UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2020.

OR

☐ **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)

(305) 575-4100

(Registrant's Telephone Number, Including Area Code)

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

Title of Each Class	Trading Symbol	Name of Each Exchange on Which Registered
Common Stock, $.01 par value per share	**OPK**	**NASDAQ Global Select Market**

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 ☒ 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 ☒

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 ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

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

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

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

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: $1,361,925,925.

As of February 8, 2021, the registrant had 670,035,399 shares of its common stock, par value $0.01 per share ("Common Stock") outstanding.

Documents Incorporated by Reference

Portions of the registrant's definitive proxy statement for its 2020 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 (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). 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, including the potential impact of the COVID-19 pandemic on our businesses, operating results, cash flows and/or financial condition. 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:

- our business may be materially adversely affected by the coronavirus (COVID-19) pandemic, including the impact on our sales and operations from continued or increasing infection rates and potential declines in testing needs should infection rates decline;
- we have had a history of losses and may not generate sustained positive cash flow sufficient to fund our operations and research and development programs;
- our need for, and ability to obtain, additional financing when needed on favorable terms, or at all;
- adverse results in material litigation matters or governmental inquiries;
- the risks inherent in developing, obtaining regulatory approvals for and commercializing new, commercially viable and competitive products and treatments;
- our research and development activities may not result in commercially viable products;
- that earlier clinical results of effectiveness and safety may not be reproducible or indicative of future results;
- that we may fail to obtain regulatory approval for hGH-CTP (Somatrogon) or successfully commercialize *Rayaldee* and hGH-CTP (Somatrogon);
- that we may not generate or sustain profits or cash flow from our laboratory operations or substantial revenue from *Rayaldee* and our other pharmaceutical and diagnostic products;
- that currently available over-the-counter and prescription products, as well as products under development by others, may prove to be as or more effective than our products for the indications being studied;
- our ability and our distribution and marketing partners' ability to comply with regulatory requirements regarding the sales, marketing and manufacturing of our products and product candidates and the operation of our laboratories;
- the performance of our third-party distribution partners, licensees and manufacturers over which we have limited control;
- our success is dependent on the involvement and continued efforts of our Chairman and Chief Executive Officer;
- availability of insurance coverage with respect to material litigation matters;
- changes in regulation and policies in the United States ("U.S.") and other countries, including increasing downward pressure on healthcare reimbursement;
- our ability to manage our growth and our expanded operations;
- increased competition, including price competition;
- changing relationships with payors, including the various state and multi-state programs, suppliers and strategic partners;

- efforts by third-party payors to reduce utilization and reimbursement for clinical testing services;
- our ability to maintain reimbursement coverage for our products and services, including *Rayaldee* and the *4Kscore* test;
- failure to timely or accurately bill and collect for our services;
- the information technology systems that we rely on may be subject to unauthorized tampering, cyberattack or other data security or privacy incidents that could impact our billing processes or disrupt our operations;
- failure to obtain and retain new clients and business partners, or a reduction in tests ordered or specimens submitted by existing clients;
- failure to establish, and perform to, appropriate quality standards to assure that the highest level of quality is observed in the performance of our testing services;
- failure to maintain the security of patient-related information;
- our ability to obtain and maintain intellectual property protection for our products;
- our ability to defend our intellectual property rights with respect to our products;
- our ability to operate our business without infringing the intellectual property rights of others;
- our ability to attract and retain key scientific and management personnel;
- the risk that the carrying value of certain assets may exceed the fair value of the assets causing us to impair goodwill or other intangible assets;
- failure to obtain and maintain regulatory approval outside the U.S.; and
- legal, economic, political, regulatory, currency exchange, and other risks associated with international operations.

Risk Factor Summary

Our business is subject to numerous risks and uncertainties, including those described in Item 1A "*Risk Factors*". These risks include, but are not limited to the following:

- Our business has been, and may continue to be, affected by the recent coronavirus disease 2019 (COVID-19) outbreak;
- We have had a history of operating losses and may not be able to sustain profitability in the near future;
- Our research and development activities may not result in commercially viable products;
- Our business is substantially dependent on our ability to generate profits and cash flow from our laboratory operations;
- Failure to timely or accurately bill and collect for our services could have a material adverse effect on our revenues and our business;
- The information technology systems that we rely on may be subject to unauthorized tampering, cyberattack or other data security incidents that could impact our billing processes or disrupt our operations;
- If we are unable to obtain and enforce patent protection for our products, our business could be materially harmed;
- Failure to maintain the security of patient-related information or compliance with security requirements could damage our reputation with customers, cause us to incur substantial additional costs and become subject to litigation;
- Failure to obtain regulatory approval outside the U.S. will prevent us from marketing our products and product candidates abroad;
- We are subject to risks associated with doing business globally; and
- Funding may not be available for us to continue to make acquisitions, investments and strategic alliances in order to grow our business.

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 diversified healthcare company that seeks to establish industry-leading positions in large and rapidly growing medical markets. Our diagnostics business includes BioReference Laboratories, Inc. ("BioReference"), one of the nation's largest full service laboratories 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* test. Our pharmaceutical business features *Rayaldee*, a, U.S. Food and Drug Administration ("FDA") approved treatment for secondary hyperparathyroidism ("SHPT") in adults with stage 3 or 4 chronic kidney disease ("CKD") and vitamin D insufficiency, and a pipeline of products in various stages of development. Our leading product in development is hGH-CTP (Somatrogon), a once-weekly human growth hormone injection which completed a successful phase 3 study in August 2019 and is partnered with Pfizer, Inc. We have submitted the initial Biologics License Application ("BLA") with the FDA for approval of Somatrogon in the United States as well as a New Drug Application (an "NDA") with the Ministry of Health, Labour and Welfare in Japan.

Through BioReference, we provide laboratory testing services, primarily to customers in the larger metropolitan areas in New York, New Jersey, Florida, Texas, Maryland, California, Pennsylvania, Delaware, Washington, DC, Illinois and Massachusetts, as well as to customers in a number of other states. We offer a comprehensive test menu of clinical diagnostics for blood, urine and tissue analysis. This includes hematology, clinical chemistry, immunoassay, infectious disease, serology, hormones, and toxicology assays, as well as Pap smear, anatomic pathology (biopsies) and other types of tissue analysis. We market our laboratory testing services directly to physicians, geneticists, hospitals, clinics, correctional and other health facilities.

We operate established pharmaceutical platforms 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. We also 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.

We have a highly experienced management team. Based on the members' respective 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.

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.

GROWTH STRATEGY

We expect our future growth to come from leveraging our commercial infrastructure, proprietary technology and development strengths.

We launched our first pharmaceutical product, *Rayaldee,* in the U.S. market in the fourth quarter of 2016. We have under development a broad and diversified portfolio of diagnostic tests, small molecules, and biologics targeting a broad range of unmet medical needs. We also operate one of the largest full service laboratories in the U.S. 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:

- continue to enhance our commercialization capability in the U.S. and internationally;
- develop and commercialize *Rayaldee* for new indications, including the treatment of SHPT in patients with vitamin D insufficiency and stage 5 CKD requiring regular hemodialysis;
- obtain requisite regulatory approval and compile clinical data for our most advanced product candidates; and

- expand into other medical markets that provide significant opportunities and that we believe are complementary to and synergistic with our business.

In addition, we expect to leverage the BioReference business and infrastructure to drive rapid and widespread uptake of our diagnostic products, including the *4Kscore* test. Our strategy with respect to BioReference Laboratories is comprised of three pillars: the core business, digital health and strategic ventures. Because of the COVID-19 outbreak, we have added a fourth pillar as the COVID-19 impacted all parts of our organization. In support of this strategy:

- We have made significant investments to rebuild and reconfigure our main laboratory in Elmwood Park, NJ and have also made significant investments in our labs in Melbourne, Florida, Houston, Texas, California and the GeneDx laboratory in Maryland.
- Increased patient access through preferred relationships with payers. We are part of the United Healthcare preferred lab network with access to 45 million patients. We now also have access to Blue Cross/Blue Shield of Texas with another 5.9 million patients and access to Blue Cross/Blue Shield of Alabama with another 2 million patients.
- We intend to continue to expand large-scale COVID-19 screening programs nationwide. We offer customized solutions to a different types of environments and to different types of clients. We are one of the largest providers of these programs, which include both PCR COVID-19 testing and point of care testing, across a variety of touch points, including the travel and leisure industry, airlines, cruise industry and education. BioReference Laboratories has been selected to support the NFL, NBA, NHL, US National Soccer Teams, Winter X Games and the US Golf Association, among other organizations.
- We intend to continue to expand our offerings among our core laboratory service businesses in clinical, genetics, women's health, oncology and urology.
- We intend to initiate digital health advances that aim to increase flexibility and convenience for patients. We recently introduced an important initiative in digital health through the launch of Scarlet™ Health, a fully-integrated digital platform providing mobile phlebotomy and laboratory services to patient's homes, offices and other preferred locations.
- We intend to continue to expand and seek new strategic ventures to provide laboratory services for large health care groups and systems.
- We intend to continue to innovate and expand our offerings at GeneDx. GeneDx is a global leader in genomics, providing testing to patients and their families from more than 55 countries, with an expertise in rare and ultra-rare genetic disorders. In 2020, we launched a new joint venture, called Detect Genomics, in partnership with Pediatrics Medical Group, a leading provider of maternal-fetal and pediatric physician services, to offer rapid exome and genome testing in neonatal intensive care units.

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") and Acuity Pharmaceuticals, Inc. ("Acuity"), both research and development companies. On June 8, 2007, we changed our name to OPKO Health, Inc. Our shares are publicly traded on the NASDAQ Stock Market under the ticker "OPK" and on the Tel Aviv Stock Exchange under the ticker "OPK". Our principal executive offices are located in leased office space in Miami, Florida.

We currently manage our operations in two reportable segments: diagnostics and pharmaceuticals. The pharmaceutical segment consists of the pharmaceutical operations we operate in Chile, Mexico, Ireland, Israel and Spain and our pharmaceutical research and development operations. The diagnostics segment primarily consists of the clinical laboratory operations of BioReference, as well as our point-of-care 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. Refer to Note 18 of our audited consolidated financial statements contained in this Annual Report on Form 10-K for financial information about our segments and geographic areas.

CURRENT PRODUCTS AND SERVICES AND RELATED MARKETS

Diagnostics

BioReference Laboratories

Through BioReference, one of the largest full service laboratories in the United States, we offer comprehensive laboratory testing services utilized by healthcare providers in the detection, diagnosis, evaluation, monitoring, and 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 in New York, New Jersey, Florida, Texas, Maryland, California, Pennsylvania, Delaware, Washington DC, Illinois and Massachusetts. BioReference is in network for over 80% of all U.S. insured lives.

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.

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. Most of our sales personnel operate in a dual capacity, as sales and client support representatives, which we believe provides better customer service and a strong connection with our customers.

We are among the largest providers of large-scale COVID-19 screening programs across the country, with the capacity to run approximately 100,000 PCR tests a day. These large-scale screening programs include both PCR COVID-19 testing and point of care testing. We offer testing across a variety of touch points, including the travel and leisure industry, airlines, cruise industry and education. We have substantial relationships with local and state governments to provide testing services across all 50 states, with substantial service relationships in New York, New Jersey, and Michigan. Through our relationships with CVS and RiteAid, we provide access to testing services for the general public and currently provide testing at more than 700 CVS and RiteAid storefronts. BioReference has also been selected to provide COVID-19 testing for the NFL, NBA, NHL, U.S. National Soccer Teams, Winter X Games and the US Golf Association, among other organizations.

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.

BioReference provides us with a significant diagnostics commercial infrastructure for marketing and sales that reached almost 19 million patients in 2020. 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 leverage the BioReference commercial infrastructure and capabilities, as well as its extensive relationships with payors, to commercialize OPKO's other diagnostic products under development.

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 serum or 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, optional Digital Rectal Exam ("DRE") status (nodule / no nodule), and prior negative biopsy status (yes, prior negative biopsy / no prior biopsy) 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 to 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 the 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 (≥20%) 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 National Comprehensive Cancer Network ("NCCN") has included the*4Kscore* test as a recommended test in its Guidelines for Prostate Cancer Early Detection since 2015. 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 and 2019 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.

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. Effective December 30, 2019, Novitas Solutions ("Novitas"), the local Medicare Administrative Contractor ("MAC") for the *4Kscore* testing laboratory in New Jersey, provided positive coverage through a local coverage determination (an "LCD") with defined coverage criteria. Since that date, *4Kscore* test orders meeting the coverage criteria have been reimbursed by Novitas and Medicare Advantage Health Plans. We have also successfully been reimbursed for *4Kscore* test orders between March and December 2019 through a reconsideration request. In addition, we have obtained a positive coverage decision from at least one national private payor and pricing agreements from several regional payors.

On June 20, 2019, we announced that we submitted a *de novo* request to the FDA seeking regulatory clearance for the *4Kscore* test. Based on feedback from the FDA, the Company withdrew its de novo request and requested a meeting with the FDA to discuss a premarket approval ("PMA") submission for the test. A PMA submission by the Company for the *4Kscore* test was accepted for review by the FDA in January 2020 and is under review.

