Opko Health, Inc.
Form 424B7
February 05, 2019
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Filed Pursuant to Rule 424(b)(7)
Registration No. 333-229400

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount of Securities to be Registered	Proposed Maximum Offering Price (1)	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee[(1)]
Common Stock, par value $0.01 per share	30,000,000.00	$3.53	$105,900,000.00	$12,835.08

(1) Estimated in accordance with Rule 457(c) promulgated under the Securities Act of 1933, as amended, solely for purposes of calculating the registration fee. The maximum price per security and the maximum aggregate offering price are based on the average of the $3.75 (high) and $3.31 (low) sale price of the Registrant s Common Stock as reported on the Nasdaq Global Select Market on February 1, 2019.

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PROSPECTUS SUPPLEMENT

(TO PROSPECTUS DATED JANUARY 28, 2019)

OPKO Health, Inc.

30,000,000 shares of Common Stock

Up to 30,000,000 shares of our common stock are being offered by the selling stockholders named herein. The selling stockholders will borrow such shares through a lending arrangement from an affiliate of the underwriter in our concurrent offering of $200,000,000 aggregate principal amount of our 4.50% convertible senior notes due 2025 (the convertible notes), not including the underwriter s option to purchase up to an additional $30,000,000 principal amount of the convertible notes from us solely to cover overallotments, if any, which affiliate (the Share Borrower) is borrowing the shares from us. The borrowed shares are newly-issued shares issued in connection with this transaction and will be cancelled or held as treasury shares by us upon the expiration or the early termination of the share lending arrangement described herein.

We expect that the selling stockholders will sell the borrowed shares and use the resulting short position to establish their initial hedge with respect to their investments in our convertible notes, which are being offered in a concurrent offering pursuant to a separate prospectus supplement and accompanying prospectus. The selling stockholders may effect such transactions by selling the borrowed shares at various prices from time to time through the Share Borrower or its affiliates. The selling stockholders will receive all of the net proceeds from the sale of the borrowed shares, and we will not receive any of those proceeds, but we will receive a one-time nominal fee of $0.01 per share for each newly-issued share from the Share Borrower for the use of the borrowed shares.

The borrowed shares may be offered for sale in transactions that may include block sales, sales on the Nasdaq Global Select Market (the Nasdaq), sales in the over-the-counter market, sales pursuant to negotiated transactions or otherwise. See Description of the Share Lending Agreement; Concurrent Offering of Convertible Notes. The delivery of the borrowed shares being offered hereby is conditioned upon the closing of the concurrent offering of the convertible notes.

Our common stock is listed on the Nasdaq under the symbol OPK. The last reported sale price of our common stock on the Nasdaq on February 1, 2019 was $3.59 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page S-15 of this prospectus supplement, as well as the documents we file with the Securities and Exchange Commission (the SEC) that are incorporated by reference herein for more information.

Neither the SEC nor any state securities commission has approved or disapproved the issuance of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

February 4, 2019

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We have not authorized anyone to provide any information or to make any representations other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectuses we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus is an offer to sell only the borrowed shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of the respective dates of such documents.

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ABOUT THIS PROSPECTUS SUPPLEMENT

Unless the context otherwise requires, all references in this prospectus supplement to OPKO, Company, our company, we, us, or our refer to OPKO Health, Inc., a Delaware corporation, including its wholly-owned subsidiaries.

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the SEC using a shelf registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part consists of the accompanying prospectus, which provides more general information, some of which may not apply to this offering. Generally, when we refer only to the prospectus, we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein.

This prospectus supplement and the accompanying prospectus relate to the offering of the borrowed shares. Before buying any borrowed shares offered hereby, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated herein and therein by reference as described under the headings Where You Can Find More Information and Incorporation of Certain Information by Reference. These documents contain important information that you should consider when making your investment decision.

You should rely only on the information contained in or incorporated by reference into this prospectus supplement, the accompanying prospectus and any free writing prospectus authorized by us. To the extent the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus or any document filed prior to the date of this prospectus supplement and incorporated by reference, the information in this prospectus supplement will control. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

The industry and market data and other statistical information contained in the documents we incorporate by reference are based on management s own estimates, independent publications, government publications, reports by market research firms or other published independent sources and, in each case, are believed by management to be reasonable estimates. Although we believe these sources are reliable, we have not independently verified the information.

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PROSPECTUS SUPPLEMENT SUMMARY

The following summary of our business highlights some of the information contained elsewhere in or incorporated by reference into this prospectus supplement or the accompanying prospectus. Because this is only a summary, however, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, which are described under Incorporation of Certain Information by Reference in this prospectus supplement and in the accompanying prospectus. You should also carefully consider the matters discussed in the section in this prospectus supplement entitled Risk Factors and in the accompanying prospectus, in our Annual Report on Form 10-K for the year ended December 31, 2017 and in the other documents incorporated herein by reference.

