 14.

On April 29, 2013, we were named in a putative class action filed in the Eighth Judicial District Court in and for Clark County, Nevada against PROLOR (now known as OPKO Biologics), the members of the PROLOR Board of Directors, individually (including Drs. Frost and Hsiao and Steven Rubin), and the Company. From May 1, 2013 through May 6, 2013, we were named in an additional five putative class actions suits filed in the Eighth Judicial District Court in and for Clark County, Nevada against the same defendants. On July 17, 2013, these suits were consolidated, for all purposes, into an amended class action complaint. The lawsuit is brought by purported holders of PROLOR's common stock, both individually and on behalf of a putative class of PROLOR's stockholders, asserting claims that PROLOR's Board of Directors breached its fiduciary duties in connection with the merger by purportedly failing to maximize stockholder value, that PROLOR and its Board of Directors failed to disclose material information to PROLOR's stockholders, and that the Company aided and abetted the alleged breaches of fiduciary duty. On May 5, 2014, the court issued an order dismissing all claims as to all defendants without prejudice, and the plaintiffs did not appeal the dismissal or file an amended complaint.

In July 2012, OPKO Lab received a letter from AdvanceMed Corporation ("AdvanceMed") regarding a post-payment review conducted by AdvanceMed (the "Post-Payment Review Letter"). The Post-Payment Review Letter originated with a post payment review audit by AdvanceMed of 183 claims submitted by OPKO Lab to the Medicare program. OPKO Lab believes that its billing practices were appropriate and it is following the appeal process set forth by Medicare. OPKO Lab received a partially favorable determination, which reduced the amount of the alleged overpayment, and it continues to appeal the remaining alleged overpayments. No assurances can be given about the outcome of the appeal.

On or around October 21, 2014, we received a Civil Investigative Demand ("Demand") from the U.S. Attorney's Office for the Middle District of Tennessee ("Attorney's Office"). The Demand concerns an investigation of allegations that the Company or one of its affiliated entities or other parties submitted false claims for payment related to services provided to government healthcare program beneficiaries in violation of the False Claims Act, 31 U.S.C. Section 3729. We intend to fully cooperate with the investigation and produce documents responsive to the Demand. It is too early to assess the probability of a favorable or unfavorable outcome in this matter or the loss or range of loss, if any.

We accrue a liability for legal contingencies when we believe that it is both probable that a liability has been incurred and that we can reasonably estimate the amount of the loss. We review these accruals and adjust them to reflect

ongoing negotiations, settlements, rulings, advice of legal counsel and other relevant information. To the extent new information is obtained and our views on the probable outcomes of claims, suits, assessments, investigations or legal proceedings change, changes in our accrued liabilities would be recorded in the period in which such determination is made. For the matters referenced in the paragraph below, the amount of liability is not probable or the amount cannot be reasonably estimated; and, therefore, accruals have not been made. In addition, in accordance with the relevant authoritative guidance, for matters which

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the likelihood of material loss is at least reasonably possible, we provide disclosure of the possible loss or range of loss; however, if a reasonable estimate cannot be made, we will provide disclosure to that effect.

We are a party to other litigation in the ordinary course of business. We do not believe that any such litigation will have a material adverse effect on our business, financial condition, or results of operations.

We expect to incur substantial losses as we continue the development of our product candidates, continue our other research and development activities, and establish a sales and marketing infrastructure in anticipation of the commercialization of our diagnostic and pharmaceutical product candidates. We currently have limited commercialization capabilities, and it is possible that we may never successfully commercialize any of our diagnostic and pharmaceutical product candidates. We do not currently generate significant revenue from any of our diagnostic and pharmaceutical product candidates. Our research and development activities are budgeted to expand over a period of time and will require further resources if we are to be successful. As a result, we believe that our operating losses are likely to be substantial over the next several years. We may need to obtain additional funds to further develop our research and development programs, and there can be no assurance that additional capital will be available to us on acceptable terms, or at all.

At December 31, 2014, we were committed to make future purchases for inventory and other items that occur in the ordinary course of business under various purchase arrangements with fixed purchase provisions aggregating $14.7 million.

Note 14 Strategic Alliances

Pfizer Inc.

We plan to develop a portfolio of product candidates through a combination of internal development and external partnerships. In December 2014, we entered into an exclusive worldwide agreement with Pfizer Inc. (“Pfizer”) for the development and commercialization of our long-acting hGH-CTP for the treatment of growth hormone deficiency (“GHD”) in adults and children, as well as for the treatment of growth failure in children born small for gestational age (“SGA”) (the “Pfizer Transaction”).

The Pfizer Transaction closed in January 2015 following the termination of the waiting period under the Hart-Scott-Rodino Act. Under the terms of the Pfizer Transaction, we received non-refundable and non-creditable upfront payments of $295 million and are eligible to receive up to an additional $275 million upon the achievement of certain regulatory milestones. Pfizer received the exclusive license to commercialize hGH-CTP worldwide. In addition, we are eligible to receive initial royalty payments associated with the commercialization of hGH-CTP for Adult GHD. Upon the launch of hGH-CTP for Pediatric GHD, the royalties will transition to a regional, tiered gross profit sharing for both hGH-CTP and Pfizer’s Genotropin®.