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 "Claros Analyzer"). The technology requires only a finger stick drop of blood introduced into the test cassette that can then be used to 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 10-15 minutes and permits the transition of 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 PMA for the Claros Analyzer and Sangia Total PSA Test with the FDA in November 2017. The FDA approved the PMA for the Sangia Total PSA Test using the Claros Analyzer in January 2019. The key clinical study with patients suspected of having prostate cancer found that the sensitivity of the Sangia Total PSA Test together with a DRE was improved versus the sensitivity of a DRE alone, to 91%, detecting 2.9 times the prostate cancers compared to a DRE alone. The FDA has categorized Sangia total PSA test as a moderately complex device under Clinical Laboratory Improvement Amendments of 1988 ("CLIA"). The Company is taking steps to obtain a CLIA waiver for the Sangia Total PSA test and the Claros system, which should permit the test to be performed by most medical office personnel with minimal additional training.

We encountered significant technical challenges for a testosterone test using the platform technology and have currently suspended further development of the testosterone test. We are currently evaluating commercialization strategies for the Claros system, as well as potential development of other tests for this platform technology, including markers with high volume assays in therapeutic areas such as nephrology, neurology, cardiology, infection and veterinary markets.

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

Renal Products-Rayaldee

Rayaldee is a patented extended release product containing 30 mcg of a prohormone, called calcifediol (25-hydroxyvitamin D_3), for oral administration. We launched *Rayaldee*, our lead renal product, in the U.S. market in November 2016, following receipt in June 2016 of FDA approval for the treatment of SHPT in adults with stage 3 or 4 CKD and vitamin D insufficiency, defined as serum total 25-hydroxyvitamin D levels less than 30 ng/mL. 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, from obesity 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 and sufficiently raise blood vitamin D prohormone levels to 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 33% and 54% of patients with stage 3 and 4 CKD respectively, and approximately 95% of patients with stage 5 CKD.

We have an approximately 75-person highly specialized sales, marketing and market access team dedicated to the commercialization of *Rayaldee* as of December 31, 2020. In the fourth quarter of 2020, total *Rayaldee* prescriptions decreased approximately 15.9% and 10.2% as compared to the fourth quarter of 2019 and the third quarter of 2020, respectively. Sales of *Rayaldee* have not increased in accordance with its expected growth trajectory as a result of challenges in onboarding new patients due to the COVID-19 pandemic. Efforts are underway to obtain broader commercial and Part D insurance coverage for *Rayaldee.* We have already achieved commercial and Medicare Part D formulary coverage for more than 82.3% of U.S. covered lives as of the end of 2020.

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.

Effective May 5, 2020, we entered into an amendment to the VFMCRP Agreement (the "VFMCRP Amendment"), pursuant to which the parties agreed to exclude Mexico, South Korea, the Middle East and all of the countries of Africa from the VFMCRP Territory. In addition, the parties agreed to certain amendments to the milestone structure and to reduce minimum royalties payable. As revised, the Company has received a $3 million payment triggered by the first marketing approval of *Rayaldee* in Europe and is eligible to receive up to an additional $17 million in regulatory milestones and $210 million in milestone payments tied to launch, pricing and sales of *Rayaldee*, and tiered, double-digit royalties.

OPKO and VFMCRP are also collaborating to develop and commercialize a new higher strength dosage form of *Rayaldee* for the treatment of SHPT in hemodialysis patients. A phase 2 study in this population commenced in the third quarter of 2018 and we expect to report topline data in the first half of 2020. OPKO granted VFMCRP an option to acquire rights to this dosage form for the U.S. market; if exercised, OPKO may receive up to $555 million in additional milestones and tiered, double digit royalties.

VFMCRP filed Marketing Authorization Application with a number of European countries, and VFMCRP has received regulatory approvals from eleven European countries to date and is preparing for product launches later in 2021.

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 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.

In October 2020, we commenced a placebo controlled Phase 2 trial with *Rayaldee* as a treatment for mild-to-moderate COVID-19. The trial is expected to enroll approximately 160 subjects, some of whom may have stage 3 or 4 CKD which may put them at higher risk for developing more severe illness due to the COVID-19 infection.

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. Plans to commence a phase 2 study in this population have been postponed from late 2020 to redirect internal resources to the ongoing conduct of the phase 2 trial in patients with COVID-19.

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 subsequently complete a final analysis of the study.

We have also completed a Phase 4 clinical trial comparing *Rayaldee* with three common treatment regimens for SHPT in adults with stage 3 or stage 4 CKD and vitamin D insufficiency. Preliminary results indicate that a daily dose of 60 micrograms of *Rayaldee* is the only treatment that reliably and sufficiently raises serum total 25-hydroxyvitamin D to effectively suppress elevated plasma parathyroid hormone levels in CKD patients. We presented interim results in an abstract titled "Comparison of Extended-Release Calcifediol (ERC), Immediate-Release Calcifediol, Cholecalciferol, and Paricalcitol for Treating Secondary Hyperparathyroidism (SHPT) in CKD" at the American Society of Nephrology's Kidney Week Annual Meeting in October 2020. We anticipate presenting the final data at an upcoming scientific meeting.

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. We intend to develop and commercialize *Rayaldee* to constitute part of the foundation for a new and markedly improved standard of care for CKD patients having SHPT and/or hyperphosphatemia.

Renal Products-Other

Another renal product in our development pipeline, *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, contributes to soft tissue mineralization, affects approximately 90% of dialysis patients and is tightly linked to the progression of SHPT and vascular calcification, both of which drive morbidity and mortality. An additional phase 3 clinical trial is required to support marketing approvals for Alpharen in North America and in Europe, and the Company is seeking potential partners to participate in this trial.

SARM

Through the acquisition of Transition Therapeutics, a Toronto-based biotechnology company ("Transition"), we acquired OPK88004, an orally administered selective androgen receptor modulator ("SARM"). 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 a 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 or lowering of 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 Benign Prostatic Hypertrophy ("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 was 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. As previously reported, 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 suspended the 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. 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 evaluated.

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.

We have evaluated OPK88003 in a dose escalation phase 2b trial in 110 type 2 diabetics where patients have been 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. The patients were treated for a total of 30 weeks in the study. In March 2019, we announced positive topline results from that phase 2b trial, which demonstrated that OPK88003 met the primary objective with a statistically significant lowering of hemoglobin A1c (HbA1c) after 30 weeks of treatment versus placebo as well as an important secondary endpoint, statistically significant weight loss versus placebo. The safety profile was similar to that expected for the incretin class of drugs, with GI side effects such as nausea, vomiting and diarrhea mostly mild and occurring during the dose-escalation phase.

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. In addition to diabetes and obesity, we are also considering development of this product candidate for additional indications, including treatment of non-alcoholic fatty liver disease and non-alcoholic steatohepatits.

Biologics-General

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 (Somatrogon)

Our lead product candidate utilizing CTP, hGH-CTP (Somatrogon), 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 (the “Pfizer Transaction”) for the development and commercialization of hGH-CTP for the treatment of GHD in adults (“Adult GHD”) and in children (“Pediatric GHD”), as well as for the treatment of growth failure in children born small for gestational age (“SGA”). In connection with the Pfizer Transaction, we granted Pfizer an exclusive license to commercialize hGH-CTP worldwide, and we received non-refundable and non-creditable upfront payments aggregating $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®.

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 was completed in August 2019. The global study was a 224-patient study in Pediatric GHD patients designed to evaluate weekly treatment with hGH-CTP versus daily injections of Genotropin. hGH-CTP is delivered in a pen device in this multi-regional study in over 21 countries. The GHD subjects were treated weekly for 12 months. On October 21, 2019, we and Pfizer announced that the global phase 3 trial met its primary endpoint of non-inferiority to daily Genotropin® (somatropin) for injection, as measured by annual height velocity ("HV") at 12 months. Results from this study demonstrated that treatment with hGH-CTP dosed once-weekly in pre-pubertal children with GHD was non-inferior to Genotropin® (somatropin) dosed once-daily with respect to HV at 12 months of treatment (the primary endpoint); the least square mean was higher in the hGH-CTP group (10.12 cm/year) than in the Genotropin® (somatropin) group (9.78 cm/year); the treatment difference (hGH-CTP—Genotropin® (somatropin)) in HV (cm/year) was 0.33 with a two-sided 95% confidence interval of the difference of (-0.39, 1.05). In addition, change in height standard deviation scores at six and 12 months, key secondary endpoints, were higher in the hGH-CTP dosed once-weekly cohort in comparison to the Genotropin® (somatropin) dosed once-daily cohort. hGH-CTP was generally well tolerated in this study and comparable to that of Genotropin® (somatropin) dosed once-daily with respect to the types, numbers and severity of the adverse events observed between the treatment arms.

We believe hGH-CTP represents a significant advancement in the treatment of children with GHD compared to the current standard of one injection per day that could enhance a patient's adherence to treatment and quality of life. Pfizer submitted a Biologics License Application ("BLA") for hGH-CTP dosed once-weekly in pre-pubertal children with GHD in October 2020. The FDA accepted the BLA for review and the target Prescription Drug User Fee Act (PDUFA) action date for a decision by the FDA is in October 2021.

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. Most of the phase 2 pediatric patients have been treated with hGH-CTP for more than six years, and some patients for more than seven years. We have switched all of the pediatric patients in this study to the disposable pen device. A 44-patient Phase 3 study in Pediatric GHD patients in Japan was completedin the first quarter of 2020. The Japan Phase 3 clinical trial met its primary and secondary objectives, and demonstrated that the efficacy and safety of hGH-CTP administered weekly was comparable to Genotropin® as measured by annual height velocity after 12 months of treatment in pre-pubertal children with GHD. The findings were consistent with the results previously reported in the Phase 3 global study. The least squared means for the annual height velocity was higher in the Somatrogon group (9.65 cm/year) than in the Genotropin group (7.87 cm/year). Pfizer submitted a New Drug Application to the Ministry of Health, Labour and Welfare in Japan for Somatrogon in January 2021. The submission to EMA is expected to occur in the first half of 2021. Somatrogon (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 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. Further, significant changes were observed with hGH-CTP treatment in secondary endpoints such as lean body mass and compared to placebo. We believe there is a path for submission of a BLA with respect to hGH-CTP for adults with GHD on the basis that the FDA may assess the totality of the data, including all relevant efficacy and safety data in adult and pediatric patients. We plan to continue to assess with Pfizer the regulatory strategy for the adult indication going forward, including the timing of a possible submission.

Factor VIIa-CTP

In addition to hGH-CTP, we have a product candidate to extend the duration of the biological activity of Factor VIIa (hemophilia) using our 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. We have completed a phase 1 single dose subcutaneously administered Factor VIIa-CTP study in healthy volunteers and a phase 2a single dose trial in Hemophilia A patients. Factor VIIa-CTP exhibited a positive safety profile in both hemophiliac patients and healthy subjects following a single IV or subcutaneous injection respectively. Pharmacodynamic assessment of coagulation markers demonstrated pharmacological activity of Factor VIIa-CTP with an extended response. We will need to conduct additional toxicity studies before we are in a position to present a clinical study plan.

Early Stage Biologics Pipeline

In addition to hGH-CTP and Factor VIIa-CTP, 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 required for treatment. We are currently engaged in research and development efforts to use the CTP technology for development of a long-acting CTP-IGF-1 for the Treatment of Severe Primary IGF-1 Deficiency.

Apart from development efforts using the CTP platform, we are also focused on development of a once weekly GLP-2 agonist for treatment of Small Bowel Syndrome and other potential indications.

APIs

FineTech Pharmaceutical, Ltd. (“FineTech”), is our Israeli-based subsidiary that develops and produces high value, high potency specialty APIs. FineTech currently manufactures commercial APIs for sale or license to pharmaceutical companies in Latin America, 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’s platform technology utilizes a short, single strand oligonucleotide to increase production of endogenous protein 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 have filed an investigational new drug application, or IND, for a lead compound to treat Dravet Syndrome. Further preclinical work has been requested by the FDA prior to initiation of a first clinical study. Orphan disease designations have been granted by FDA and EMA.

Commercial Operations

We may 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 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.

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.

RESEARCH AND DEVELOPMENT EXPENSES

During the years ended December 31, 2020, 2019, and 2018, we incurred $75.3 million, $117.9 million, and $125.6 million, respectively, of research and development expenses related to our various product candidates. During the years ended December 31, 2020, 2019, and 2018, our research and development expenses primarily consisted of hGH-CTP and *Rayaldee* development programs.

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.

We own or license-in thousands of U.S. and foreign patents and applications for our products, product candidates and our outlicensed product candidates. These patents cover pharmaceuticals, diagnostics and other products and their uses, pharmaceutical and diagnostic compositions and formulations and product manufacturing processes. Our patents are filed in various locations worldwide as is appropriate to the particular patent and its use.