Our Company

We are a diversified healthcare company that seeks to establish industry-leading positions in large and rapidly growing medical markets. Our diagnostics business includes BioReference Laboratories, the nation s third-largest clinical laboratory with a core genetic testing business and an almost 300-person sales and marketing team to drive growth and leverage new products, including the *4Kscore* prostate cancer diagnostic test and the *Claros 1* in-office immunoassay platform (in development). Our pharmaceutical business features *Rayaldee*, a U.S. Food and Drug Administration (FDA) approved treatment for secondary hyperparathyroidism in adults with stage 3 or 4 chronic kidney disease and vitamin D insufficiency (launched in November 2016), OPK88004, a selective androgen receptor modulator which we have studied for benign prostatic hyperplasia but for which we are exploring other potential indications, and OPK88003, a once or twice weekly oxyntomodulin for type 2 diabetes and obesity which is a clinically advanced drug candidate among the new class of GLP-1 glucagon receptor dual agonists (phase 2b). Our pharmaceutical business also features hGH-CTP, a once-weekly human growth hormone injection (in phase 3 and partnered with Pfizer Inc. (Pfizer)).

We operate established pharmaceutical business operations in Spain, Ireland, Chile and Mexico, which are generating revenue and from which we expect to generate positive cash flow and facilitate future market entry for our products currently in development. We have a development and commercial supply pharmaceutical company, as well as a global supply chain operation and holding company in Ireland, which we expect will play an important role in the development, manufacturing, distribution and approval of a wide variety of drugs with an emphasis on high potency products. We also own a specialty active pharmaceutical ingredients 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.

We are a Delaware corporation. We maintain our principal executive offices at 4400 Biscayne Blvd., Miami, FL 33137. Our telephone number is (305) 575-4100. We maintain a website at *www.opko.com*. The information contained on our website or that can be accessed through our website does not constitute part of this prospectus supplement or the accompanying prospectus.

Current Products and Services and Related Markets

Diagnostics

BioReference Laboratories

Through BioReference, the third largest full service clinical laboratory in the U.S., we offer comprehensive laboratory testing services utilized by healthcare providers in the detection, diagnosis, evaluation, monitoring and

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treatment of diseases, including esoteric testing, molecular diagnostics, anatomical pathology, genetics, women s health and correctional healthcare. We market and sell these services to physician offices, clinics, hospitals, employers and governmental units nationally, with the largest concentration of business in the larger metropolitan areas across New York, New Jersey, Florida, Texas, Maryland, California, Pennsylvania, Delaware, Washington DC, Illinois and Massachusetts.

BioReference has an almost 300-person sales and marketing team and operates a network of approximately 200 patient service centers.

Our BioReference laboratory testing business consists of routine testing and esoteric testing. Routine tests measure various health parameters, such as the functions of the heart, kidney, liver, thyroid and other organs, including such tests as blood cell counts, cholesterol levels, pregnancy, substance abuse and urinalysis. We typically operate 24 hours per day, 365 days per year and perform and report most routine test results within 24 hours.

The esoteric tests we perform require sophisticated equipment and materials, highly skilled personnel and professional attention. Esoteric tests are ordered less frequently than routine tests and typically are priced higher than routine tests. Esoteric tests include tests related to endocrinology, genetics and genomics, immunology, microbiology, HIV tests, molecular diagnostics, next generation sequencing, oncology, serology and toxicology.

Through BioReference, we operate in the following highly specialized laboratory divisions:

BioReference Laboratories. BioReference constitutes our core clinical testing laboratory offering automated, high volume routine testing services, STAT testing, informatics, HIV, Hep C and other molecular tests.

GenPath (Oncology). National oncology presence with expertise in cancer pathology and diagnostics, as well as molecular diagnostics. Core tests include FLOW, IHC, MicroArray, FISH, ISH, Morphology and full-service oncology.

GenPath (Women s Health). Innovative technology platform for sexually transmitted infections has enabled expansion nationally with specimens coming from 41 states, including Image Directed Paps analysis, HPV Plus and STI Testing.

GeneDx. Industry leading national laboratory for testing rare and ultra-rare genetic diseases with international reach, performing testing on specimens from more than 50 countries.

Laboratorio Bueno Salud. National testing laboratory dedicated to serving the Spanish-speaking population in the U.S., where all business is conducted in Spanish including patient and physician interaction.

We have one of the largest marketing staffs of any laboratory in the country with sales and marketing groups dedicated to urology, oncology, women s health, genetic testing and correctional health, as well as cross-over groups selling to large institutions. All of our sales and marketing personnel operate in a dual capacity, as both marketing and client support representatives, which we believe provides better customer service and a strong connection with our customers.

We expect the clinical laboratory testing industry will continue to experience growth in testing volumes due to aging of the population in the U.S., patient awareness of the value of laboratory tests, a decrease in the cost of tests, the development of sophisticated and specialized tests for detection and management of disease, increased recognition of early detection and prevention as a means of reducing healthcare costs and ongoing research and development in genetics and genomics and personalized medicine. Our mission is to be recognized by our clients as the premier provider of clinical laboratory testing, information and related services.

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BioReference provides us with a significant diagnostics commercial infrastructure for marketing and sales that reached almost 11 million patients in 2018. In addition, its large team of managed care experts complement our efforts to ensure that payors recognize the value of our diagnostic and laboratory tests for reimbursement purposes. We continue to leverage the national marketing, sales and distribution resources of BioReference, along with its almost 300-person sales and marketing team, to enhance sales of and reimbursement for our 4Kscore test, a laboratory developed blood test that provides a personalized risk score for aggressive prostate cancer. We plan to continue to leverage the BioReference commercial infrastructure and capabilities, as well as its extensive relationships with payors, to commercialize OPKO s other diagnostic products under development, including the *Claros 1*.