We will lead the clinical activities and will be responsible for funding the development programs for the key indications, which includes Adult and Pediatric GHD and Pediatric SGA. Pfizer will be responsible for all development costs for additional indications as well as all post-marketing studies. In addition, Pfizer will fund the commercialization activities for all indications and lead the manufacturing activities covered by the global development plan.

As the Pfizer Transaction was completed in January 2015, no revenue was recognized for the year ended December 31, 2014 for the Pfizer Transaction. See further discussion of the Pfizer Transaction in Note 20.

TESARO

In November 2009, we entered into an asset purchase agreement (the “NK-1 Agreement”) under which we acquired rolapitant and other neurokinin-1 (“NK-1”) assets from Schering Plough Corporation, now Merck. In December 2010, we entered into an exclusive license agreement with TESARO, in which we out-licensed the development, manufacture, commercialization and distribution of our lead NK-1 candidate, rolapitant (the “TESARO License”). Under the terms of the TESARO License, we are eligible for payments of up to $121.0 million, including an up-front payment of $6.0 million, which has been received, and additional payments based upon achievement of specified regulatory and commercialization milestones. In addition, TESARO will pay us double digit tiered royalties on sales of licensed products. We will share future profits from the commercialization of licensed products in Japan with TESARO and we will have an option to market the products in Latin America.

In September 2014, TESARO submitted a New Drug Application (“NDA”) to the FDA for approval of oral rolapitant, an investigational neurokinin-1 receptor antagonist in development for the prevention of chemotherapy-induced nausea and vomiting. Under the terms of our agreement with TESARO, TESARO paid us a milestone payment of $5.0 million upon acceptance by the FDA of the NDA in the fourth quarter 2014 which was recognized in Revenue from transfer of intellectual

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property in the Consolidated Statement of Operations.

Under the terms of the NK-1 Agreement, upon acceptance by the FDA of TESARO's NDA in the fourth quarter of 2014, we were required to make a $2.0 million milestone payment to Merck. We accounted for the NK-1 Agreement as an asset acquisition and allocated the entire $2.0 million payment to In-process research and development expense in the Consolidated Statement of Operations. Under the terms of the NK-1 Agreement, we are required to pay up to an additional $25.0 million upon achievement of certain development milestones. Future payments to be made under the NK-1 Agreement will be recognized when the milestones are achieved and consideration is issued or becomes issuable.

RXi Pharmaceuticals Corporation

In March 2013, we completed the sale to RXi Pharmaceuticals Corporation ("RXi") of substantially all of our assets in the field of RNA interference (the "RNAi Assets") (collectively, the "Asset Purchase Agreement"). In accounting for the sale of the RNAi Assets, we determined that we did not have any continuing involvement in the development of the RNAi Assets or any other future performance obligations and, as a result, during the year ended December 31, 2013, we recognized $12.5 million of revenue from transfer of intellectual property in our Consolidated Statement of Operations.

Pursuant to the Asset Purchase Agreement, RXi will be required to pay us up to $50.0 million in milestone payments upon the successful development and commercialization of each drug developed by RXi, certain of its affiliates or any of its or their licensees or sublicensees utilizing patents included within the RNAi Assets (each, a "Qualified Drug"). In addition, RXi will also be required to pay us royalties equal to: (a) a mid single-digit percentage of "Net Sales" (as defined in the Asset Purchase Agreement) with respect to each Qualified Drug sold for an ophthalmologic use during the applicable "Royalty Period" (as defined in the Asset Purchase Agreement); and (b) a low single-digit percentage of net sales with respect to each Qualified Drug sold for a non-ophthalmologic use during the applicable royalty period.

Other

We have also completed strategic deals with the UT Southwestern, Washington University, INEOS Healthcare, TSRI, the President and Fellows of Harvard College, and Academia Sinica, among others. In connection with these license agreements, upon the achievement of certain milestones we are obligated to make certain payments and have royalty obligations upon sales of products developed under the license agreements. At this time, we are unable to estimate the timing and amounts of payments as the obligations are based on future development of the licensed products.

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Note 15 Leases

We conduct certain of our operations under operating lease agreements. Rent expense under operating leases was approximately $2.6 million, $1.9 million, and $1.3 million for the years ended December 31, 2014, 2013, and 2012, respectively.

As of December 31, 2014, the aggregate future minimum lease payments under all non-cancelable operating leases with initial or remaining lease terms in excess of one year are as follows:

Year Ending	(In thousands)
2015	$2,744
2016	2,290
2017	1,478
2018	1,149
2019	653
Thereafter	3,256
Total minimum lease commitments	$11,570

Note 16 Segments

We currently manage our operations in two reportable segments, pharmaceuticals and diagnostics. The pharmaceuticals segment consists of two operating segments, our (i) pharmaceutical research and development segment which is focused on the research and development of pharmaceutical products, and vaccines, and (ii) the pharmaceutical operations we acquired in Chile, Mexico, Israel, Spain, Brazil, and Uruguay. The diagnostics segment consists of two operating segments, our (i) pathology operations we acquired through the acquisition of OPKO Lab and (ii) point-of-care and molecular diagnostics operations. There are no inter-segment sales. We evaluate the performance of each segment based on operating profit or loss. There is no inter-segment allocation of interest expense and income taxes.