Rayaldee

We have multiple U.S. patent families relating to *Rayaldee.* These patents are also filed in multiple countries worldwide. One patent family claims a sustained release oral dosage formulation and a method of treating 25-hydroxyvitamin D insufficiency or deficiency and will not expire until at least February 2027. A second patent family claims a method of administering 25-hydroxyvitamin D_3 by controlled release, a formulation for controlled release of a vitamin D compound, a controlled release oral dosage formulation of a vitamin D compound and a method of treatment, and will not expire until at least April 2028. We also have additional patents and patent applications pending relating to the sustained release formulation and its use which will expire in 2034. The patents issued in the U.S. covering *Rayaldee* are listed in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. OPKO and/or its affiliates have entered into two exclusive license agreements with respect to *Rayaldee* patents in certain territories outside of North America with VFMCRP (Europe and many other countries throughout the rest of the world) and JT (Japan). We intend to seek patent term extensions in those countries for which such protection is potentially available. We also continue to file and seek patent protection on various uses of extended release dosage forms of 25-hydroxyvitamin D3 and new formulations of this drug.

hGH-CTP (somatrogon)

The hGH-CTP line of patents, which is exclusively licensed to Pfizer, includes multiple U.S. patent families that cover modified human grown hormone (somatrogon), uses of somatrogon in adult and pediatric patient populations, and methods of making somatrogon. Equivalent patents have also been filed in multiple countries around the world. One patent family covers certain CTP modified hGH polypeptides relating to growth hormones and their method of use and expires in February of 2027 (with the exception of two U.S. patents, namely US 8304386 and US 8097435, which expire in January 2028 and April 2027, respectively, due to Patent Term Adjustment for each). Additional U.S. patent applications are pending which cover somatrogon formulations, methods of manufacture and pediatric dosing regimens and, if granted, would expire in 2033. Equivalent patents are granted in Europe and Japan and which expire in 2032 and 2034. A subset of cases in the patent estate covers cytokine-based polypeptides relating to human growth hormone treatment and will expire in February 2027 (in the U.S., these cases include registered patents 8,048,849; 8,426,166; 8,999,670; and 9,896,494, and no Patent Term Adjustment was issued). Multiple other U.S. patents cover somatrogon and its uses or methods of making including U.S. Pat. Nos. 7,553,941; 8,450,269; 8,946,155; and 10,351,615, where no Patent Term Adjustment was awarded by the USPTO. The equivalent foreign patents and applications are granted or pending in several major market countries and regions. In addition to the CTP patents and applications licensed to Pfizer, OPKO has multiple patent families covering similar biologicals with patents and applications pending in the U.S. and internationally. Patent term extensions will be sought in those countries where somatrogon is approved.

OPK88003 and OPK88004

In 2016, we acquired Transition which is developing multiple drug candidates that include OPK88003 (a long acting oxyntomodulin) and OPK88004 (SARM), each of which are licensed from Eli Lilly and have granted patents worldwide covering the compounds and their use in their respective indications. U.S. Pat. No. 8367607 covers OPK88003 and expires in December 2030, without extension. OPKO has also filed a formulation patent on a long acting oxyntomodulin formulation. U.S. Pat. No. 7968587 covers OPK88004 (SARM) and expires, without extension, in November 2027. In addition to the molecule patent covering the selective androgen receptor modulator, Transition Therapeutics exclusively licensed a method of use patent family covering its use in treating androgen deprivation therapy associated symptoms. These patents expire in 2035. OPKO has also filed additional patent applications on expanded uses of OPK88004. In addition, Transition and its affiliates have patented compounds (scyllo-inositol) for the treatment of Alzheimer's disease. The patents are pending or granted in many countries of the world. OPKO and/or its affiliates or licensees will seek all available patent term extensions for our product candidates and products.

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.

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 October 2017, we entered into a license and development agreement with JT for the development and commercialization of *Rayaldee* in Japan for the treatment of SHPT in non-dialysis and dialysis patients with CKD. In May 2016, we entered into a license and collaboration with 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 CKD and vitamin D insufficiency, which was amended in May 2020 to exclude Mexico, South Korea, the Middle East and all of the countries of Africa from the VFMCRP Territory. In December 2014, we entered into the Pfizer Transaction 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 President and Fellows of Harvard College, Academia Sinica, The Scripps Research Institute, TESARO, INEOS Healthcare, and Arctic Partners, among others.

COMPETITION

The pharmaceutical and diagnostic testing 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.

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 are or intend to commercialize ourselves and through our partners. Competitors to our diagnostics business 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 and diagnostics industry include industry consolidation, product quality and price, product technology, reputation, customer service, and access to technical information.

With regard to our pharmaceutical products, *Rayaldee's* competition includes, among other products, activated (1-alpha-hydroxylated) vitamin D analogs such as calcitriol, doxercalciferol, and paricalcitol, and vitamin D supplements such as ergocalciferol and cholecalciferol. Although we believe that *Rayaldee* offers substantial benefits over these products, *Rayaldee* may be competing with these and other lower priced products and products which are marketed by larger pharmaceutical companies with substantially greater resources.

We are aware of a number of pharmaceutical and biopharmaceutical companies that have commenced clinical studies of products or have successfully commercialized products addressing areas that we are targeting with our long acting hGH-CTP. For example, several companies are developing sustained release or long-acting products for the treatment of growth hormone deficiency (GHD), and a number of companies currently market generic daily human growth hormone products for GHD.

In our clinical laboratory operations, we compete with three types of providers in a highly fragmented and competitive industry: hospital laboratories, physician-office laboratories and other independent clinical laboratories. Our major competitors in the New York metropolitan area are two of the largest national laboratories, Quest Diagnostics and Laboratory Corporation of America. Although we are much smaller than these national laboratories, we believe that we compete successfully with them in our region due to our innovative testing services and our level of service. We believe our responses to medical consultation are faster and more personalized than those of the national laboratories. Our client service staff deals only with basic technical questions and those that have medical or scientific significance are referred directly to our senior scientists and medical staff.

We are commercializing our *4Kscore* product in the U.S., Europe and Mexico in a laboratory setting and seek to capitalize on commercialization opportunities for our proprietary diagnostic point-of-care system by transitioning laboratory-based tests, including PSA and other tests to our point-of-care system. We expect to leverage BioReference's national marketing, sales and distribution resources, along with its almost 300-person sales and marketing team to support commercialization of the *4Kscore* and other diagnostic products. Competitors to our diagnostics business are many and include major diagnostic companies, molecular diagnostic firms, universities, and research institutions.

Pricing and reimbursement coverage positions could substantially impact the competitiveness of the *4Kscore* test and our other diagnostic products. 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;
- 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 Civil Monetary Penalty Law (including the beneficiary inducement prohibition) ("CMP"), 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, as well as the performance of clinical testing services, 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.

Clinical Laboratory Operations

Our clinical laboratory operations are subject to 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 CMS under the Federal Clinical Laboratory Improvement Amendments ("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 New York, California, Maryland, Pennsylvania, and Rhode Island, 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.

Our clinical laboratory operations are subject to complex laws, regulations and licensure requirements relating to billing and payment for laboratory services, sales and marketing interactions with ordering physicians and other health care providers, security and confidentiality of health information, and environmental and occupational safety, among others. Changes in regulations often increase the cost of testing or processing claims. Also, these laws may be interpreted or applied by a prosecutorial, regulatory or judicial authority in a manner that could require us to make changes in our operations, including in our pricing, billing and/or marketing practices in a manner that could adversely affect operations.

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, failure to meet anticipated clinical success, patient safety concerns, 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- and are sometimes required - after approval to gain additional experience from the treatment of patients in the intended therapeutic indication. There are also certain situations when drugs and biologics are eligible for one of FDA's expedited approval programs, designed to shorten review and development time.

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 Biologics License Application (BLA) or an NDA is submitted to the FDA for its review. Since the early 1990s, the FDA has managed a user fee program whereby sponsors of drug applications pay a fee to the agency and the agency commits to meeting a series of performance goals designed to reduce drug review times. 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 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.

In addition to clinical trial rules, FDA imposes other requirements on applicants including obligations related to Good Manufacturing Practices (GMPs), proper labeling, and other issues related to manufacturing and marketing a drug.

Other than *Rayaldee*, 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

Medical devices are subject to varying levels of premarket regulatory control, the most comprehensive of which requires human clinical trials be conducted before a device receives approval for commercial distribution. The FDA classifies medical devices into one of three classes based upon their risk profile (both to the patient and provider): Class I devices are relatively

simple “low risk” technologies, and can be manufactured and distributed with general controls without a premarket clearance or approval from the FDA; Class II devices are somewhat more complex “moderate risk” devices, and require greater scrutiny from the agency, requiring a premarket clearance from the FDA before market entry; Class III devices are “high risk” technologies inserted or implanted in the body, intended to treat life sustaining functions. These Class III technologies require a premarket approval from the FDA before market entry.

In the U.S., a company generally can obtain permission to distribute a new device in one of two ways. The first applies to a Class II 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. To obtain FDA permission to distribute the device, a company generally must submit a section 510(k) premarket notification, 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.

In December of 2016, Congress enacted the 21st Century Cures Act (P.L. 114-255) which contained provisions establishing a new Breakthrough Device pathway to allow faster patient access to devices and breakthrough technologies that provide for more effective treatment or diagnosis for life-threatening or irreversibly debilitating diseases, for which no approved or cleared treatment exists or that offer significant advantages over existing approved or cleared alternatives. FDA has just begun to implement this program and it is not clear if any of our products would be eligible.

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 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, since 2012, the FDA has collected 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 approved PMA supplement or a 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

Certain of our diagnostic products in development are subject to regulation by the FDA and similar international health authorities. For these products, 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, it 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 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.

However, the FDA indicated in November 2016 that it would delay implementation of the Framework Guidance and the Notification Guidance, and seek additional input from industry. In addition, on January 13, 2017, the FDA published a synthesis of feedback on the Framework Guidance and Notification Guidance titled, Discussion Paper on Laboratory Developed Tests (the "Discussion Paper"). The Discussion Paper provided notice that the FDA would not issue a final guidance on the oversight of LDTs to allow for further public discussion on appropriate oversight approach, and to give congressional authorizing committees the opportunity to develop a legislative solution.

If finalized in the October 2014 format, the Framework Guidance and the Notification Guidance may have a materially adverse effect 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 regulatory situation remains fluid. The FDA has indicated that it will continue dialogue with the industry, and the timeline and process for finalizing the draft guidance documents is unknown. To date, the FDA has not issued any further guidance to the laboratory community at large (although it does from time to time issue warning letters to individual laboratories), nor has Congress enacted any specific legislative solution. We will continue to monitor changes to all domestic and international LDT regulatory policy so as to ensure compliance with the current regulatory scheme.

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 drug or device 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 payors 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 payors, such as the government or private insurance plans. Third party payors 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 are established by calculating a weighted mean of private payor rates with new rates. Effective January 1, 2018, clinical laboratory fee schedule rates were based on weighted median private payor rates as required by PAMA. 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.

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.

Additionally, as we operate in Europe, we may be subject to laws governing the collection, use, disclosure and transmission of personal and/or patient information. In December 2015, the European Union approved a General Data Protection Regulation ("GDPR") to replace the current data protection directive, Directive 95/46/EC, which took effect May 25, 2018. The GDPR governs the use and transfer of personal data and imposes enhanced penalties for noncompliance. We have made, and will continue to make, certain adjustments to our operations so as to comply with the GDPR.

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 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 ("Affordable Care Act"), 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, the beneficiary inducement prohibition of the federal Civil Monetary Penalty 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. On December 7, 2016, the OIG released amendments to the CMP. Some of the amendments may impact our business, such as allowing certain remuneration to financially needy individuals. 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.

Open Payments Program

With the launch of *Rayaldee*, part of our business is now subject to the federal Physician Payments Sunshine Act under the Affordable Care Act, and its implementing regulations, which is implemented though the physicians Open Payments Program (the "Open Payments Program"). The Open Payments Program requires manufacturers of drugs, devices, biological and medical supplies covered by Medicare, Medicaid or the Children's Health Insurance Program, to report information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals. Manufacturers must also report, on an annual basis, certain ownership and investment interests held by physicians and their immediate family members and payments or other "transfers of value" made to such physician owners. A failure to report each payment, other transfer of value, or ownership/investment interest in a timely, accurate, and complete manner may result in civil monetary penalties of up to $150,000 annually. Further, the "knowing" failure to report each payment, other transfer of value, or ownership/investment interest may result in a one million dollar annual penalty. Several other states and a number of countries worldwide have adopted or are considering the adoption of similar transparency laws. Any failure by us to implement proper procedures to track and report on a timely basis transfers of value to physicians and teaching hospitals could result in substantial penalties.

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.

MANUFACTURING AND QUALITY

Our current pharmaceutical manufacturing facilities are located in Waterford, Ireland, Guadalajara, Mexico, Nesher, Israel, and Banyoles, Spain. In addition to such 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 continue 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

Our diagnostics business includes BioReference's almost 300-person sales and marketing team in the U.S. to drive growth and leverage new products, including the *4Kscore* prostate cancer test. We have a highly specialized, field based 75-person sales and marketing team in the United States dedicated to the launch and commercialization of *Rayaldee.* We also have limited sales and marketing personnel in Ireland, Chile, Spain, Mexico and Israel.

HUMAN CAPITAL RESOURCES

Employees and Labor Relations

As of December 31, 2020, we had 5,269 full-time employees worldwide. With the exception of the employees of one of our subsidiaries, OPKO Spain, based in one of our factories in Spain, none of our employees are represented by a collective bargaining agreement. Overall, we consider our employee relations to be good.