4Kscore Test

We offer the *4Kscore* test through our BioReference laboratory located in Elmwood Park, New Jersey. We began selling the *4Kscore* test in the U.S. in March 2014 and in Europe and Mexico in September 2014 and January 2015, respectively. The *4Kscore* test is a laboratory developed test that 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, 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 a Gleason Score 7 or higher prostate cancer. The four kallikrein panel of biomarkers utilized in the *4Kscore* test is based on decades of research conducted by scientists at Memorial Sloan-Kettering Cancer Center and leading European institutions. Investigators at the Lund University, Sweden, University of Turku, Finland and Memorial Sloan Kettering Cancer Center, New York, have also demonstrated that the *4Kscore* test can risk stratify the 20-year risk for development of prostate metastases and mortality in men who present at age 50 or 60 years old with an elevated PSA.

The *4Kscore* test was developed by OPKO and validated in two prospective, blinded studies of 1,012 and 366 men, respectively. The first study was done in collaboration with 26 urology centers across the U.S. and the second study was conducted at eight VA centers in the U.S. with a predominantly African American cohort. African Americans are 1.7 times more likely to be diagnosed with prostate cancer than Caucasian men and 2.2 times more likely to die from the disease. 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, regardless of race. The full data from the blinded, prospective U.S. clinical validation studies have been published in peer reviewed medical journals.

The clinical data from both studies 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 greater than 0.80 and is significantly higher than previously developed tests. Furthermore, the *4Kscore* test demonstrated excellent risk calibration, indicating the accuracy of the result for an individual patient, both Caucasian and African American. The high value of AUC and the excellent risk calibration make the *4Kscore* test result valuable information for the shared decision-making between the urologist and patient on whether or not to perform a prostate biopsy.

A separate clinical utility study indicated that the *4Kscore* test led to 64.6% fewer biopsies. The study, The *4Kscore*® Test Reduces Prostate Biopsy Rates in Community and Academic Urology Practices , was published in a peer reviewed medical journal. The study, which included 611 patients seen by 35 academic and community urologists across the U.S., evaluated the influence of the *4Kscore* test on urologist- patient decisions about whether to perform a biopsy in men who had an abnormal PSA and or DRE result. Test results for patients were stratified into low risk (< 7.5%), intermediate risk (7.5%-19.9%) and high risk (³20%) for developing aggressive prostate cancer. Nearly half (49.3%) of the men were categorized as low risk; 25.7% and 25.0% fell into the intermediate-risk and high-risk categories, respectively. Notably, the *4Kscore* test results influenced biopsy

decisions in 88.7% of the men. In the three risk groups, a biopsy was avoided in 94.0%, 52.9% and 19.0% of men in the low, intermediate and high-risk categories, respectively.

The *4Kscore* test has been granted a Category I CPT® code by the AMA (CPT Code 81539). A CPT code is used by insurance companies and government payors to describe health care services and procedures. A Category I CPT code is critical to facilitate reimbursement in government programs such as Medicare and Medicaid, as well as private insurance programs.

The National Comprehensive Cancer Network (NCCN) included the *4Kscore* test as a recommended test in their 2015, 2016, 2017 and 2018 Guidelines for Prostate Cancer Early Detection. The panel making this recommendation concluded that the *4Kscore* test is indicated for use prior to a first prostate biopsy, or after a negative biopsy, to assist patients and physicians in further defining the probability of high-grade cancer. In addition, the European Association of Urology (EAU) Prostate Cancer Guidelines Panel included the *4Kscore* test in the 2018 EAU Guidelines for Prostate Cancer, concluding that the *4Kscore*, as a blood test with greater specificity over the PSA test, is indicated for use prior to a first prostate biopsy or after a negative biopsy to assist patients and physicians in further defining the probability of high-grade cancer.

We have and will continue to commit substantial efforts to obtaining broad reimbursement coverage for the *4Kscore* test. We have obtained a positive coverage decision from at least one national private payor and pricing agreements from several regional payors. Novitas Solutions, the local Medicare Administrative Contractor (MAC) for our laboratory in New Jersey, issued a proposed non-coverage policy for the *4Kscore* test in May 2018 subject to a public comment period ending July 5, 2018. We made oral presentations at a Novitas open meeting and submitted substantial evidence and data to address the comments raised in the draft non-coverage determination. In January 2019, Novitas issued a notice of a future non-coverage determination for the *4KScore* test to be effective March 20, 2019. We are evaluating options to appeal the decision and undertake other steps with the Center for Medicare and Medicaid Services (CMS) in an effort to have this determination rescinded or reversed.

Point-of-Care Diagnostics

OPKO Diagnostics, LLC (OPKO Diagnostics), formerly Claros Diagnostics, Inc., has developed a novel diagnostic instrument system to provide rapid, high performance blood test results in the point-of-care setting. The technology only requires a finger stick drop of blood introduced into the test cassette that can then run a quantitative test. The instrument performs the tests on a disposable, one-time usable cassette that is a microfluidics-based diagnostic test system. The credit card-sized test cassette works with a sophisticated desktop analyzer to provide high performance quantitative blood test results within minutes and permits the transition of complex immunoassays from the centralized reference laboratory to the physician s office, hospital nurses station or other decentralized location.