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Information regarding our operations and assets for our operating segments and the unallocated corporate operations as well as geographic information are as follows:

	For the years ended December 31,		
(In thousands)	2014	2013	2012
Product revenues:			
Pharmaceuticals	$76,983	$68,161	$45,295
Diagnostics	—	—	—
Corporate	—	—	—
	$76,983	$68,161	$45,295
Revenue from services:			
Pharmaceuticals	$—	$—	$—
Diagnostics	8,426	10,833	395
Corporate	240	825	1,354
	$8,666	$11,658	$1,749
Revenue from transfer of intellectual property:			
Pharmaceuticals	$5,285	$15,160	$—
Diagnostics	191	1,551	—
Corporate	—	—	—
	$5,476	$16,711	$—
Operating (loss) income:			
Pharmaceuticals	$(94,401)	$(29,809)	$(6,797)
Diagnostics	(21,647)	(22,199)	(14,259)
Corporate	(27,725)	(24,473)	(15,628)
Less: Operating loss attributable to noncontrolling interests	(2,042)	(3,151)	(585)
	$(145,815)	$(79,632)	$(37,269)
Depreciation and amortization:			
Pharmaceuticals	$7,936	$8,234	$6,367
Diagnostics	6,894	6,833	3,614
Corporate	97	149	179
	$14,927	$15,216	$10,160
Net loss from investment in investees:			
Pharmaceuticals	$(3,587)	$(11,456)	$(2,062)
Diagnostics	—	—	—
Corporate	—	—	—
	$(3,587)	$(11,456)	$(2,062)
Revenues:			
United States	$14,142	$28,369	$1,749
Chile	29,154	31,650	26,514
Spain	21,323	18,800	6,124
Israel	20,638	13,252	7,655
Mexico	5,807	4,459	5,002
Other	61	—	—
	$91,125	$96,530	$47,044

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(In thousands)	December 31, 2014	December 31, 2013
Assets:		
Pharmaceuticals	$1,064,498	$1,065,033
Diagnostics	108,072	116,944
Corporate	95,094	209,539
	$1,267,664	$1,391,516
Goodwill:		
Pharmaceuticals	$173,327	$175,408
Diagnostics	50,965	50,965
Corporate	—	—
	$224,292	$226,373

During the year ended December 31, 2014, one customer of our pharmaceutical segment represented 13% of our total revenue. During the years ended December 31, 2013, and 2012, no customer represented more than 10% of our total revenue. As of December 31, 2014, 2013, and 2012, no customer represented more than 10% of our accounts receivable balance.

Note 17 Fair Value Measurements

We record fair values at an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. We utilize a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. These tiers include: Level 1, defined as observable inputs such as quoted prices in active markets; Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable; and Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring an entity to develop its own assumptions.

A summary of our investments classified as available for sale and carried at fair value, is as follows:

	As of December 31, 2014				
(In thousands)	Amortized Cost	Gross unrealized gains in Accumulated OCI	Gross unrealized losses in Accumulated OCI	Gain/(Loss) in Accumulated Deficit	Fair value
Common stock investments, available for sale	$11,479	$293	$(4,573)	$(1,441)	$5,758
Common stock options/warrants	1,425	216	—	4,673	6,314
Total assets	$12,904	$509	$(4,573)	$3,232	$12,072

	As of December 31, 2013				
(In thousands)	Amortized Cost	Gross unrealized gains in Accumulated OCI	Gross unrealized losses in Accumulated OCI	Gain/(Loss) in Accumulated Deficit	Fair value
Common stock investments, available for sale	$3,376	$2,698	$—	$—	$6,074
Common stock options/warrants	925	1,041	—	4,022	5,988
Total assets	$4,301	$3,739	$—	$4,022	$12,062

Any future fluctuation in fair value related to these instruments that is judged to be temporary, including any recoveries of previous write-downs, will be recorded in Accumulated other comprehensive income or loss. If we determine that any future valuation adjustment was other-than-temporary, we will record a loss during the period such

determination is made.

As of December 31, 2014, we have money market funds that qualify as cash equivalents, forward contracts for inventory purchases (Refer to Note 18) and contingent consideration related to the acquisitions of CURNA, OPKO Diagnostics, OPKO Health Europe, and OPKO Renal that are required to be measured at fair value on a recurring basis. In addition, in connection with our investment and our consulting agreement with Neovasc, we record the related Neovasc options at fair value as well as the warrants from Cocrystal, ARNO and Sevion.