Health and Safety

As a company in the healthcare industry, employee safety is a key focus of our leadership, communications, and training. We are required to comply with the College of American Pathologists and Clinical Laboratory Improvement Amendments laboratory safety requirements in addition to OSHA regulations. With a clear leader in our EHS Manager, direction, standards of practice, training and auditing are consolidated and then disseminated to our managers, supervisors and all employees. We continually align our health and safety goals with those prescribed by applicable regulatory agencies and balance these goals with the needs of our employees. During the COVID-19 pandemic, we transitioned non-essential workers from the office to working from home, and we optimized our essential worker stations in our laboratories and other key process areas to provide for appropriate sanitation, social distancing and other appropriate measures to address the risks of the pandemic. Using guidance provided by the CDC and OSHA among other agencies, we worked to ensure proper personal protective equipment, spacing, workstation design and information support were available to our essential employees who continued working in our offices and facilities during the pandemic.

Competitive Pay and Benefits

We are committed to fair pay and we offer competitive medical benefits to all of our employees. Our U.S. health benefits package is above the competitive range for similar companies in our comparative industries and is one of the key tools we use for recruitment.

Inclusion and Diversity

We recognize the importance of and value diversity and inclusion in our workplace. As such, we have celebrated our diversity through employee and social media announcements in conjunction with company newsletters and employee events. We welcome discussions about our differences, embracing them and learning from them to move forward as a stronger, more productive organization. These differences are not limited to ethnicity or religion, but also in the way we process information

and communicate with our colleagues. We are in a unique position where our workforce is already quite diverse and according to feedback from employee surveys, there is great pride and respect shared among our teams.

In addition, one of our strategic business goals is to recognize and serve diverse communities. Through BioReference, we work closely with clients in these communities by offering excellent customer service and patient care.

Talent Development

We recognize it is important that our employees are able to develop and grow their careers. We recently hired a Head of Learning and Training to enhance employee training and development as well as to ensure compliance while working in a collaborative environment. Our talent acquisition team is undergoing a transformation that is changing recruitment strategies to source from more diverse channels, which we anticipate will lead to more candidate hiring options, enhance our recruitment platform and eventually strengthen employee retention.

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 are required to file annual, quarterly and current reports, proxy statements and other information with the SEC. Information that we file with the SEC is available at the SEC's web-site at www.sec.gov. We also 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. The information on our website is not, and shall not be deemed to be, a part hereof or incorporated into this or any of our other filings with the SEC.

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

Our business has been, and may continue to be, affected by the coronavirus disease 2019 (COVID-19) outbreak.

The outbreak of the coronavirus disease 2019 (COVID-19) has evolved into a global pandemic, significantly affecting the U.S. and most countries around the world. The extent to which this coronavirus impacts our business and operating results will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning the virus, including variants of the virus, and the actions to contain the spread of or to detect, prevent, or treat COVID-19, among others.

As a result of the demand for COVID-19 testing, the Company's overall testing volume has increased significantly, which has positively impacted its operations. Simultaneously, however, demand for tests that comprise the Company's core testing business has declined. Should the demand for COVID-19 PCR testing decline, whether from the introduction of new technologies, vaccines or therapies or a reduction in infection rates, our business, including our sales and operations, could be materially adversely affected. Because the demand and duration of the need for COVID-19 testing are uncertain, the Company could experience significant volatility in its results of operations if the demand for testing declines and such demand is not offset by an increase in demand for the services provided by the Company's core testing business.

We may also experience supply chain disruptions, including shortages, delays and price increases in testing equipment and supplies as a result of global disruptions in healthcare markets, which could materially adversely impact our business. It is also possible that the Company will experience an adverse impact on cash collections as a result of the COVID-19 pandemic.

Governments have implemented travel restrictions and quarantine policies which may have a material adverse economic effect on our business. Such restrictions may present challenges in connection with our laboratory business, our ability to

successfully commercialize *Rayaldee*, our ability to manufacture pharmaceutical products in Ireland, Mexico, Spain, Chile and Israel, and our ability to continue clinical development of our product candidates. Further, if the spread of the coronavirus pandemic continues and our operations are adversely impacted, our ability to meet performance obligations under contracts may be impacted.

COVID-19 could also disrupt our operations due to absenteeism by infected or ill members of management or other employees, or absenteeism by members of management and other employees who elect not to come to work due to the illness affecting others in our office or laboratory facilities, or due to quarantines.

The regulatory framework governing laboratories, diagnostic and pharmaceutical companies may be affected as governmental authorities divert resources to respond to the COVID-19 outbreak, which may have an unanticipated and unforeseen impact on our operations. It is possible that the timing of regulatory submissions and approvals for our products, including hGH-CTP, will be adversely impacted or delayed. With respect to our ongoing and planned clinical trials, restrictions and efforts to avoid further spread of COVID-19 may present challenges to the conduct of these trials consistent with normally applicable approaches and good clinical practice standards, and although regulators including the FDA have offered guidance applicable during the COVID-19 pandemic allowing for flexibility of standards in certain areas and alternate methods of meeting trial oversight obligations (for example, via remote monitoring), the potential impact of these challenges cannot be fully predicted at this time.

We have had a history of operating losses and may not be able to sustain profitability in the near future.

BioReference's COVID-19 testing volume has positively impacted our profitability, but we had, until recently, incurred losses since our inception. We may not continue to generate substantial revenue from COVID-19 testing as vaccine use is adopted and infection rates decline, unless such decline is offset by significant revenue generation from our other income streams. We have historically generated only limited revenue from operations and we may not generate substantial revenue from the sale of proprietary pharmaceutical products or certain of our diagnostic products for some time, if at all. *Rayaldee* is our only proprietary pharmaceutical product that has been approved for marketing by us to date. We continue to incur substantial research and development and general and administrative expenses related to our operations including our pre-clinical development activities and clinical trials. We may incur losses from our operations in the 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, particularly if we are unable to generate or sustain profits and cash flow from sales of *Rayaldee* or our operations at BioReference. If we are unable to generate or sustain profits and cash flow from our operations, 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 no longer be profitable. In particular, if we are unable to successfully commercialize *Rayaldee*, we may never generate substantial revenues from *Rayaldee.* 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.

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

As of December 31, 2020, we had cash and cash equivalents of $72.2 million. Prior to 2020, we had not generated sustained positive cash flows sufficient to offset our operating and research and development expenses and our primary sources of cash has been from the public and private placement of stock, the issuance of convertible notes and credit facilities available to us. While we have generated significant cash from operations as a result of testing related to the COVID-19 pandemic, we are unable to predict how long the demand will continue for our COVID-19 related testing, whether pricing and reimbursement policies for testing will sustain, or whether further restrictions will be placed on elective procedures or if stay at home orders will be reinstated and accordingly, the sustainability of the cash flow is uncertain.

If we are unable to generate a sufficient amount of product and service revenue to finance our cash requirements for research, development and operations, we will need 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, as well as our ability to comply with credit facilities and other loan requirements. Our line of credit with JPMorgan Chase Bank, N.A. ("CB") contains and other agreements that govern our indebtedness may contain restrictive and financial covenants that impose restrictions on us and certain of our subsidiaries, including covenants that require us to maintain specified financial ratios. We have obtained waivers and/or amended our credit facility with CB from time to time in the past to avoid a default under certain covenants, and our ability to comply with these financial covenants may be adversely affected in the future. Failure to comply with specified financial covenants and other requirements could result in an event of default under our line of credit with CB and/or other lenders, which, if not cured or waived, could restrict us from utilizing the facility or accelerate any repayment obligations we may have under the facility and which could have a material adverse effect on our financial condition.

Disruptions in the U.S. and global financial markets may also 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 or cease operations altogether. 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 and other onerous terms. 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 products and product candidates or grant licenses on terms that may not be favorable to us.

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 for 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-regulatory authorities may disagree with our trial design and our interpretation of data from pre-clinical studies and 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.

We rely on licensing agreements with Vifor Fresenius Medical Renal Care Pharma Ltd ("VFMCRP") and Japan Tobacco ("JT") for the international development and marketing of Rayaldee. Failure to maintain these license agreements could prevent us from successfully developing and commercializing Rayaldee worldwide.

In May 2016, EirGen, our wholly-owned subsidiary, partnered with VFMCRP through a Development and License Agreement for the development and marketing of *Rayaldee* in Europe, Canada, Mexico, Australia, South Korea and certain other international markets. The license to VFMCRP potentially covers all therapeutic and prophylactic uses of the product in human patients, provided that initially the license is for the use of the product for the treatment or prevention of secondary hyperparathyroidism related to patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency. Effective May 5, 2020, we entered into the VFMCRP Amendment, pursuant to which the parties agreed to exclude Mexico, South Korea, the Middle East and all of the countries of Africa from the VFMCRP Territory. In addition, the parties agreed to certain amendments to the milestone structure and to reduce minimum royalties payable. As revised, the Company is eligible to receive up to $17 million in regulatory milestones and $210 million in milestone payments tied to launch, pricing and sales of *Rayaldee*, and tiered, double-digit royalties. The success of the Development and License Agreement with VFMCRP is dependent in part on, among other things, the skills, experience and efforts of VFMCRP's employees responsible for the project, VFMCRP's commitment to the arrangement, and the financial condition of VFMCRP, all of which are beyond our control. In the event that VFMCRP, for any reason, including but not limited to early termination of the agreement, fails to devote sufficient resources to successfully develop and market *Rayaldee* internationally, our ability to earn milestone payments or receive royalty payments would be adversely affected, which would have a material adverse effect on our financial condition and prospects.

In October 2017, we entered into a Development and License Agreement (the "JT Agreement") with JT under which JT was granted the exclusive rights for the development and commercialization of *Rayaldee* in Japan. 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, we are eligible to receive up to $31 million upon the achievement of certain regulatory and development milestones by JT for *Rayaldee* in Japan, and $75 million upon the achievement of certain sales based milestones by JT. We will also receive tiered, double digit royalty payments at rates ranging from low double digits to mid-teens on net sales within Japan. 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 we have agreed to reimburse JT up to a capped amount. If JT, for any reason, including but not limited to early termination of the JT Agreement, fails to devote sufficient resources to successfully develop and market *Rayaldee* in Japan, our ability to earn milestone payments or receive royalty payments would be adversely affected, which could have a material adverse effect on our financial condition and prospects.

Our exclusive worldwide agreement with Pfizer Inc. is important to our business. If we do not successfully develop hGH- CTP (somatrogon) and/or Pfizer Inc. does not successfully commercialize hGH-CTP (somatrogon), 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 GHD in adults and children (the "Pfizer Agreement"). Under the Pfizer Agreement, we are eligible to receive up to $275 million upon the achievement of certain regulatory milestones. Upon the launch of hGH-CTP for Pediatric GHD, we are eligible to receive a regional, tiered gross profit share based upon sales of both hGH-CTP and Pfizer's Genotropin® (somatropin). We are responsible for the development program and are obligated to pay for the development up to an agreed cap, which has been exceeded. In May 2020, we entered into an Amended and Restated Development and Commercialization License Agreement (the "Restated Agreement") with Pfizer, effective January 1, 2020, pursuant to which the parties agreed, among other things, to share all costs for Manufacturing Activities, as defined in the Restated Agreement, for developing a licensed product for the three indications included in the Agreement. In the event that the parties are able to obtain regulatory approvals to market a product covered by the Pfizer 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 and Pfizer's commitment to the arrangement. The Pfizer Agreement is terminable for any reason by Pfizer upon ninety days written notice to OPKO. In the event that Pfizer terminates the Agreement or 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 effect on our financial condition and prospects and the trading prices of our securities.

Our business is substantially dependent on our ability to achieve regulatory approval for the marketing of hGH-CTP (somatrogon) in pediatric and adult patients and the commercial success of this product.

On October 21, 2019, we and Pfizer announced that the global phase 3 trial evaluating hGH-CTP (somatrogon) dosed once-weekly in pre-pubertal children with GHD met its primary endpoint of non-inferiority to daily Genotropin® (somatropin) for injection, as measured by annual height velocity at 12 months. In addition, change in height standard deviation scores at six and 12 months, key secondary endpoints, were higher in the hGH-CTP dosed once-weekly cohort in comparison to the Genotropin® (somatropin) dosed once-daily cohort. hGH-CTP was generally well tolerated in this study and comparable to Genotropin® (somatropin) dosed once-daily with respect to the types, numbers and severity of the adverse events observed between the treatment arms. Although the primary endpoint and key secondary endpoints were met and the safety profile for hGH-CTP was consistent with that observed with those treated with Genotropin® (somatropin), further testing and analysis, other clinical trials or patient use may undermine those determinations or unexpected side effects may arise. We previously announced topline data from an earlier phase 3, double blind, placebo controlled study of hGH-CTP in adults with GHD. 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 exceptional value of trunk fat mass reduction in the placebo group that may have affected the primary outcome. We completed post-hoc sensitivity analyses for the adult study 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. There can be no assurance that the FDA will consider the sensitivity analysis or consider the product for approval for adults with GHD.

In January 2021, we and Pfizer announced that the FDA had accepted for filing the BLA submission for the pediatric indication which was submitted in October 2020. There can be no assurance that a BLA will be submitted for the adult indication or that we will obtain marketing approval for either the pediatric or adult indication. 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 marketing approval is both time-consuming and costly, with no certainty of a successful outcome. If we are unable to achieve regulatory approval for hGH-CTP to treat pediatric patients or adults with GHD, our business will be significantly adversely impacted, which could have a materially adverse effect on our business, financial condition and results of operations.