We completed multiple in vitro analytical validation and field use tests for the PSA test in mid-2017 and filed the pre-marketing authorization (PMA) for the Claros Analyzer and Sangia Total PSA Test with the FDA in November 2017. The key clinical study with patients who were suspicious for prostate cancer found that the Sangia Total PSA test improved the sensitivity of a DRE to 91%, detecting 2.9 times the prostate cancers compared to DRE alone. The FDA approved the PMA for the Sangia Total PSA Test using the Claros Analyzer in January 2019. We also intend to commence a clinical trial of a testosterone diagnostic test for our point-of-care system. We expect to fully leverage BioReference s marketing, sales and distribution resources for the launch of the *Claros 1* system and associated diagnostic tests in the U.S.

We are also presently working to add additional tests for our point-of-care system, including parathyroid hormone (PTH) 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.

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Pharmaceutical Business

We currently have one commercial stage pharmaceutical product and several pharmaceutical compounds and technologies in various stages of research and development for a broad range of indications and conditions, including the following:

Renal Products

We launched *Rayaldee*, our lead renal product, in the U.S. market in November 2016. In June 2016, the FDA approved *Rayaldee* extended release capsules for the treatment of secondary hyperparathyroidism (SHPT) in adults with stage 3 or 4 chronic kidney disease (CKD) and vitamin D insufficiency, defined as serum total 25-hydroxyvitamin D levels less than 30 ng/mL. *Rayaldee* is a patented extended release product containing 30 mcg of a prohormone called calcifediol (25-hydroxyvitamin D3).

We have a 79-person highly specialized sales, marketing and market access team dedicated to the launch and commercialization of *Rayaldee* as of December 31, 2018. As compared to the fourth quarter of 2017 and the third quarter of 2018, total *Rayaldee* prescriptions increased approximately 141% and 17%, respectively, in the fourth quarter of 2018. Efforts are underway to obtain broader commercial and Part D insurance coverage for *Rayaldee*. We have already contracted for commercial and Part D coverage for more than seventy percent (70%) of U.S. covered lives as of the end of 2018.

In connection with the launch of *Rayaldee*, we have also engaged in a comprehensive ongoing market education campaign highlighting the unmet need in treating SHPT, including by leveraging key opinion leaders in community outreach programs such as speakers bureaus and patient advocacy programs.

In May 2016, we entered into a collaboration with Vifor Fresenius Medical Care Renal Pharma (VFMCRP) for the development and commercialization of *Rayaldee* in Europe, Canada, Mexico, Australia, South Korea and certain other international markets for the treatment of SHPT in patients with stage 3, 4 or 5 CKD and vitamin D insufficiency. Under the terms of the agreement, OPKO received an upfront payment of $50 million. We also received a $2 million payment triggered by the marketing approval of *Rayaldee* in Canada and will receive up to $230 million in additional regulatory and sales-based milestones. In addition, VFMCRP will pay OPKO tiered, double digit royalties on sales of the product at percentage rates that range from the mid-teens to the mid-twenties or a minimum royalty, whichever is greater, upon commencement of sales of the product. OPKO and VFMCRP are also collaborating to develop and commercialize a new dosage form of *Rayaldee* for the treatment of SHPT in hemodialysis patients. OPKO granted VFMCRP an option to acquire rights to this dosage form for the U.S. market; if exercised, OPKO will receive up to $555 million in additional milestones and double digit royalties.

On October 12, 2017, we entered into a Development and License Agreement (the JT Agreement) with Japan Tobacco Inc. (JT) granting JT the exclusive rights for the development and commercialization of *Rayaldee* in Japan (the JT Territory). The license grant to JT covers the therapeutic and preventative use of the product for (i) SHPT in non-dialysis and dialysis patients with CKD, (ii) rickets, and (iii) osteomalacia, as well as such additional indications as may be added to the scope of the license subject to the terms of the JT Agreement. Under the terms of the JT Agreement, OPKO received an initial upfront payment of $6 million and we received another $6 million milestone payment triggered by the initiation of OPKO s U.S. phase 2 study with *Rayaldee* in dialysis patients. OPKO is also eligible to receive up to an additional aggregate amount of $31 million upon the achievement of certain regulatory and development milestones by JT for *Rayaldee* in the JT Territory, and $75 million upon the achievement of certain sales based milestones by JT in the JT Territory. OPKO will also receive tiered, double digit royalty payments at rates ranging from low double digits to mid-teens on net product sales within the JT Territory. JT will, at its sole cost and

expense, be responsible for performing all development

activities necessary to obtain all regulatory approvals for *Rayaldee* in Japan and for all commercial activities pertaining to *Rayaldee* in Japan, except for certain preclinical expenses which OPKO has agreed to reimburse JT up to a capped amount.

The FDA approval of *Rayaldee* was supported by successful results from two identical randomized, double-blind, placebo-controlled, multi-site phase 3 studies which established the safety and efficacy of *Rayaldee* as a new treatment for SHPT in adults with stage 3 or 4 CKD and vitamin D insufficiency.

Vitamin D insufficiency arises in CKD due to the abnormal upregulation of CYP24A1, an enzyme that destroys vitamin D and its metabolites, and from many other causes as well.