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Our financial assets and liabilities measured at fair value on a recurring basis are as follows:

	Fair value measurements as of December 31, 2014			
(In thousands)	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)	Total
Assets:				
Money market funds	$71,286	$—	$—	$71,286
Certificates of deposit	—	—	—	—
Common stock investments, available for sale	5,758	—	—	5,758
Common stock options/warrants	—	6,314	—	6,314
Forward contracts	—	36	—	36
Total assets	$77,044	$6,350	$—	$83,394
Liabilities:				
Embedded conversion option	$—	$—	$65,947	$65,947
Contingent consideration:				
CURNA	—	—	440	440
OPKO Diagnostics	—	—	13,578	13,578
OPKO Renal	—	—	55,780	55,780
OPKO Health Europe	—	—	1,769	1,769
Total liabilities	$—	$—	$137,514	$137,514

	Fair value measurements as of December 31, 2013			
(In thousands)	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)	Total
Assets:				
Money market funds	$168,418	$—	$—	$168,418
Certificates of deposit	—	827	—	827
Pharmsynthez Notes Receivable & Purchase Option	—	6,151	—	6,151
Common stock investments, available for sale	6,074	—	—	6,074
Common stock options/warrants	—	5,988	—	5,988
Forward contracts	—	49	—	49
Total assets	$174,492	$13,015	$—	$187,507
Liabilities:				
Embedded conversion option	$—	$—	$101,087	$101,087
Deferred acquisition payments, net of discount	—	—	5,465	5,465
Contingent consideration:				
CURNA	—	—	573	573
OPKO Diagnostics	—	—	13,776	13,776
FineTech	—	—	3,124	3,124
OPKO Renal	—	—	53,092	53,092
OPKO Health Europe	—	—	1,043	1,043

Total liabilities	$—	$—	$178,160	$178,160

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The carrying amount and estimated fair value of our long-term debt, as well as the applicable fair value hierarchy tiers, are contained in the table below. The fair value of the 2033 Senior Notes is determined using a binomial lattice approach in order to estimate the fair value of the embedded derivative in the 2033 Senior Notes. Refer to Note 6.

	December 31, 2014				
(In thousands)	Carrying Value	Total Fair Value	Level 1	Level 2	Level 3
2033 Senior Notes	$65,507	$63,062	$—	$—	$63,062

There have been no transfers between Level 1 and Level 2 and no transfers to or from Level 3 of the fair value hierarchy.

As of December 31, 2014 and 2013, the carrying value of our other assets and liabilities approximates their fair value due to their short-term nature.

The following tables reconcile the beginning and ending balances of our Level 3 assets and liabilities as of December 31, 2014 and 2013:

	December 31, 2014		
(In thousands)	Contingent consideration	Deferred acquisition payments, net of discount	Embedded conversion option
Balance at December 31, 2013	$71,620	$5,465	$101,087
Additions	—	—	—
Total losses (gains) for the period:			
Included in results of operations	24,446	(735)	12,213
Foreign currency impact	(130)	—	—
Payments	(24,369)	(4,730)	—
Conversion	—	—	(47,353)
Balance at December 31, 2014	$71,567	$—	$65,947

	December 31, 2013			
(In thousands)	BZNE Note and conversion feature	Contingent consideration	Deferred acquisition payments, net of discount	Embedded conversion option
Balance at December 31, 2012	$2,040	$20,056	$10,103	$—
Additions	—	47,710	—	59,204
Total losses (gains) for the period:				
Included in results of operations	—	6,947	829	52,742
Foreign currency remeasurement		31		
Conversion	(2,040)	—	—	(10,859)
Payments	—	(3,124)	(5,467)	—
Balance at December 31, 2013	$—	$71,620	$5,465	$101,087

The estimated fair values of our financial instruments have been determined by using available market information and what we believe to be appropriate valuation methodologies. We use the following methods and assumptions in estimating fair value:

Contingent consideration – We estimate the fair value of the contingent consideration utilizing a discounted cash flow model for the expected payments based on estimated timing and expected revenues. We use several discount rates depending on each type of contingent consideration related to OPKO Diagnostics, CURNA, OPKO Health Europe, OPKO Renal and rolapitant transactions. The discount rates used range from 6% to 27% and were based on the weighted average cost of capital for those businesses. If the discount rates were to increase by 1%, on each transaction, the contingent consideration would decrease by $1.2 million. If estimated future sales were to decrease by 10%, the contingent consideration related to OPKO Renal would decrease by $1.5 million. As of December 31, 2014,

of the $71.6 million of contingent consideration, $27.4 million is recorded in Accrued expenses and $44.2 million is recorded in Other long-term liabilities. As of December 31, 2013,

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of the $71.6 million of contingent consideration, $28.0 million is recorded in Accrued expenses and $43.6 million is recorded in Other long-term liabilities.

Deferred payments – We estimate the fair value of the deferred payments utilizing a discounted cash flow model for the expected payments.

Embedded conversion option – We estimate the fair value of the embedded conversion option related to the 2033 Senior Notes using a binomial lattice model. Refer to Note 6 for detail description of the binomial lattice model and the fair value assumptions used.

BZNE Notes and conversion feature - The stock market activity in BZNE does not represent an active market and as such, we determined the fair market value utilizing a business enterprise valuation approach in order to determine the fair value of our investment. The most significant assumptions are the projected revenue growth and operating income (loss). The impact of a change in any of our significant underlying assumptions +/- 1% would not result in a materially different fair value. We converted the BZNE Notes into common stock in December 2013.