Protein therapeutics have the potential to cause an immune or antibody response in patients.

Antibodies may be transient or persistent and can have no effect or can neutralize the therapeutic effect of the protein. Antibodies that neutralize the activity of a therapeutic protein are known as neutralizing antibodies. As previously reported, low titers of anti-hGH-CTP non-neutralizing antibodies were noted over a four year period in 17 subjects, or approximately 35% of the subjects, in our phase 2 open label extension study in children with GHD. The low titer non-neutralizing antibodies did not affect growth parameters or IGF-1 levels in the patients. Immunogenicity testing and analysis for our phase 3 study is ongoing, and we expect that the full results of the study will be submitted for presentation at a future scientific meeting. The FDA reviews information on immune responses observed during clinical studies and the implications on safety and efficacy and could request additional studies or analysus of hGH-CTP or could decline to approve hGH-CTP for the indications we seek. Any of these occurrences could have a material adverse impact on our business, results of operation and financial condition.

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

Our business is dependent on our ability to successfully commercialize the *4Kscore* test and other diagnostic products. We are committing significant resources to the development and commercialization of these products, and there is no guarantee that we will be able to successfully commercialize these tests. We have limited experience in developing, manufacturing, selling, marketing and distributing innovative 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, or obtain favorable reimbursement, we will not generate any meaningful revenue from the sale of such tests.

Our business is substantially dependent on our ability to generate profits and cash flow from our laboratory operations.

We have made a significant investment in our laboratory operations through the acquisition of BioReference.We compete in the clinical laboratory market primarily on the basis of the quality of testing, reporting and information systems, reputation in the medical community, the pricing of services and ability to employ qualified personnel. Our failure to successfully compete on any of these factors could result in the loss of clients and a reduction in our revenues and profits. To offset efforts by payors to reduce the cost and utilization of clinical laboratory services, we will need to obtain and retain new clients and business partners and grow the laboratory operations. In response to the global pandemic, BioReference has been conducting a substantial amount of COVID-19 testing that has positively impacted our revenues. Simultaneously, however, the volume of its core testing business has decreased as a result of COVID-19. A significant reduction in COVID-19 tests ordered,

specimens submitted by existing clients, or payment rates, without offsetting growth in our core business testing or client base, would impact our ability to successfully maintain the growth our business has experienced and could have a material adverse impact on our ability to generate profits and cash flow from the laboratory operations in the future.

Discontinuation or recalls of existing testing products, failure to develop, or acquire, licenses for new or improved testing technologies or our clients using new technologies to perform their own tests could adversely affect our business.

From time to time, manufacturers discontinue or recall reagents, test kits or instruments used by us to perform laboratory testing. Such discontinuations or recalls could adversely affect our costs, testing volume and revenue.

The clinical laboratory industry is subject to changing technology and new product introductions. Our success in maintaining a leadership position in genomic and other advanced testing technologies will depend, in part, on our ability to develop, acquire or license new and improved technologies on favorable terms and to obtain appropriate coverage and reimbursement for these technologies. We may not be able to negotiate acceptable licensing arrangements and it cannot be certain that such arrangements will yield commercially successful diagnostic tests. If we are unable to license these testing methods at competitive rates, our research and development costs may increase as a result. In addition, if we are unable to license or develop new or improved technologies to expand our esoteric testing operations, our testing methods may become outdated when compared with our competition and testing volume and revenue may be materially and adversely affected.

Currently, most clinical laboratory testing is categorized as "high" or "moderate" complexity, and thereby is subject to extensive and costly regulation under CLIA. The cost of compliance with CLIA makes it impractical for most physicians to operate clinical laboratories in their offices, and other laws limit the ability of physicians to have ownership in a laboratory and to refer tests to such a laboratory. Manufacturers of laboratory equipment and test kits could seek to increase their sales by marketing point-of-care laboratory equipment to physicians and by selling test kits approved for home or physician office use to both physicians and patients. Diagnostic tests approved for home use are automatically deemed to be "waived" tests under CLIA and may be performed in physician office laboratories as well as by patients in their homes with minimal regulatory oversight. Other tests meeting certain FDA criteria also may be classified as "waived" for CLIA purposes. The FDA has regulatory responsibility over instruments, test kits, reagents and other devices used by clinical laboratories and has taken responsibility from the Centers for Disease Control for classifying the complexity of tests for CLIA purposes. Increased approval of "waived" test kits could lead to increased testing by physicians in their offices or by patients at home, which could affect our market for laboratory testing services and negatively impact our revenues. If our competitors develop and market products that are more effective, safer or less expensive than our products and product candidates, our net revenues, profitability and commercial opportunities will be negatively impacted.

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

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 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. Our competitors may also have more experience and expertise in obtaining marketing approvals from the FDA and other regulatory authorities. We cannot predict with accuracy the timing or impact of the introduction of potentially competitive products or their possible effect on our sales. In addition to product development, testing, approval, and promotion, other competitive factors in the pharmaceutical and diagnostics industry include industry consolidation, product quality and price, product technology, reputation, customer service, and access to technical information.

The clinical laboratory business is intensely competitive both in terms of price and service. Pricing of laboratory testing services is often one of the most significant factors used by health care providers and third-party payors in selecting a laboratory. As a result of the clinical laboratory industry undergoing significant consolidation, larger clinical laboratory providers are able to increase cost efficiencies afforded by large-scale automated testing. This consolidation results in greater price competition. We may be unable to increase cost efficiencies sufficiently, if at all, and as a result, our net earnings and cash flows could be negatively impacted by such price competition. Additionally, we may also face changes in contracting with third party payors, fee schedules, competitive bidding for laboratory services or other actions or pressures reducing payment schedules as a result of increased or additional competition.

If our competitors market products that are more effective, safer, easier to use or less expensive than our current products and product candidates, or that reach the market sooner than our products and product candidates, we may not achieve commercial success. In addition, the biopharmaceutical, diagnostic, medical device, and laboratory 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, products 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;
- delay or failure to obtain institutional review board ("IRB") approval to conduct or renew a clinical trial at a prospective site; and
- insufficient liquidity to fund our preclinical and clinical studies.

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;
- inability to monitor patients adequately during or after treatment; and
- insufficient liquidity to fund ongoing studies.

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 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.

Our inability to meet regulatory quality standards applicable to our manufacturing and quality processes and to address quality control issues in a timely manner could delay the production and sale of our products or result in recalls of products.

Manufacturing or design defects, unanticipated use of our products, or inadequate disclosure of risks relating to the use of our products could lead to injury or other adverse events. These events could lead to recalls or safety alerts relating to our products (either voluntary or required by governmental authorities) and could result, in certain cases, in the removal of a product from the market. Any recall could result in significant costs as well as negative publicity that could reduce demand for our products. Personal injuries relating to the use of our products can also result in product liability claims being brought against us. In some circumstances, such adverse events could also cause delays in new product approvals.

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 Ireland, 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.

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 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.

Failure to establish, and perform to, appropriate quality standards to assure that the highest level of quality is observed in the performance of our testing services could adversely affect the results of our operations and adversely impact our reputation.

The provision of clinical testing services, including anatomic pathology services, and related services, and the design, manufacture and marketing of diagnostic products involve certain inherent risks. The services that we provide and the products that we design, manufacture and market are intended to provide information for healthcare providers in providing patient care. Therefore, users of our services and products may have a greater sensitivity to errors than the users of services or products that are intended for other purposes.

Similarly, negligence in performing our services can lead to injury or other adverse events. We may be sued under physician liability or other liability law for acts or omissions by our pathologists, laboratory personnel and other employees. We are subject to the attendant risk of substantial damages awards and risk to our reputation.

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

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
- changes in the standard of care for the targeted indications for any of our products or product candidates, which could reduce the marketing impact of any claims that we could make following applicable regulatory authority approval.

In addition, our efforts to educate the medical community and health care payors on the benefits of our products and 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 products 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, diagnostic and laboratory tests is uncertain, and failure of our pharmaceutical products, diagnostic tests or laboratory 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. The commercial success of our existing and future products 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, as well as our ability to obtain in network status with such 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 restricting in network status of laboratory providers. As a result, they may not cover or provide adequate payment for our product candidates. These payors may conclude that our products 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 products for insurance coverage and adequate reimbursement or approve our laboratory for in network status.

The failure to obtain adequate coverage or any reimbursement for our products, or health care cost containment initiatives that limit or restrict reimbursement for our products, 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. Private health plans, such as managed care plans and pharmacy benefit management ("PBM") programs may also not include our products on formularies, and may use other techniques that restrict access to our products or set a lower reimbursement rate than anticipated.

A significant portion of our revenues come from government subsidized healthcare programs such as Medicaid and Medicare. 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 governmental payor program, a substantial portion of our consolidated revenues would be lost, which would adversely affect our results of operations and financial condition. In addition, if a federal government shutdown were to occur for a prolonged period of time, federal government payment obligations, including its obligations under Medicaid and Medicare, may be delayed. Similarly, if state government shutdowns were to occur, state payment obligations may be delayed. If the federal or state governments fail to make payments under these programs on a timely basis, our business could suffer, and our financial position, results of operations or cash flows may be materially affected.

As we evolve from a company primarily involved in development to a company also involved in commercialization of our pharmaceutical and diagnostic products as well as our laboratory testing services, we may encounter difficulties in managing our growth and expanding our operations successfully.

As we advance our product candidates and expand our business, we will need to expand our development, regulatory and commercial infrastructure. As our operations expand, we expect that we will need to manage additional relationships with various third parties, 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 and operations effectively; manage our clinical trials effectively; hire, train and integrate additional management, 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.

Our success is dependent to a significant degree upon the involvement, efforts and reputation 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 CEO, 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 us, both in terms of a credit agreement and equity investments. If we lost his services or if his reputation was damaged for whatever reason, including, but not limited to, as a result of the allegations underlying various past SEC and shareholder lawsuits against us and Dr. Frost, our relationships with acquisition and investment targets, joint ventures, customers and investors, as well as our ability to obtain additional funding on acceptable terms, or at all, 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 operate our business and develop or commercialize our products and product candidates.

We will need to expand and effectively manage our managerial, operational, sales, financial, development, and other resources in order to successfully operate our business and pursue our research, development, and commercialization efforts for our products and 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 could delay or prevent the development and commercialization of our products and product candidates.

If the FDA or other applicable regulatory authorities approve generic products that compete with any of our products or product candidates, the sale of our products or product candidates may be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "listed drug" which, in turn can be relied upon by potential competitors in support of an approval of an abbreviated new drug application, or ANDA, or 505(b)(2) application. U.S. laws and other applicable policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for a generic substitute. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredient(s), dosage form, strength, route of administration, and conditions of use, or labeling, as our product or product candidate and that the generic product is bioequivalent to ours, meaning it is absorbed in the body at the same rate and to the same extent as our product or product candidate. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than ours to bring to market and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of sales of any branded product is typically lost to the generic product. Accordingly, competition from generic equivalents to our products or product candidates would materially adversely impact our revenues, profitability and cash flows and substantially limit our ability to obtain a return on the investments that we have made in our products and product candidates.

We rely on third parties to manufacture and supply our pharmaceutical and diagnostic products and product candidates.

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 products and 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 products and 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 products or 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.

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 are independent contractors 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.

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 as required by applicable laws and we work to ensure that the subjects from whom our data and samples 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.

Failure to timely or accurately bill and collect for our services could have a material adverse effect on our revenues and 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 and payor practices 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 and the World Health Organization establishes diagnostic codes using a data set called International Statistical Classification of Diseases, or ICD-10, 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 the ICD-10 code selected by the ordering or performing physician. 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.

In addition to the items described above, third-party payors, including government programs, may decide to deny payment or recoup payments for testing that they contend was improperly billed or not medically necessary, against their coverage determinations, or for which they believe they have otherwise overpaid (including as a result of their own error), and we may be required to refund payments already received. Our revenues may be subject to retroactive adjustment as a result of these factors among others, including without limitation, differing interpretations of billing and coding guidance and changes by government agencies and payors in interpretations, requirements, and "conditions of participation" in various programs.

We have in the ordinary course of business been the subject of recoupments by payors and have from time to time identified and reimbursed payors for overpayments.

Incorrect or incomplete documentation and billing information, as well as the other items described above, among other factors, 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 the 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 information technology systems that we rely on may be subject to unauthorized tampering, cyberattack or other data security incidents that could impact our billing processes or disrupt our operations

In addition to our internal information technology systems, we rely on the IT systems of certain third parties to whom we outsource certain of our services or functions, or with whom we store confidential information, including patient data. These IT systems are subject to potential cyberattacks or other security breaches. If such attacks are successful, they could disrupt our operations and result in unauthorized persons gaining access to confidential or proprietary information. A breach or security incident affecting these third parties could harm our business, results of operations and reputation, and subject us to liability, governmental investigation, significant damage to our reputation or otherwise adversely affect our business.