Studies in CKD patients have demonstrated that currently available over-the-counter and prescription vitamin D supplements 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 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 CKD.

The completed phase 3 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 decrease in PTH of at least 30% from pre-treatment baseline during the last six weeks of the 26-week treatment period. A significantly higher response rate was observed with *Rayaldee* compared to placebo treatment in both trials and safety and tolerability data were comparable in both treatment groups. The PTH-lowering response rates with *Rayaldee* were similar in both stage 3 and 4 CKD. Patients completing the two pivotal trials were treated, at their election, for an additional six months with *Rayaldee* during an open-label extension study. Data from the extension study indicated that the PTH lowering response rate steadily increased with duration of *Rayaldee* treatment without deterioration in safety profile.

We also are developing *Rayaldee* for other indications, including for SHPT in patients with vitamin D insufficiency and stage 5 CKD requiring regular hemodialysis. A phase 2 study of a higher dose product commenced in this patient population during the third quarter of 2018. We expect to receive data from the study in the second half of 2020.

In August 2014, we also 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 were receiving anti-resorptive therapy. The study, which has been completed, was designed to evaluate safety, markers of vitamin D and mineral metabolism and tumor progression. We are currently collecting the final data and will shortly complete a final analysis of the study.

We filed an IND for *Rayaldee* in January 2019 for the treatment of SHPT arising from vitamin D insufficiency in patients who have undergone bariatric surgery. We intend to commence a phase 2 study in this population in the first half of 2019.

Our second most advanced renal product, Alpharen (Fermagate Tablets), is a new and potent non-absorbed phosphate binder to treat hyperphosphatemia in stage 5 CKD patients requiring regular hemodialysis. 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 and vascular calcification, both of which drive morbidity and

mortality. The kidneys provide the primary route of excretion for

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excess phosphorus absorbed from ingested food. As kidney function worsens, serum phosphorus levels increase and directly stimulate PTH secretion. Stage 5 CKD patients requiring dialysis must reduce their dietary phosphate intake and usually require regular treatment with orally administered phosphate binding agents to lower serum phosphorus to meet the recommendations of the Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guidelines that elevated serum phosphorus levels should be lowered. 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. A single additional phase 3 clinical trial is required to support marketing approvals for Alpharen in North America and in Europe.

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 global market opportunity. According to the National Kidney Foundation, CKD afflicts over 40 million people in the U.S., including more than 21 million patients with stage 3 or 4 CKD. In stage 5 CKD, kidney function is minimal to absent and most 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 and commercialize *Rayaldee* and Alpharen to constitute part of the foundation for a new and markedly improved standard of care for CKD patients having SHPT and/or hyperphosphatemia.

SARM

Through the acquisition of Transition Therapeutics, a Toronto-based biotechnology company (Transition), we acquired OPK88004, an orally administered selective androgen receptor modulator (SARM) which we have been developing for the treatment of Benign Prostatic Hypertrophy (BPH) and other urologic and metabolic conditions. The selective and antagonistic properties of OPK88004 on the prostate appear to be well suited to potentially reduce prostate hyperplasia and volume, as well as provide anabolic therapeutic benefits such as increased lean body mass and physical function, and decreased fat mass in specific patient populations. We believe that SARMs hold considerable promise as new class of anabolic therapies for a variety of clinical indications, such as frailty and functional limitations associated with aging and chronic illnesses, cancer and osteoporosis.

A phase 2 study of 350 male subjects for another indication showed significantly increased lean body mass and muscle strength and significant fat mass reduction with no change in lower PSA levels. OPK88004 is currently being studied in a phase 2 study in prostate cancer patients who have undergone radical prostatectomy. The main objective of the study is to examine the effect of OPK88004 on sexual function and quality of life issues associated with this patient population. An additional phase 2b study to determine the optimal dose to treat patients with BPH commenced in November 2017 and we completed enrollment and randomized 114 patients in the U.S. in December 2018. The main focus of the study is to determine the optimal dose of OPK88004 that will reduce prostate volume and PSA levels, and increase anabolic effects such as lean body and decreased fat mass in BPH patients. Blinded data from the phase 2b study have shown significant variability in the measurement of prostate volume, rendering the assessment of prostate volume from treatment impractical. Additionally, a small number of subjects have shown increased liver enzymes. We plan to suspend the current trial but continue to analyze data relating to the study s other primary endpoint, the effect of OPK88004 on serum PSA levels, and the secondary endpoints, changes in lean body mass and fat mass. The results of this data analysis are expected in the second quarter of 2019. Additional indications including treatment of symptoms associated with androgen deprivation therapy in prostate cancer patients and low testosterone levels, muscle weakness and general frailty in kidney dialysis patients are being planned.

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Oxyntomodulin

Our internal product development program is also currently focused on developing a once weekly administered oxyntomodulin for type 2 diabetes and obesity. Our most advanced oxyntomodulin product candidate, OPK88003, a once-weekly administered peptide for the treatment of type 2 diabetes and associated obesity, is a dual agonist of the Glucagon-Like Peptide-1 (GLP-1) and glucagon receptors. The receptors play an integral role in regulating appetite, food intake, satiety and energy utilization in the body. Stimulating both of the receptors, OPK88003 has the potential to regulate blood glucose.