Note 18 Derivative Contracts

The following table summarizes the fair values and the presentation of our derivative financial instruments in the Consolidated Balance Sheets:

(In thousands)	Balance Sheet Component	December 31, 2014	December 31, 2013
Derivative financial instruments:			
Pharmsynthez Note Receivable and Purchase Option	Prepaid expenses and other current assets	$ —	$ 6,151
Common stock options/warrants	Investments, net	$ 6,314	$ 5,988
Embedded conversion option	2033 Senior Notes, net of discount and estimated fair value of embedded derivatives	$ 65,947	$ 101,087
Forward contracts [1]	Current portion of lines of credit and notes payable	$ 36	$ 49

[1] Gains on forward contracts are recorded in Prepaid expenses and other current assets. Losses on forward contracts are recorded in Accrued expenses.

We enter into foreign currency forward exchange contracts to cover the risk of exposure to exchange rate differences arising from inventory purchases on letters of credit. Under these forward contracts, for any rate above or below the fixed rate, we receive or pay the difference between the spot rate and the fixed rate for the given amount at the settlement date.

To qualify the derivative instrument as a hedge, we are required to meet strict hedge effectiveness and contemporaneous documentation requirements at the initiation of the hedge and assess the hedge effectiveness on an ongoing basis over the life of the hedge. At December 31, 2014 and 2013, our derivative financial instruments do not meet the documentation requirements to be designated as hedges. Accordingly, we recognize the changes in Fair value of derivative instruments, net in our Consolidated Statements of Operations. The following table summarizes the losses and gains recorded for the years ended December 31, 2014 and 2013:

	For the years ended December 31,		
(In thousands)	2014	2013	2012
Derivative gain (loss):			
Common stock options/warrants [1]	$1,193	$6,544	$1,350
2033 Senior Notes	(12,213)	(52,742)	—
Forward contracts	$388	$256	$(132)
Total	$(10,632)	$(45,942)	$1,218

[1] Includes the Pharmsynthez Note Receivable and the Purchase Option.

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The outstanding forward contracts at December 31, 2014 and 2013, have been recorded at fair value and their maturity details are as follows:

(In thousands) Days until maturity	Contract value	Fair value at December 31, 2014	Effect on income (loss)
0 to 30	$750	$780	$30
31 to 60	90	93	3
61 to 90	—	—	—
91 to 120	68	71	3
121 to 180	—	—	—
Total	$908	$944	$36

(In thousands) Days until maturity	Contract value	Fair value at December 31, 2013	Effect on income (loss)
0 to 30	$472	$489	$17
31 to 60	561	579	18
61 to 90	503	517	14
91 to 120	—	—	—
121 to 180	—	—	—
More than 180	—	—	—
Total	$1,536	$1,585	$49

Note 19 Selected Quarterly Financial Data (Unaudited)

	For the 2014 Quarters Ended			
(In thousands, except per share data)	March 31	June 30	September 30	December 31
Total revenues	$22,274	$23,545	$19,773	$25,533
Total costs and expenses	52,550	58,429	67,974	57,987
Net loss	(45,088)	(26,075)	(50,014)	(53,461)
Net loss attributable to common shareholders	(44,548)	(25,478)	(48,669)	(52,971)
(Loss) income per share, basic and diluted:	$(0.11)	$(0.06)	$(0.11)	$(0.12)

	For the 2013 Quarters Ended			
(In thousands, except per share data)	March 31	June 30	September 30	December 31
Total revenues	$31,376	$23,821	$20,641	$20,692
Total costs and expenses	38,149	41,805	39,650	56,558
Net loss	(34,763)	(4,353)	(60,801)	(17,429)
Net loss attributable to common shareholders	(34,635)	(3,394)	(59,998)	(16,800)
(Loss) income per share, basic and diluted:	$(0.11)	$(0.01)	$(0.17)	$(0.04)

Note 20 Subsequent Events

The Pfizer Transaction was completed in January 2015 following the termination of the waiting period under the Hart-Scott-Rodino Act. In the first quarter of 2015, we expect to make a payment $25.6 million to the Office of the Chief Scientist of the Israeli Ministry of Economy (“OCS”) in connection with repayment obligations resulting from grants previously made by the OCS to OPKO Biologics to support development of hGH-CTP and the outlicense of the technology outside of Israel.

We have reviewed all subsequent events and transactions that occurred after the date of our December 31, 2014 Consolidated Balance Sheet date, through the time of filing this Annual Report on Form 10-K.

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ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, have evaluated the effectiveness of the Company's disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) as of December 31, 2014. Our disclosure controls and procedures are designed to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the rules and forms of the Securities and Exchange Commission. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Based on this evaluation, management concluded that our disclosure controls and procedures were effective as of December 31, 2014.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined effective could provide only reasonable assurance with respect to financial statement preparation and presentation.