Although the Company has security measures implemented, cyber-attacks and threats against us and our third-party providers continue to evolve and are often not recognized until such attacks are launched against a potential target. A successful cybersecurity attack or other data security incident could result in the misappropriation and/or loss of confidential or personal information, create system interruptions, or deploy malicious software that attacks our systems. The unauthorized dissemination of sensitive personal information or proprietary or confidential information due to a breach of these IT systems could expose us or other third-parties to regulatory fines or penalties, litigation and potential liability, or otherwise harm our business. Any mitigation or remediation efforts that we undertake may require expenditures of significant resources and the diversion of the attention of management. In addition, we have taken, and continue to take, precautionary measures to reduce the risk of, and detect and respond to, future cyber threats, and prevent or minimize vulnerabilities in our IT systems. We have also taken, and will continue to take, measures to assess the cybersecurity protections implemented by our third-party providers. There can be no assurances that our precautionary measures or measures used by our third-party providers will prevent, contain or successfully defend against cyber or information security threats that could have a significant impact on our business, results of operations and reputation and subject us to liability.

Healthcare plans have taken steps to control the utilization and reimbursement of healthcare services, including clinical test services.

We also face efforts by non-governmental third-party payors, including healthcare plans, to reduce utilization and reimbursement for clinical testing services.

The healthcare industry has experienced a trend of consolidation among healthcare insurance plans, resulting in fewer but larger insurance plans with significant bargaining power to negotiate fee arrangements with healthcare providers, including clinical testing providers. These healthcare plans and independent physician associations, may demand that clinical testing providers accept discounted fee structures or assume all or a portion of the financial risk associated with providing testing services to their members through capped payment arrangements. In addition, some healthcare plans limit the laboratory network to only a single national or regional laboratory to obtain improved fee-for-service pricing. There is also an increasing number of patients enrolling in consumer driven products and high deductible plans that involve greater patient cost-sharing.

The increased consolidation among healthcare plans also has increased the potential adverse impact of ceasing to be a contracted provider with any such insurer.

We expect continuing efforts to limit the number of participating laboratories in payor networks, reduce reimbursements, to impose more stringent cost controls and to reduce utilization of clinical test services. These efforts, including future changes in third-party payor rules, practices and policies, or failing to become a contracted provider or ceasing to be a contracted provider to a healthcare plan, may have a material adverse effect on our business.

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 products and product candidates. Because certain U.S. patent applications are confidential, 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. 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. 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.

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 products and product candidates, thus allowing others to more effectively compete with us. Therefore, any patents that we own or license may not adequately protect our products and product candidates or our future products, which could have a material adverse effect on our business, results of operations, and financial condition. We cannot be assured that our filings for patent term extensions or supplementary protection certificates to potentially extend a patent term of a patent covering an approved drug or biological product will be granted in any particular jurisdiction in which the Company or its licensee obtains approval for a drug or biological product.

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 and may in the future obtain licenses from third party owners that are necessary or useful for our business. 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 or may determine not to pursue litigation against other companies that are infringing these patents. 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.

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. The U.S. case law pertaining to statutory exemptions to patent infringement for those who are using third party patented technology in the process of pursuing FDA regulatory approval 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 may 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 have faced, and may in the future face, intellectual property infringement claims that could be time-consuming and costly to defend, and could result in our loss of significant rights and the assessment of treble damages.

We may from time to time receive notices of claims of infringement and misappropriation or misuse of other parties' proprietary rights. Some of these additional claims may also lead to litigation. We cannot assure you that we will prevail in such actions, or that other actions alleging misappropriation or misuse by us of third-party trade secrets, infringement by us of third-party patents and trademarks or the validity of our patents, will not be asserted or prosecuted against us.

We may also initiate claims to defend our intellectual property or to seek relief on allegations that we use, sell, or offer to sell technology that incorporates third party intellectual property. Intellectual property litigation, regardless of outcome, is expensive and time-consuming, could divert management's attention from our business and have a material negative effect on our business, operating results or financial condition. If there is a successful claim of infringement against us, we may be required to pay substantial damages (including treble damages if we were to be found to have willfully infringed a third party's patent) to the party claiming infringement, develop non-infringing technology, stop selling our tests or using technology that contains the allegedly infringing intellectual property or enter into royalty or license agreements that may not be available on acceptable or commercially practical terms, if at all. Our failure to develop non-infringing technologies or license the proprietary rights on a timely basis could harm our business.

It is possible that in the patent laws related to the field of genomic-based products and diagnostics and patents covering such products changes to permit the patenting of genes and/or gene based products and/or related diagnostic methods. In such a case, we might be required to pay royalties, damages and costs to firms who own the rights to these patents, or we might be restricted from using any of the inventions claimed in those patents.

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 product or 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 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. Additionally, as previously disclosed and further explained in Legal Proceedings, we are subject to pending legal proceedings with respect to alleged violations of securities laws, specifically, the class action lawsuits for which we await a final order approving the settlement terms.

From time to time, we may receive inquiries, document requests, Civil Investigative Demands ("CIDs") or subpoenas from the Department of Justice, the Office of Inspector General and Office for Civil Rights ("OCR") of the Department of Health and Human Services, the Centers for Medicare and Medicaid Services, various payors and fiscal intermediaries, and other state and federal regulators regarding investigations, audits and reviews. We are currently responding to CIDs, subpoenas or document requests for various matters relating to our laboratory operations. Some pending or threatened proceedings against us may involve potentially substantial amounts as well as the possibility of civil, criminal, or administrative fines, penalties, or other sanctions, which could be material. Settlements of suits involving the types of issues that we routinely confront may require monetary payments as well as corporate integrity agreements. Additionally, qui tam or "whistleblower" actions initiated under the civil False Claims Act may be pending but placed under seal by the court to comply with the False Claims Act's requirements for filing such suits. The Company generally has cooperated, and intends to continue to cooperate, with appropriate regulatory authorities as and when investigations, audits and inquiries arise.

Such legal actions and government investigations could result in substantial monetary damages, negatively impact our ability to obtain additional funding on acceptable terms, or at all, and damage to our reputation with customers, business partners and other third parties, all of which could have a material adverse effect upon our results of operations and financial position. Further, the legal actions and government investigations could damage our reputation with investors and adversely affect the trading prices of our securities.

RISKS RELATED TO REGULATORY COMPLIANCE

Our ability to successfully operate our laboratories and develop and commercialize certain of our diagnostic tests and LDTs will depend on our ability to maintain required regulatory licensures and comply with all the CLIA requirements.

In order to successfully operate our laboratory business and offer certain of our diagnostic tests and LDTs, we must maintain our CLIA certification 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. Our laboratories are 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 laboratories 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.

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 Biologics License Application (BLA), an 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. To date, we have only submitted one NDA which was approved in June 2016, and one BLA which was approved for filing in January 2021. We have received FDA approval of the PMA for our Sangia Total PSA Test using the Claros Analyzer, a novel diagnostic instrument system to provide rapid, high performance blood test results in the point-of-care setting, in January 2019 but we have not received marketing approval or clearance for any of our other diagnostic product candidates, 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, BLA, 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. 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;
- 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
- 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.

The terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products and product candidates, which could materially impair our ability to generate anticipated revenues.

We, our approved or cleared products, and the manufacturers of our products are subject to continual review. Our approved or cleared products may only be promoted for their indicated uses. Marketing, labeling, packaging, adverse event reporting, storage, advertising, and promotion for our approved products will be subject to extensive regulatory requirements. We train our marketing and sales force against promoting our products for uses outside of the cleared or approved indications for use, known as "off-label uses." If the FDA determines that our promotional materials or training constitute promotion of

unsupported claims or an off-label use, it could request that we modify our training or promotional materials or subject us to regulatory or enforcement actions, including the issuance of an untitled letter, a warning letter, injunction, seizure, civil fine or criminal penalties. It is also possible that other federal, state or foreign enforcement authorities might take action if they consider our business activities to constitute promotion of an off-label use, which could result in significant penalties, including, but not limited to, criminal, civil and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government healthcare programs, and the curtailment of our operations.

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 or product candidate or our ability to manufacture and promote a product or 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 products or product candidates and we may not achieve or sustain profitability, which would materially impair our ability to generate anticipated revenues.

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:

- federal and state laws applicable to billing and claims payment;
- federal and state laboratory anti-mark-up laws;
- federal and state anti-kickback laws;
- physician self-referral law;
- federal and state false claims laws;
- federal self-referral and financial inducement prohibition laws, commonly known as the Stark Law, and the state equivalents;
- federal and state laws governing laboratory licensing and testing, including CLIA;
- federal and state laws governing the development, use and distribution of LDTs;
- HIPAA, along with the revisions to HIPAA as a result of the amendments from the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH Act"), and analogous state laws and non-US laws, including the General Data Protection Regulation;
- federal, state and foreign regulation of privacy, security, electronic transactions and identity theft;
- federal, state and local laws governing the handling, transportation and disposal of medical and hazardous waste;
- Occupational Safety and Health Administration rules and regulations;
- changes to laws, regulations and rules as a result of the implementation and/or repeal of part or all of 2010 Health Care Reform Legislation; and
- changes to other federal, state and local laws, regulations and rules, including tax laws.

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. Different interpretations and enforcement policies of existing statutes and regulations applicable to our business could subject our current practices to allegations of impropriety or illegality, or could require us to make significant changes to

our operations. Under the FCA, whistleblower or qui tam provisions 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 and we may be subject to such suits. Violations of the FCA could result in enormous economic liability and could have a material impact on us. 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 maintain the security of patient-related information or compliance with security requirements could damage our reputation with customers, cause us to incur substantial additional costs and become subject to litigation.

Pursuant to HIPAA, including the HITECH amendments thereunder, and certain similar state laws, we must comply with comprehensive privacy and security standards with respect to the use and disclosure of protected health information. If we do not comply with existing or new laws and regulations related to protecting privacy and security of personal or health information, we could be subject to monetary fines, civil penalties, or criminal sanctions.

We may also be required to comply with the data privacy and security laws of other countries in which we operate or from which we receives data transfers, including the General Data Protection Regulation (GDPR), which affects our European operations and possibly our laboratory and clinical development operations. The GDPR, which is wide-ranging in scope, governs the collection and use of personal data in the European Union and imposes operational requirements for companies that receive or process personal data of residents of the European Union that are different than those currently in place in the European Union. We have implemented policies and procedures required to comply with the new EU regulations but may be subject for penalties if we are found to be non-compliant.

We have had data and security breaches in the ordinary course and such breaches may continue to happen from time to time despite our best efforts to prevent such breaches and safeguard private information. Some of these other data and security breaches have been reported to OCR and we have received requests for information from OCR in connection with certain of these matters, or we are awaiting discussion, investigation or action by OCR. Any action by OCR may require us to pay fines or take remedial actions that may be expensive and require the attention of management, any of which may have a material adverse effect on us and our results of operations.

We have and will continue to receive certain personal and financial information about our clients and their patients. In addition, we depend upon the secure transmission of confidential information over public networks. While we take reasonable and prudent steps to protect this protected information, a compromise in our security systems that results in client or patient personal information being obtained by unauthorized persons or our failure to comply with security requirements for financial transactions could adversely affect our reputation with our clients and result in litigation against us or the imposition of penalties, all of which may adversely impact our results of operations, financial condition and liquidity.

Failure to comply with environmental, health and safety laws and regulations, including the Federal Occupational Safety and Health Administration Act, the Needlestick Safety and Prevention Act and the Comprehensive Medical Waste Management Act, could result in fines and penalties and loss of licensure, and have a material adverse effect upon our business.

We are subject to licensing and regulation under federal, state and local laws and regulations relating to the protection of the environment and human health and safety, including laws and regulations relating to the handling, transportation and disposal of medical specimens, infectious and hazardous waste and radioactive materials, as well as regulations relating to the safety and health of laboratory employees. The Federal Occupational Safety and Health Administration has established extensive requirements relating to workplace safety for health care employers, including clinical laboratories, whose workers may be exposed to blood-borne pathogens such as HIV and the hepatitis B virus. These requirements are designed to minimize exposure to, and transmission of, blood-borne pathogens. In addition, the Needlestick Safety and Prevention Act requires, among other things, that we include in our safety programs the evaluation and use of engineering controls such as safety needles if found to be effective at reducing the risk of needlestick injuries in the workplace.

Waste management is subject to federal and state regulations governing the transportation and disposal of medical waste including bodily fluids. In New Jersey, we are subject to the Comprehensive Medical Waste Management Act (“CMWMA”), which requires us to register as a generator of special medical waste. All of our medical waste is disposed of by a licensed interstate hauler. These records are audited by the State of New Jersey on a yearly basis. We are also subject to the Federal Hazardous Materials Transportation Law, 49 U.S.C. 5101 et seq., and the Hazardous Materials Regulations (“HMR”), 49 CFR

parts 171-180. The federal government has classified hazardous medical waste as hazardous materials for the purpose of regulation.

Failure to comply with such federal, state and local laws and regulations could subject us to denial of the right to conduct business, fines, criminal penalties and/or other enforcement actions, any of which could have a material adverse effect on our business. In addition, compliance with future legislation could impose additional requirements us, which may be costly.

Our failure or the failure of third-party payors or physicians to comply with ICD-10-CM Code Set, and our failure to comply with other emerging electronic transaction standards could adversely impact our business.

We continue our assessment of information systems, applications and processes for compliance with ICD-10-CM Code Set requirements. Clinical laboratories are typically required to submit health care claims with diagnosis codes to third party payors. The diagnosis codes must be obtained from the ordering physician for clinical laboratory testing and from the interpreting pathologist for anatomic pathology services. Our failure or the failure of third party payors or physicians to comply with these requirements could have an adverse impact on reimbursement, delay sales and cash collections.