OPK88003 has been evaluated in a phase 2 study enrolling 420 type 2 diabetes subjects in a 24-week study consisting of a 12-week randomized blinded stage followed by a 12-week open-label stage. The study included four once-weekly dose arms of OPK88003 (10mg, 15mg, 30mg, 50mg), a placebo arm and an active comparator arm (exenatide extended release 2mg). The study was completed in February 2016.

Subjects receiving the highest dose of OPK88003 peptide once weekly in the study demonstrated significantly superior weight loss compared with currently approved extended release exenatide and placebo after 12 and 24 weeks of treatment. OPK88003 also provided a reduction in HbA1c, a marker of sugar metabolism, similar to exenatide at weeks 12 and 24.

OPK88003 is currently being evaluated in a dose escalation phase 2b trial in 110 type 2 diabetics in which patients are treated with a dose escalation regimen over 3 months intended to optimize dose levels, and increase body weight loss and reduce the adverse event profile, such as nausea and vomiting. Patient enrollment was completed in June 2018. The patients will be treated for a total of 30 weeks in the study. We expect to receive data from the study in the first quarter of 2019. The key primary endpoint will be HbA1c and secondary endpoints such as weight loss, lipid profile and safety will also be analyzed.

We believe oxyntomodulin has potential to be a safe, long term therapy for obesity 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.

Biologics

Our biologics business focuses on developing and commercializing longer-acting proprietary versions of already approved therapeutic proteins. One of our innovative platform technologies uses a short, naturally-occurring amino acid sequence, carboxl terminal peptide (CTP), which 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.

hGH-CTP

Our lead product candidate utilizing CTP, hGH-CTP, is a recombinant human growth hormone product under development for the treatment of growth hormone deficiency (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 (Adult GHD) and in children (Pediatric

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GHD), 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 tiered royalty payments associated with the commercialization of hGH-CTP for Adult GHD with percentage rates ranging from the high teens to mid-twenties. Upon the launch of hGH-CTP for Pediatric GHD in certain major markets, 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, SGA, 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.

Our phase 3 trial of hGH-CTP in pediatric patients was initiated in December 2016 and patient enrollment was completed in August 2018. The global study is a 225-patient study in Pediatric GHD patients designed to evaluate weekly treatment with hGH-CTP versus daily injections of Genotropin. The hGH-CTP is delivered in a pen device in this multi-regional study in over 21 countries. The GHD subjects will be treated weekly for 12 months. We expect to perform topline data analysis from the study in the fourth quarter of 2019. In addition to the phase 3 pediatric study, we have continued without interruption our ongoing phase 2 pediatric open label extension study for hGH-CTP. The phase 2 pediatric patients have been treated with hGH-CTP for over four years, and some patients for over five years. We have switched all of the pediatric patients in this study to the disposable pen device. We have also initiated a 44-patient study in Pediatric GHD patients in Japan which is nearing completion of enrollment. hGH-CTP has orphan drug designation in the U.S. and Europe for both adults and children with GHD.

In December 2016, we announced preliminary topline data from our phase 3, double blind, placebo controlled study of hGH-CTP in adults with GHD. The multinational, multi-center study, which utilized a 2:1 randomization between hGH-CTP and placebo, enrolled 203 subjects, 198 of whom received at least one dose of study treatment. Treatment was administered through a weekly injection. The topline results showed:

The active group had a mean change in trunk fat mass of -0.4kg and placebo group was 0;

There was no statistically significant difference (£ 0.05 (p value)) between the active and placebo group;

97% of hGH-CTP vs 6% of placebo group showed IGF-1 normalization; and

The safety profile of hGH-CTP is consistent with that observed with those treated with daily growth hormone.

Although there was no statistically significant difference between hGH-CTP and placebo on the primary endpoint of change in trunk fat mass from baseline to 26 weeks, after unblinding the study, we identified an

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exceptional value of trunk fat mass reduction in the placebo group that may have affected the primary outcome. We have completed post-hoc sensitivity analyses to evaluate the influence of outliers on the primary endpoint results using multiple statistical approaches. Analyses that excluded outliers showed a statistically significant difference between hGH-CTP and placebo on the change in trunk fat mass. Additional analyses that did not exclude outliers showed mixed results. Following completion of the analyses, OPKO and Pfizer have agreed that OPKO may communicate with the FDA regarding a potential biologics license application (BLA) submission.

Factor VII

In addition to hGH-CTP, we are developing a product to extend 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. 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.

We have conducted a phase 1/2a dose escalation study and a phase 1 dose escalating subcutaneous study in healthy volunteers to determine safety of our long acting Factor VIIa-CTP for the treatment of bleeding episodes in hemophilia A or B patients with inhibitors to Factor VIII or Factor IX. These two studies are completed and data assessment is on-going. Further regulatory and development strategies will be planned.

We believe that the CTP technology may also be broadly applicable to other therapeutic proteins in the market and provide a reduction in the number of injections.

APIs

FineTech Pharmaceutical, Ltd. (FineTech) is our Israeli-based subsidiary 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

OPKO CURNA, LLC (CURNA), previously CURNA Inc., is 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 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.

CURNA has identified and developed potential active 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. A lead compound has been identified for the treatment of Dravet Syndrome. Orphan disease designations are granted by FDA and EMA.