Our management conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2014, based on the framework in the Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "2013 Internal Control-Integrated Framework"). As permitted, our management's assessment of and conclusion on the effectiveness of our internal controls over financial reporting did not include the internal controls of SciVac Ltd, a consolidated variable interest entity. SciVac Ltd constituted $7.6 million and $(4.5) million of our total and net assets, respectively, as of December 31, 2014 and $2.8 million and $(2.6) million of revenues and net loss attributable to common shareholders, respectively, for the year then ended. Based on our evaluation under the framework in 2013 Internal Control-Integrated Framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2014.

The effectiveness of the Company's internal control over financial reporting as of December 31, 2014 has been audited by Ernst & Young LLP, our independent registered public accounting firm, who also audited our Consolidated Financial Statements included in this Annual Report on Form 10-K, as stated in their report which appears with our accompanying Consolidated Financial Statements.

Changes to the Company's Internal Control Over Financial Reporting

As previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2013, we concluded there was a material weakness in the design and operating effectiveness of our internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act, as of December 31, 2013. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis. The material weakness in internal control over financial reporting related to the Company's financial statement close process at its Chilean subsidiary due to the lack of sufficient controls to assure that inventory and accounts receivable balances were recorded correctly in accordance with U.S. generally accepted accounting principles.

With the oversight of senior management and our audit committee, we took additional measures to remediate the underlying causes of the material weakness. During the year ended December 31, 2014, we have worked with a global accounting firm in preparation for reporting on the effectiveness of our internal controls, and we have engaged an additional accounting firm to assist our local management team in addressing the underlying cause of the material weakness primarily through the development and implementation of additional policies, improved processes and documented procedures, as well as the hiring of additional finance personnel. Upon completion of our testing of the design and operating effectiveness of these

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new control procedures, management concluded that it has remediated the previously identified material weakness as of December 31, 2014.

Except as described above, there have been no changes in our internal control over financial reporting during the most recent quarter ended December 31, 2014 that has materially affected or is reasonably likely to materially affect, our internal control over financial reporting.

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ITEM 9B. OTHER INFORMATION

None.

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PART III

The information required in Items 10 (Directors, Executive Officers and Corporate Governance), Item 11 (Executive Compensation), Item 12 (Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters), Item 13 (Certain Relationships and Related Transactions, and Director Independence), and Item 14 (Principal Accounting Fees and Services) is incorporated by reference to the Company's definitive proxy statement for the 2015 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2014.

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PART IV.

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

(a) (1) Financial Statements: See Part II, Item 8 of this report.

We filed our consolidated financial statements in Item 8 of Part II. Additionally, the financial statement schedule entitled “Schedule II – Valuation and Qualifying Accounts” has been omitted since the information required is included in the consolidated financial statements and notes thereto.

(2) Exhibits: See below.

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Exhibit Number	Description
1.1[13]	Underwriting Agreement, dated March 9, 2011, by and among OPKO Health, Inc., Jefferies & Company, Inc. and J.P. Morgan Securities LLC, as representatives for the underwriters named therein.
2.1[1]	Merger Agreement and Plan of Reorganization, dated as of March 27, 2007, by and among Acuity Pharmaceuticals, Inc., Froptix Corporation, eXegenics, Inc., e-Acquisition Company I-A, LLC, and e-Acquisition Company II-B, LLC.
2.2[4]+	Securities Purchase Agreement, dated May 2, 2008, by and among Vidus Ocular, Inc., OPKO Instrumentation, LLC, OPKO Health, Inc., and the individual sellers and noteholders named therein.
2.3[10]	Purchase Agreement, dated February 17, 2010, by and among Ignacio Levy García and José de Jesús Levy García, Inmobiliaria Chapalita, S.A. de C.V., Pharmacos Exakta, S.A. de C.V., OPKO Health, Inc., OPKO Health Mexicana S. de R.L. de C.V., and OPKO Manufacturing Facilities S. de R.L. de C.V.
2.4[15]+	Agreement and Plan of Merger, dated January 28, 2011, by and among CURNA Inc., KUR, LLC, OPKO Pharmaceuticals, LLC, OPKO CURNA, LLC, and certain individuals named therein.
2.5[16]	Agreement and Plan of Merger, dated October 13, 2011, by and among OPKO Health, Inc., Claros Merger Subsidiary, LLC, Claros Diagnostics, Inc., and Ellen Baron, Marc Goldberg and Michael Magliochetti on behalf of the Shareholder Representative Committee.
2.6[18]+	Stock Purchase Agreement, dated December 20, 2011, by and among FineTech Pharmaceutical Ltd., Arie Gutman, OPKO Holdings Israel Ltd., and OPKO Health, Inc.
2.7[19]	Purchase Agreement, dated January 20, 2012, by and among OPKO Health, Inc., OPKO Chile S.A., Samuel Alexandre Arama, Inversiones SVJV Limitada, Bruno Sergiani, Inversiones BS Limitada, Pierre-Yves LeGoff, and Inversiones PYTT Limitada.
2.8[20]+	Stock Purchase Agreement, dated August 2, 2012, by and among Farmadiet Group Holding, S.L., the Sellers party thereto, OPKO Health, Inc., and Shebeli XXI, S.L.U.
2.9[22]+	Agreement and Plan of Merger, dated October 18, 2012, by and among Prost-Data, Inc. d/b/a OurLab, Our Labs, Endo Labs and Gold Lab, Jonathan Oppenheimer, M.D., OPKO Health, Inc., OPKO Laboratories Inc., and OPKO Labs, LLC.
2.10[23]+	Share Purchase Agreement, dated January 8, 2013, by among Cytochroma Inc., Cytochroma Holdings ULC, Cytochroma Canada Inc., Cytochroma Development Inc., Proventiv Therapeutics, LLC, Cytochroma Cayman Islands, Ltd., OPKO Health, Inc., and OPKO IP Holdings, Inc.
2.11[24]	Asset Purchase Agreement, dated March 1, 2013, by and between RXi Pharmaceuticals Corporation and OPKO Health, Inc.
2.12[25]	Agreement and Plan of Merger, dated April 23, 2013, by and among OPKO Health, Inc., POM Acquisition Inc., and PROLOR Biotech, Inc.