Also, the failure of our IT systems to keep pace with technological advances may significantly reduce our revenues or increase our expenses. Public and private initiatives to create healthcare information technology ("HCIT") standards and to mandate standardized clinical coding systems for the electronic exchange of clinical information, including test orders and test results, could require costly modifications to our existing HCIT systems. If we fail to adopt or delay in implementing HCIT standards, we could lose customers and business opportunities.

Failure to comply with complex federal and state laws and regulations related to submission of claims for clinical laboratory services could result in significant monetary damages and penalties and exclusion from the Medicare and Medicaid programs.

We are subject to extensive federal and state laws and regulations relating to the submission of claims for payment for clinical laboratory services, including those that relate to coverage of our services under Medicare, Medicaid and other governmental health care programs, the amounts that may be billed for our services and to whom claims for services may be submitted. These rules may also affect us in light of the practice management products that we market, to the extent that these products are considered to affect the manner in which our customers submit their own claims for services. Submission of our claims is particularly complex because we provide both anatomic pathology services and clinical laboratory tests, which generally are paid using different reimbursement principles. The clinical laboratory tests are often paid under a clinical laboratory fee schedule, and the anatomic pathology services are often paid under a physician fee schedule.

Our failure to comply with applicable laws and regulations could result in our inability to receive payment for our services or result in attempts by third-party payors, such as Medicare and Medicaid, to recover payments from us that have already been made. Submission of claims in violation of certain statutory or regulatory requirements can result in penalties, including substantial civil money penalties for each item or service billed to Medicare in violation of the legal requirement, and exclusion from participation in Medicare and Medicaid. Government authorities may also assert that violations of laws and regulations related to submission or causing the submission of claims violate the federal False Claims Act ("FCA") or other laws related to fraud and abuse, including submission of claims for services that were not medically necessary. Under the FCA, whistleblower or qui tam provisions 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 and we may be subject to such suits. Violations of the FCA could result in enormous economic liability. The FCA provides that all damages are trebled, and each false claim submitted is subject to a penalty of up to $21,916. For example, we could be subject to FCA liability if it was determined that the services we provided were not medically necessary and not reimbursable, particularly if it were asserted that we contributed to the physician's referrals of unnecessary services to us. It is also possible that the government could attempt to hold us liable under fraud and abuse laws for improper claims submitted by an entity for services that we performed if we were found to have knowingly participated in the arrangement that resulted in submission of the improper claims.

Changes in regulation and policies, including increasing downward pressure on health care reimbursement, may adversely affect reimbursement for diagnostic services and could have a material adverse impact on our business.

Reimbursement levels for health care services are subject to continuous and often unexpected changes in policies, and we face a variety of efforts by government payors to reduce utilization and reimbursement for diagnostic testing services. Changes in governmental reimbursement may result from statutory and regulatory changes, retroactive rate adjustments, administrative rulings, competitive bidding initiatives, and other policy changes.

The U.S. Congress has considered, at least yearly in conjunction with budgetary legislation, changes to one or both of the Medicare fee schedules under which we receive reimbursement, which include the physician fee schedule for anatomical pathology services, and the clinical laboratory fee schedule for our clinical laboratory services. For example, currently there is no copayment or coinsurance required for clinical laboratory services, although there is for our services that are paid under the physician fee schedule. However, Congress has periodically considered imposing a 20 percent coinsurance on laboratory services. If enacted, this would require us to attempt to collect this amount from patients, although in many cases the costs of collection would exceed the amount actually received.

The Center for Medicare and Medicaid Services ("CMS") pays laboratories on the basis of a fee schedule that is reviewed and re-calculated on an annual basis. CMS may change the fee schedule upward or downward on billing codes that we submit for reimbursement on a regular basis. Our revenue and business may be adversely affected if the reimbursement rates associated with such codes are reduced. Even when reimbursement rates are not reduced, policy changes add to our costs by increasing the complexity and volume of administrative requirements. Medicaid reimbursement, which varies by state, is also subject to administrative and billing requirements and budget pressures. In recent years, state budget pressures have caused states to consider several policy changes that may impact our financial condition and results of operations, such as delaying payments, reducing reimbursement, restricting coverage eligibility and service coverage, and imposing taxes on our services.

Third party payors 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 is established by calculating a weighted mean of private payor rates. Effective January 1, 2018, clinical laboratory fee schedule rates are based on weighted median private payor rates as required by PAMA. Even though the permitted annual decrease are capped through 2023, 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.

The federal government is faced with significant economic decisions in the coming years. Some solutions being offered in the government could substantially change the way laboratory testing is reimbursed by government entities. We cannot be certain what or how any such government changes may affect our business.

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. As such, 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 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 U. S. However, there are legal challenges to 2010 Health Care Reform Legislation pending before the Supreme Court and we cannot ascertain the outcome of those challenges and how any such challenge might affect the Company.

It is uncertain whether any efforts to amend the Affordable Care Act will be successful or enacted into law, and if enacted, what the impact might be on our business. It is also uncertain how the current administration intends to alter 2010 Health Care Reform Legislation, if at all including whether regulatory changes to the implementation of the 2010 Health Care Reform Legislation will restrict patient access to affordable insurance or other third-party payor sources and impact their access to novel, biosimilar and complex generic products. In addition, litigation may prevent some or all of the legislation from taking effect. We cannot assure you as to the ultimate content, timing, or effect of changes, nor is it possible at this time to estimate the impact of any such potential legislation.

To enhance compliance with applicable health care laws, and mitigate potential liability in the event of noncompliance, regulatory authorities, such as the U. S. Health and Human Services Department Office of Inspector General (the "OIG"), have recommended the adoption and implementation of a comprehensive health care compliance program that generally contains the elements of an effective compliance and ethics program. In addition, certain states, such as New York, require that certain health care providers have a compliance program that generally adheres to the standards set forth in a model compliance program. Also, under the 2010 Health Care Reform Legislation, the U.S. Department of Health and Human Services, or HHS,

requires suppliers, such as us, to adopt, as a condition of Medicare participation, compliance programs that meet a core set of requirements. While we have adopted U.S. healthcare compliance and ethics programs that generally incorporate the OIG's recommendations and train our employees in such compliance, having such a program can be no assurance that we will avoid any compliance issues.

RISKS RELATED TO INTERNATIONAL OPERATIONS

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

We intend to market certain of our products and product candidates in non-U.S. markets. In order to market our products and 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 products and 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 products and 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 product and product candidates to other available products. If reimbursement of our products and 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. 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 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 differ in some respects from those associated with our U.S. business and our exposure to such risks may increase if our international business continues to grow. 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 and 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.

Our international business is subject to both U.S. and foreign laws and regulations, including, without limitation, regulations relating to import-export controls, technology transfer restrictions, repatriation of earnings, data privacy and protection, investment, exchange rates and controls, the FCPA and other anti-corruption laws, the anti-boycott provisions of the U.S. Export Administration Act, labor and employment, works councils and other labor groups, taxes, environment, security restrictions, intellectual property, changes in taxation, including legislative changes in U.S. and international taxation of income earned outside of the U.S., handling of regulated substances, and other commercial activities. Failure by us, our employees, affiliates, partners or others with whom we work to comply with these laws and regulations could result in administrative, civil or criminal liabilities. New regulations and requirements, or changes to existing ones in the various countries in which we operate can significantly increase our costs and risks of doing business internationally. 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.

Changes in regulations, political leadership and environment, or security risks may dramatically affect our ability to conduct or continue to conduct business in international markets. Our international business may also be impacted by changes in foreign national policies and priorities, which may be influenced by changes in the environment, geopolitical uncertainties, government budgets, and economic and political factors more generally, any of which could impact funding for programs or delay purchasing decisions or customer payments. We also could be affected by the legal, regulatory and economic impacts of Britain's exit from the European Union, the impact of which is not known at this time. The occurrence and impact of these

factors is difficult to predict, but one or more of them could have a material adverse effect on our financial position, results of operations and/or cash flows.

RISKS RELATED TO ACQUISITIONS AND INVESTMENTS

We have a large amount of goodwill and other intangible assets on our balance sheet that are subject to periodic impairment evaluations.

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, 2020, we have goodwill and other intangible assets of $1.7 billion. 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. 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 previously performed.

Sales of *Rayaldee* and our operations at EirGen, are currently underperforming expectations and if we do not achieve our planned operating results, we may be required to incur a non-cash impairment charge. There can be no assurance that future reviews of our goodwill and other intangible assets will not result in impairment charges. 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 and the trading price of our securities.

RISKS RELATED TO OWNERSHIP OF OUR COMMON STOCK

The trading prices of our securities may fluctuate significantly.

The trading prices 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 announcement and/or commencement and/or settlement of lawsuits or similar claims against us or any of our officers, directors and affiliates;
- 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.

Further, the securities 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 trading prices of our Common Stock, which could cause a decline in the value of our securities.

Directors, executive officers, principal stockholders and affiliated entities own a substantial amount 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 January 31, 2021, our directors, executive officers, principal stockholders and affiliated entities beneficially owned, in the aggregate, approximately 41.3% of our outstanding voting securities. Phillip Frost, M.D., our Chairman and CEO, is

deemed to beneficially own, in the aggregate, approximately 34.2% of our Common Stock as of January 31, 2021. As a result, Dr. Frost, acting with other members of management, would have the ability to significantly impact the election of our Board of Directors, the adoption or amendment of provisions in our 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 holders of our securities might otherwise recover a premium for their securities over current market prices.

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 January 29, 2021, investors held a short position of approximately 104,766,092 million shares of our Common Stock which represented approximately 15.6% of our outstanding Common Stock. 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, including with respect to companies we acquire, 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 and remediated control deficiencies in the past, and we cannot assure you that we will at all times in the future be able to report that our internal controls are effective. In addition, material weaknesses in the design and operation of the internal control over financial reporting of companies that we acquire could have a material adverse effect on our business and operating results. 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 Nasdaq Global Select Market 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

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, we lease approximately 29,500 square feet, which encompasses space for our corporate offices and administrative services.

The table below summarizes certain information as to our significant physical properties as of December 31, 2020:

Location	Segment and Purpose	Type of Occupancy
Miami, FL	Diagnostics & Pharmaceutical: Corporate Headquarters	Leased
Elmwood Park, NJ	Diagnostics: Main Laboratory	Leased
Gaithersburg, MD	Diagnostics: Genetics Laboratory	Leased
Kiryat Gat, Israel	Pharmaceutical: Research and Development, CTP	Leased
Woburn, MA	Diagnostics	Leased
Nesher, Israel	Pharmaceuticals: API Manufacturing	Leased
Guadalajara, Mexico	Pharmaceuticals: Pharmaceutical Manufacturing	Owned
Banyoles, Spain	Pharmaceuticals: Pharmaceutical Manufacturing	Owned
Palol de Revardit, Spain	Warehouse	Leased
Barcelona, Spain	Pharmaceuticals: Research and Development	Leased
Waterford, Ireland	Pharmaceuticals: Pharmaceutical Manufacturing	Leased
Santiago, Chile	Pharmaceuticals: Office; Warehouse	Leased

ITEM 3. LEGAL PROCEEDINGS.

We are involved from time to time in various claims and legal actions arising in the ordinary course of business.

As previously disclosed, on September 7, 2018, the Securities and Exchange Commission ("SEC") filed a lawsuit in the Southern District of New York (the "SEC Complaint" or "SEC Lawsuit") against a number of individuals and entities, including the Company and its CEO and Chairman, Phillip Frost ("Dr. Frost"), alleging violations of securities laws. The Company entered into a settlement agreement with the SEC on December 27, 2018, pursuant to which, without admitting or denying any of the allegations of the SEC Complaint, the Company is enjoined from violating Section 13(d) of the Exchange Act and paid a $100,000 penalty.

Following the SEC's announcement of the SEC Complaint, a number of class actions and derivative suits were filed concerning the allegations in the SEC Complaint and related matters. On June 26, 2020, The Amitim Funds, the lead plaintiff in the class action lawsuits filed a Stipulation of Settlement in the Southern District of Florida of behalf of itself and the remainder of the class, which, if approved, will provide for the settlement of and release of the class action claims for an aggregate of $16.5 million, a significant portion of which has been paid into escrow by our insurance carriers. On September 4, 2020, an Order Preliminarily Approving Settlement was entered and a settlement hearing was held on December 15, 2020. We are awaiting the Court's final order approving the settlement. Additional information on the class action lawsuits is provided below.

On November 2, 2020, the derivative suit was settled in the Delaware Chancery Court for an aggregate amount of $3.1 million (the "Settlement"). Several derivative lawsuits that were filed in Florida State and federal courts were stayed pending the resolution of the Delaware derivative action and all of those matters have now been dismissed. The specific information relating to each lawsuit is provided below.