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NK-1 Program

We acquired rolapitant and other neurokinin-1 (NK-1) assets from Merck & Co. In December 2010, we exclusively out-licensed the development, manufacture and commercialization of our lead NK-1 candidate, VARUBI (rolapitant), to TESARO, Inc. (TESARO). VARUBI , a potent and selective competitive antagonist of the NK-1 receptor, had successfully completed clinical testing for prevention of chemotherapy induced nausea and vomiting (CINV) and post-operative induced nausea and vomiting. TESARO s NDA for oral VARUBI was approved by the FDA in September 2015, and in November 2015, TESARO commenced the commercial launch of oral VARUBI in the U.S. TESARO s IV formulation of VARUBI was approved by the FDA in October 2017 and commercial sales commenced in November 2017. In January 2018, the package insert for VARUBI was updated to include mention of new adverse effects, including anaphylaxis, anaphylactic shock and other serious hypersensitivity reactions which were reported following its introduction to the market in November 2017. In late February 2018, TESARO announced it would suspend distribution of VARUBI IV, but would continue to support the oral product.

Under the terms of the license, we received a $6.0 million upfront payment from TESARO and we received $30.0 million of milestone payments upon achievement of certain regulatory and commercial sale milestones. We are eligible to receive additional commercial milestone payments of up to $85.0 million if specified levels of annual net sales are achieved. TESARO is also obligated to pay us tiered royalties on annual net sales achieved in the U.S. and Europe at percentage rates that range from the low double digits to the low twenties, and outside of the U.S. and Europe at low double-digit percentage rates. TESARO assumed responsibility for clinical development and commercialization of licensed products at its expense. Under the agreement, we will continue to receive royalties on a county-by-country and product-by-product basis until the later of the date that all of the patents rights licensed from us and covering rolapitant expire, are invalidated or are not enforceable, and 12 years from the date of the first commercial sale of the product.

If TESARO elects to develop and commercialize VARUBI in Japan through a third-party licensee, TESARO will share equally with us all amounts it receives in connection with such activities, subject to certain exceptions and deductions. The term of the license will remain in force until the expiration of the royalty term unless we terminate the license earlier for TESARO s material breach of the license or bankruptcy. TESARO has a right to terminate the license during the term for any reason on three month s written notice. TESARO assigned its rights and obligations under the agreement to TerSera Therapeutics LLC (TerSera) in June 2018 pursuant to an asset purchase agreement. Under the asset purchase agreement, TerSera is responsible for VARUBI in the United States and Canada and TESARO can continue to commercialize VARUBY® in Europe and the rest of the world though a sublicense with TerSera.

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. During 2015, we acquired EirGen Pharma Ltd. (EirGen), a specialty pharmaceutical company based in Ireland. EirGen is focused on the development and commercial supply of high potency, high barrier to entry, pharmaceutical products. Through its facility in Waterford, Ireland, EirGen currently manufactures high potency pharmaceutical products and exports to over 50 countries. High potency drugs such as those used for cancer chemotherapy are typically unsuitable for manufacture in normal multi-product facilities due to cross contamination risks.

To date, EirGen and its commercial partners have filed several product applications with the FDA in Europe and in Japan. EirGen has a strong research and development portfolio of high barrier to entry drugs and we expect to rapidly expand its drug portfolio. We believe EirGen will play an important role in the development, manufacturing,

distribution and approval of a wide variety of drugs in a variety of dosage forms with an emphasis on high potency products.

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OPKO Health Europe (previously Farmadiet Group Holding, S.L.) operates primarily in Spain and has more than 20 years of experience in the development, manufacture, marketing and sale of pharmaceutical, nutraceutical and veterinary products in Europe.

OPKO Mexico (previously Pharmacos Exakta S.A. de C.V.), is engaged in the manufacture, marketing, sale and distribution of ophthalmic and other pharmaceutical products to private and public customers in Mexico. OPKO Mexico is commercializing food supplements and over the counter products, and manufactures and sells products primarily in the generics market in Mexico, although it also has some proprietary products as well.

OPKO Chile (previously Pharma Genexx, S.A.) markets, sells and distributes pharmaceutical 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. ALS Distribuidora Limitada (ALS) is 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 acquisition of ALS, OPKO acquired all of the product registrations and trademarks previously owned by Arama, as well as the Arama name. We distribute food supplements and over the counter products through Arama.

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.

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The Offering

Issuer	OPKO Health, Inc., a Delaware corporation.
Shares of our common stock outstanding as of December 31, 2018	586,331,543 shares.
Shares of our common stock offered	Up to 30,000,000 borrowed shares.
Shares of our common stock outstanding following this offering	616,331,543 shares (including 30,000,000 shares, the maximum number of shares of our common stock that may be offered hereby), but excluding any shares of our common stock that may be issuable upon conversion of the convertible notes).
Nasdaq symbol for our common stock	Our common stock is listed on the Nasdaq under the symbol OPK.
Use of proceeds	The shares of our common stock offered hereby by the selling stockholders have been borrowed through a share lending arrangement from an affiliate of the underwriter in our concurrent offering of convertible notes, which is borrowing the shares from us. We refer to the entity that is borrowing shares from us as the Share Borrower. The borrowed shares are newly-issued shares issued in connection with this transaction and will be cancelled or held as treasury shares by us upon the expiration or the early termination of the share lending arrangement described herein. We expect that the selling stockholders will sell the borrowed shares and use the resulting short position to establish their initial hedge with respect to their investments in the convertible notes. The selling stockholders may effect such transactions by selling the borrowed shares at various prices from time to time through the Share Borrower or its affiliates. The selling stockholders will receive all of the net proceeds from the sale of the borrowed shares, and we will not receive any of those proceeds, but we will receive a one-time nominal fee of $0.01 per share for each newly-issued share from the Share Borrower for the use of the borrowed shares. See Use of Proceeds , Description of the Share Lending Agreement; Concurrent Offering of Convertible Notes and Plan of Distribution.