3.1[(28)]	Amended and Restated Certificate of Incorporation, as amended.

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3.2[3]	Amended and Restated Bylaws.
3.3[8]	Certificate of Designation of Series D Preferred Stock.
4.1[1]	Form of Common Stock Warrant.
4.2[8]	Form of Common Stock Warrant.
4.3[26]	Indenture, dated January 30, 2013, between OPKO Health, Inc. and Wells Fargo Bank, National Association.
10.1[1]	Form of Lockup Agreement.
10.2[2]	Office Lease dated November 13, 2007, by and between Frost Real Estate Holdings, LLC, and the OPKO Health, Inc.
10.3[3]	Stock Purchase Agreement, dated December 4, 2007, by and between OPKO Health, Inc. and the members of The Frost Group, LLC.
10.4[3]*	OPKO Health, Inc. 2007 Equity Incentive Plan.
10.5[27]*	Amendment to OPKO Health, Inc. 2007 Equity Incentive Plan.
10.6[4]	Form of Director Indemnification Agreement.
10.7[4]	Form of Officer Indemnification Agreement.
10.8[5]	Stock Purchase Agreement, dated August 8, 2008 by and between OPKO Health, Inc. and the Purchasers named therein.
10.9[6]	Stock Purchase Agreement, dated February 23, 2009 by and between OPKO Health, Inc. and Frost Gamma Investments Trust.
10.10[6]	Promissory Note to Frost Gamma Investments Trust, dated March 4, 2009.
10.11[7]	Form of Stock Purchase Agreement for transactions between OPKO Health, Inc. and Nora Real Estate SA., Vector Group Ltd., Oracle Partners LP, Oracle Institutional Partners, LP., Chung Chia Company Limited, Gold Sino Assets Limited, and Grandtime Associates Limited.
10.12[7]	Stock Purchase Agreement, dated June 10, 2009, by and among OPKO Health, Inc. and Sorrento Therapeutics, Inc.
10.13[8]	Form of Securities Purchase Agreement for Series D Preferred Stock.
10.14[9]*	Form of Restricted Share Award Agreement for Directors.
10.15[9]	Cocrystal Discovery, Inc. Agreements.
10.16[12]	

	Stock Purchase Agreement, dated October 1, 2009, by and among the Laboratoria Volta S.A., Farmacias Ahumada S.A., FASA Chile S.A., OPKO Chile Limitada and Inversones OPKO Limitada, subsidiaries of OPKO Health, Inc.
10.17(11)+	Asset Purchase Agreement, dated October 12, 2009, by and between OPKO Health, Inc. and Schering Corporation.
10.18(11)	Letter Agreement, dated June 29, 2010, by and between OPKO Health, Inc. and Schering Corporation.

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10.19[17]+	Exclusive License Agreement by and between TESARO, Inc. and OPKO Health, Inc. dated December 10, 2010.
10.20[14]	Third Amended and Restated Subordinated Note and Security Agreement, dated February 22, 2011, between OPKO Health, Inc. and The Frost Group, LLC.
10.21[16]+	Asset Purchase Agreement dated September 21, 2011, by and among Optos plc, Optos Inc., OPKO Health, Inc., OPKO Instrumentation, LLC, Ophthalmic Technologies, Inc., and OTI (UK) Limited.
10.22[21]	Form of Note Purchase Agreement, dated as of January 25, 2013, by and among OPKO Health, Inc. and each purchaser a party thereto.
10.23[+]	Development and Commercialization License Agreement by and between OPKO Ireland, Ltd., a subsidiary of OPKO Health, Inc., and Pfizer, Inc. dated December 13, 2014.
21	Subsidiaries of the Company.
23.1	Consent of Ernst & Young LLP.
31.1	Certification by Phillip Frost, Chief Executive Officer, pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities and Exchange Act of 1934 as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for the quarterly period ended December 31, 2014.
31.2	Certification by Adam Logal, Chief Financial Officer, pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities and Exchange Act of 1934 as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for the quarterly period ended December 31, 2014.
32.1	Certification by Phillip Frost, Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 for the quarterly period ended December 31, 2014.
32.2	Certification by Adam Logal, Chief Financial Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 for the quarterly period ended December 31, 2014.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Denotes management contract or compensatory plan or arrangement.

+ Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission.

(1) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on April 2, 2007, and incorporated herein by reference.

(2) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 14, 2007 for the Company's three-month period ended September 30, 2007, and incorporated herein by reference.

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(3) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 31, 2008 and incorporated herein by reference.

(4) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 8, 2008 for the Company's three-month period ended June 30, 2008, and incorporated herein by reference.

(5) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 12, 2008 for the Company's three-month period ended September 30, 2008, and incorporated herein by reference.

(6) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 8, 2009 for the Company's three-month period ended March 31, 2009, and incorporated herein by reference.

(7) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 7, 2009 for the Company's three-month period ended June 30, 2009, and incorporated herein by reference.

(8) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on September 24, 2009, and incorporated herein by reference.

(9) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 9, 2009 for the Company's three-month period ended September 30, 2009, and incorporated herein by reference.

(10) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 10, 2010 for the Company's three-month period ended March 31, 2010, and incorporated herein by reference.

(11) Filed with the Company's Amendment to Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 3, 2011.

(12) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 17, 2010.

(13) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 10, 2011, and incorporated herein by reference.

(14) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 10, 2011 for the Company's three-month period ended March 31, 2011, and incorporated herein by reference.

(15) Filed with the Company's Quarterly Report on Form 10-Q/A filed with the Securities and Exchange Commission on July 5, 2011, and incorporated herein by reference.

(16) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 9, 2011 for the Company's three-month period ended September 30, 2011, and incorporated herein by reference.

(17) Filed with the Company's Annual Report on Form 10-K/A filed with the Securities and Exchange Commission on July 28, 2011.

(18) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 15, 2012.

(19) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 10, 2012 for the Company's three-month period ended March 31, 2012, and incorporated herein by reference.

(20) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 9, 2012 for the Company's three-month period ended September 30, 2012, and incorporated herein by reference.

(21) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on January 29, 2013, and incorporated herein by reference.

(22) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 18, 2013.

(23) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 10, 2013 for the Company's three-month period ended March 31, 2013, and incorporated herein by reference.

(24) Filed with the Company's Schedule 13D filed with the Securities and Exchange Commission on March 22, 2013, and incorporated herein by reference.

(25)

Filed as Annex A to the Company's Preliminary Joint Proxy Statement/Prospectus, Form S-4, with the Securities Exchange Commission on June 27, 2013, as amended, and incorporated herein by reference.

(26) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on February 5, 2013, and incorporated herein by reference.

(27) Filed with the Company's Current Report on Form 8-K filed with the Securities Exchange Commission on August 30, 2013, and incorporated herein by reference.

(28) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 12, 2013 for the Company's three month period ended September 30, 2013, and incorporated herein by reference.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: February 27, 2015

OPKO HEALTH, INC.

By: /s/ Phillip Frost, M.D.
Phillip Frost, M.D.
Chairman of the Board and
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Phillip Frost, M.D. Phillip Frost, M.D.	Chairman of the Board and Chief Executive Officer (Principal Executive Officer)	February 27, 2015
/s/ Jane H. Hsiao, Ph.D., MBA Jane H. Hsiao, Ph.D., MBA	Vice Chairman and Chief Technical Officer	February 27, 2015
/s/ Steven D. Rubin Steven D. Rubin	Director and Executive Vice President – Administration	February 27, 2015
/s/ Adam Logal Adam Logal	Senior Vice President, Chief Financial Officer, Chief Accounting Officer and Treasurer (Principal Financial Officer)	February 27, 2015
/s/ Robert Baron Robert Baron	Director	February 27, 2015
/s/ Thomas E. Beier Thomas E. Beier	Director	February 27, 2015
/s/ Dmitry Kolosov Dmitry Kolosov	Director	February 27, 2015
/s/ Richard A. Lerner, M.D. Richard A. Lerner, M.D.	Director	February 27, 2015
/s/ John A. Paganelli John A. Paganelli	Director	February 27, 2015
/s/ Richard C. Pfenniger, Jr. Richard C. Pfenniger, Jr.	Director	February 27, 2015
/s/ Alice Lin-Tsing Yu, M.D., Ph.D. Alice Lin-Tsing Yu, M.D., Ph.D.	Director	February 27, 2015

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Exhibit Index

Exhibit Number	Description
10.23(+)	Development and Commercialization License Agreement by and between OPKO Ireland, Ltd., a subsidiary of OPKO Health, Inc., and Pfizer, Inc. dated December 13, 2014.
21	Subsidiaries of the Company.
23.1	Consent of Ernst & Young LLP.
31.1	Certification by Phillip Frost, Chief Executive Officer, pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities and Exchange Act of 1934 as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for the quarterly period ended December 31, 2014.
31.2	Certification by Adam Logal, Chief Financial Officer, pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities and Exchange Act of 1934 as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for the quarterly period ended December 31, 2014.
32.1	Certification by Phillip Frost, Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 for the quarterly period ended December 31, 2014.
32.2	Certification by Adam Logal, Chief Financial Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 for the quarterly period ended December 31, 2014.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document