Risk factors	You should carefully consider the information set forth in the Risk Factors section of this prospectus supplement and accompanying prospectus as well as the other information included in or incorporated by reference into this prospectus supplement and the accompanying prospectus and similar sections in our filings with the SEC before deciding whether to invest in our common stock.

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Description of Concurrent Offerings	Concurrently with this offering and by means of a separate prospectus supplement and accompanying prospectus, we are offering $200,000,000 aggregate principal amount of convertible notes, not including the underwriter s option to purchase up to an additional $30,000,000 principal amount of the convertible notes from us solely to cover overallotments, if any. See Description of the Share Lending Agreement; Concurrent Offering of Convertible Notes.

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RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should carefully consider the risks described below, as well as the other risks and uncertainties described in our Annual Report on Form 10-K for the year ended December 31, 2017, the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed.

Risks Related to Our Business

We have a history of operating losses and may not become profitable in the near future.

We are not profitable and have incurred losses since our inception. We may not generate substantial 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 the U.S., Chile, Mexico, Israel, Spain and Ireland, and from sale of the *4Kscore* test. We may not successfully leverage the national marketing, sales and distribution resources of BioReference to enhance sales of, and reimbursement for, our *4Kscore* test and our other diagnostic products under development, which would adversely impact our ability to generate substantial revenue from the sale of these products for some time. *Rayaldee* is our only pharmaceutical product that has been approved for marketing, other than those products sold by our Chilean, Mexican, Israeli, Spanish and Irish subsidiaries. We continue to incur substantial 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 may incur losses from our operations for the foreseeable future and these losses could 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, particularly if we are unable to generate profits and cash flow from BioReference and our other commercial businesses. If we are unable to generate profits and cash flow from BioReference and our other commercial businesses, our product candidates fail in clinical trials or do not gain regulatory approval or clearance, or if our approved products and product candidates do not achieve market acceptance, we may never become profitable. In particular, if we are unable to successfully commercialize *Rayaldee*, we may never generate substantial revenues from *Rayaldee* or achieve profitability. In addition, if we are required by the 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 will continue to require additional funding, which may not be available to us on acceptable terms, or at all.

As of September 30, 2018, we had cash and cash equivalents of approximately $43.7 million. We have not generated sustained positive cash flows sufficient to offset our operating and research and development expenses and our primary source of cash has been from the public and private placement of stock, our issuance on January 30, 2013 of $175.0 million in original principal amount of 3.00% Senior Convertible Notes (the 2033 Senior Notes) to qualified institutional buyers and accredited investors in a private placement in reliance on exemptions from registration under the Securities Act of 1933, as amended (the Securities Act), our issuance in February 2018 of a series of 5% Convertible Promissory Notes in the aggregate principal amount of $55.0 million and credit facilities available to us.

On November 8, 2018, we entered into stock purchase agreements with certain investors pursuant to which we agreed to sell to such investors in private placements (the Private Placements) an aggregate of approximately 26.5 million

shares of our common stock (the Shares) at a purchase price of $3.49 per share, which was the closing bid price of our common stock on the Nasdaq Global Select Market on

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such date, for an aggregate purchase price of $92.5 million. In addition, we entered into a credit agreement with an affiliate of our Chairman and Chief Executive Officer, Phillip Frost, M.D., pursuant to which the lender committed to provide us with an unsecured line of credit in the amount of $60 million. Borrowings under the line of credit will bear interest at a rate of 10% per annum and may be repaid and reborrowed at any time. The line of credit matures on November 8, 2023. On February 1, 2019, we borrowed $28.8 million under the line of credit; no amounts were previously outstanding under the line of credit. We intend to use the proceeds of the $28.8 million borrowing to repurchase the 2033 Senior Notes tendered by holders thereof pursuant to such holders option to require us to repurchase such 2033 Senior Notes pursuant to the terms of the indenture governing the 2033 Senior Notes.

We believe that the cash and cash equivalents on hand or available to us from operations or through our lines of credit, together with the proceeds of this offering, are sufficient 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 products and product candidates, the success of our relationships with Pfizer, VFMCRP and JT and the success of our integration of BioReference and other acquisitions, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials and our expanded commercial operations. Our future capital requirements will depend on a number of factors, including the successful commercialization of *Rayaldee*, our relationships with Pfizer, VFMCRP and JT, cash flow generated by BioReference and costs associated with the integration of the BioReference and other acquisitions, 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 products and product candidates. Until we can generate a sufficient amount of product and service revenue to finance our cash requirements for research, dev