On or about September 12, 2018, Jason Kerznowski ("Kerznowski"), a purported stockholder, filed a putative class action lawsuit in the United States District Court for the District of New Jersey against the Company and certain of its current and former executive officers (the "Kerznowski Lawsuit"). This lawsuit was brought by Kerznowski both individually and on behalf of a putative class of the Company's stockholders, claiming that in connection with the facts and circumstances

underlying the allegations in the SEC Complaint, the Company engaged in fraudulent conduct and made false and misleading statements of material fact or omitted to state material facts necessary to make the statements made not misleading. The Kerznowski Lawsuit sought to declare the action to be a class action and certify Kerznowski as the class representative, monetary damages, including prejudgment and post judgment interest, an award of reasonable attorneys' fees, expert fees, and other costs, and such other relief as the Court may deem just and proper.

On or about September 14, 2018, Charles Steinberg ("Steinberg"), a purported stockholder, filed a putative class action lawsuit in the United States District Court for the Southern District of Florida against the Company and certain of its current and former executive officers (the "Steinberg Lawsuit"). This lawsuit was brought by Steinberg both individually and on behalf of a putative class of the Company's stockholders claiming that in connection with the facts and circumstances underlying the allegations in the SEC Complaint, the Company engaged in fraudulent conduct and made false and misleading statements of material fact or omitted to state material facts necessary to make the statements made not misleading. The Steinberg Lawsuit sought to declare the action to be a class action, monetary damages, including prejudgment and post judgment interest, an award of reasonable attorneys' fees and expert fees and other costs, and such additional or different relief as the interests of law or equity may require.

On February 4, 2019, the United States District Court for the District of New Jersey appointed the Amitim Funds as lead plaintiff in the Kerznowski Lawsuit and subsequently transferred the matter to the United States District Court for the Southern District of Florida. Amitim Funds was also appointed as lead plaintiff in the Steinberg Lawsuit. On May 3, 2019, plaintiffs in each of the Kerznowski Lawsuit and Steinberg Lawsuit, filed an identical consolidated class action complaint, and the Court consolidated these actions on May 8, 2019. On May 29, 2020, the parties informed the Court they had reached a settlement in principle, settling the class action suit for $16.5 million, subject to certain terms and conditions, and the Court issued an Order on Notice of Settlement denying all pending motions as moot and administratively closing the case. On September 4, 2020, an Order Preliminarily Approving Settlement was entered and a settlement hearing was held on December 15, 2020. We are awaiting the Court's final order approving the settlement.

On or about September 13, 2018, Idan Sharon filed an Application for Approval of a Class Action in the Tel Aviv Israel District Court against the Company and certain of its current and former executive officers, and certain members of its Board of Directors (the "Sharon Claim"). This application was filed by a purported stockholder, both individually and on behalf of a putative class of the Company's stockholders, claiming that in connection with the facts and circumstances underlying the allegations in the SEC Complaint, the Company engaged in fraudulent conduct and made false and misleading statements of material fact or omitted to state material facts necessary to make the statements made not misleading. The Sharon Claim seeks both to declare the action a class action and monetary damages. The Court closed this case pending resolution of the U.S.-based class actions relating to the allegations in the SEC Complaint. The Court has ordered plaintiff's counsel to update the court with respect to whether there has been a ruling in the U.S. class action matter by February 17, 2021.

On or about September 16, 2018, Dalia Avraham filed an Application for Approval of a Class Action in the Tel Aviv Israel District Court against the Company and Dr. Frost. This application was filed by a purported stockholder, both individually and on behalf of a putative class of the Company's stockholders (the "Avraham Claim"). The Avraham Claim alleges a negligent and/or deliberate act related to the trade of the Company's shares on the Tel Aviv Stock Exchange ("TASE") which was intended to or which in fact caused damage to the Company's investors based on the Company's decision to delist from TASE in April 2018 and its subsequent decision to continue to be listed on TASE. The Avraham Claim seeks to declare the action to be a class action and an estimated NIS 20 million (approximately USD $6.1 million) in damages. The parties have been asked to submit dates for a hearing on a motion to dismiss. We believe that this action is without merit and the Company intends to vigorously defend itself.

On October 2, 2018 Andy Yu ("Yu"), a purported stockholder, filed a shareholder derivative complaint in the United States District Court for the Southern District of Florida against the Company as a nominal defendant, certain of the Company's current and former executive officers, certain current and former members of its Board of Directors, and Frost Gamma Investments Trust (the "Yu Lawsuit"). The Yu Lawsuit alleged violations of the federal securities laws based on alleged false and misleading statements of material fact or omissions, breach of fiduciary duty based on the allegations raised by the SEC in the SEC Complaint, and unjust enrichment. Yu sought to maintain the action on behalf of the Company, alleging that he was a proper and adequate representative of the Company, and also sought to direct the Company to improve its corporate governance and internal procedures, monetary damages, restitution, an award of reasonable attorneys' fees and expert fees and other costs, and such additional or different relief as the Court may deem just and proper. Following the Settlement, the Yu Lawsuit was dismissed with prejudice on January 13, 2021.

On October 31, 2018, Lisette Demetriades ("Demetriades"), a purported stockholder, filed a shareholder derivative complaint in the United States District Court for the Southern District of Florida against the Company as a nominal defendant, certain of the Company's current and former executive officers, certain current and former members of its Board of Directors,

and Frost Gamma Investment Trust (the "Demetriades Lawsuit"). The Demetriades Lawsuit alleged violations of the federal securities laws based on alleged false and misleading statements of material fact or omissions, breach of fiduciary duty based on the allegations raised by the SEC in the SEC Complaint, and unjust enrichment. Demetriades sought to maintain the action on behalf of the Company, and alleged that he was a proper and adequate representative of the Company, and also sought to direct the Company to improve its corporate governance and internal procedures, monetary damages, restitution, an award of reasonable attorneys' fees and expert fees and other costs, and such additional or different relief as the Court may deem just and proper. Following the Settlement, a Joint Stipulation for Dismissal with Prejudice was filed on January 5, 2021 and the Demetriades Lawsuit was dismissed.

On September 27, 2018, Frank Lipsius ("Lipsius"), a purported stockholder, filed a shareholder derivative complaint in the Circuit Court of the Eleventh Judicial Circuit in and for Miami-Dade County, Florida against the Company as a nominal defendant, certain of the Company's current and former executive officers, and members of its Board of Directors (the "Lipsius Lawsuit"). This lawsuit was brought by Lipsius and alleged breach of fiduciary duty against the officers and directors named therein, based on the allegations raised by the SEC in the SEC Lawsuit that the Company made misleading statements, and based on a purported failure to maintain proper internal controls. Lipsius sought to maintain the action on behalf of the Company, alleged that he is a proper and adequate representative of the Company, and also sought to direct the Company to improve its corporate governance and internal procedures, monetary damages, restitution, an award of reasonable attorneys' fees and expert fees and other costs, and such additional or different relief as the Court may deem just and proper. Following the Settlement, a Joint Stipulation for Dismissal with Prejudice was filed on December 18, 2020 and the Lipsius Lawsuit was dismissed.

On or about November 2, 2018, Louis T. Alexander ("Alexander"), a purported stockholder, filed a shareholder derivative complaint in the Circuit Court of the Eleventh Judicial Circuit of Florida serving Miami-Dade County against the Company, as a nominal defendant, Dr. Frost, certain current and former members of the Company's Board of Directors and executive officers (the "Alexander Lawsuit"). This lawsuit alleged breach of fiduciary duty against the officers and directors named therein, based on the allegations raised by the SEC in the SEC Lawsuit that the Company made misleading statements, and based on a purported failure to maintain proper internal controls. Alexander sought to maintain the action on behalf of the Company, alleged that he was a proper and adequate representative of the Company, and also sought to direct the Company to improve its corporate governance and internal procedures, monetary damages, restitution, an award of reasonable attorneys' fees, and experts' fees, and other costs, and such other and further relief as the Court deems just and proper. Following the Settlement, a Joint Stipulation for Dismissal with Prejudice was filed on December 21, 2020 and the Alexander Lawsuit was dismissed.

On January 28, 2019, Robert Davydov ("Davydov"), a purported stockholder, filed a shareholder derivative complaint in the Circuit Court of the Eleventh Judicial Circuit of Florida serving Miami-Dade County against the Company as a nominal defendant and the certain members of its Board of Directors (the "Davydov Lawsuit"). The Davydov Lawsuit alleged breach of fiduciary duty based on the allegations raised by the SEC in the SEC Complaint, breach of the duties of care, loyalty and good faith, corporate waste and unjust enrichment. Davydov sought to maintain the action on behalf of the Company, alleged that he was a proper and adequate representative of the Company, and also sought a declaration that the defendants breached their fiduciary duties, an award of monetary damages, restitution, an award of reasonable attorneys' fees and expert witness fees and other costs, and such other and further equitable relief as the Court deems just and proper. Following the Settlement, a Joint Stipulation for Dismissal with Prejudice was filed on December 15, 2020 and the Davydov Lawsuit was dismissed.

On November 14, 2018, Sammy Lee ("Lee"), a purported stockholder, filed a shareholder derivative complaint in the United States District Court for the Southern District of Florida against the Company as a nominal defendant, Dr. Frost, Frost Gamma Investments Trust, an entity controlled by Dr. Frost, and certain of the Company's current and former executive officers, and current and former members of its Board of Directors (the "Lee Lawsuit"). The Lee Lawsuit alleged violations of the federal securities laws based on alleged false and misleading statements of material fact or omissions, breach of fiduciary duty based on the allegations raised by the SEC in the SEC Complaint, and unjust enrichment. Lee sought to maintain the action on behalf of the Company, alleged that he was a proper and adequate representative of the Company, and sought to direct the Company to improve its corporate governance and internal procedures, monetary damages, restitution, an award of reasonable attorneys' fees and expert fees and other costs, and such other and further relief as the Court may deem just and proper. The action was dismissed sua sponte by the Judge for failure to state a claim. An amended complaint was filed on November 30, 2018. Following the Settlement, a Joint Stipulation for Dismissal with Prejudice was filed and the Lee Lawsuit was dismissed on January 11, 2021.

On December 17, 2018, Thaddeus R. Sobieski and Donnis W. King, purported stockholders of the Company, filed a shareholder derivative complaint in the United States District Court for the Southern District of Florida against the Company as a nominal defendant, Dr. Frost, Frost Gamma Investments Trust, and certain of the Company's current and former executive officers, and current and former members of its Board of Directors (the "Sobieski King Lawsuit"). The Sobieski King Lawsuit

alleged breach of fiduciary duty based on the allegations raised by the SEC in the SEC Complaint, violations of the federal securities laws based on alleged false and misleading statements of material fact or omissions, unjust enrichment, and waste of corporate assets. The lawsuit sought to declare that the action was a proper derivative action, a declaration that defendants breached their fiduciary duties, monetary damages, current and former directors to remit all salaries and other compensation received during the period of alleged breach of fiduciary duties, to have the Company improve its corporate governance and internal procedures, an award of pre-judgement and post- judgement interest, reasonable attorneys' fees, experts' fees, costs and expenses, and such other and further relief as the Court may deem just and proper. Following the Settlement, the Sobieski King Lawsuit was dismissed with prejudice on January 7, 2021.

On December 31, 2018, Connie Wendt ("Wendt"), a purported stockholder, filed a shareholder derivative complaint in the United States District Court for the Southern District of Florida against the Company as a nominal defendant, certain of its current and former executive officers, certain current and former members of its Board of Directors, Frost Gamma Investments Trust, and certain other individuals and an entity named in the SEC Complaint (the "Wendt Lawsuit"). The Wendt Lawsuit alleged breach of fiduciary duty based on the allegations raised by the SEC in the SEC Complaint, breach of duty of loyalty, breach of fiduciary duty for insider selling and misappropriation of information, unjust enrichment, and violations of the federal securities laws. Wendt sought to maintain the action on behalf of the Company, alleged that she was a proper and adequate representative of the Company, and sought a declaration that each of the Company's named officers and directors breached their fiduciary duties to the Company, monetary damages, disgorgement of alleged profits, an award of costs and disbursements including reasonable attorneys' fees, accountants' and experts' fees and costs and expenses, and such other and further relief as the Court deems just and proper. Following the Settlement, the Wendt Lawsuit was dismissed with prejudice on December 18, 2020.

Between October 2018 and January 2019, five shareholder derivative complaints were filed by purported stockholders in the Delaware Court of Chancery against the Company as a nominal defendant, Dr. Frost and the Company's Board of Directors. In the first quarter of 2019, the five lawsuits were consolidated into *In re OPKO Health, Inc. Derivative Action*, Case No. 2018-0740-SG (the "Consolidated Delaware Action"). On February 11, 2019, a Verified Consolidated Derivative Complaint was filed in the Consolidated Delaware Action, and Richard Tunick, Jamie Gewirtz, Emily Gewirtz Stiebel, Esther Susan Lutzker and Ivan Pawlenko were named as Co-Lead Plaintiffs in the filing. The Consolidated Derivative Complaint alleged breach of fiduciary duty based on the allegations raised by the SEC in the SEC Complaint, and breach of the duty of loyalty. The lead plaintiffs sought to declare the action a proper derivative action, monetary damages, disgorgement of all remuneration during the relevant time period, to direct the Company to improve its internal controls, equitable and injunctive relief, pre- and post-judgment interest, an award of reasonable attorneys' fees and expert fees, and such other and further relief as the Court deemed just and proper. The Settlement was approved on November 2, 2020.

On April 8, 2019, MabVax Therapeutics Holdings, Inc. filed a lawsuit in the Superior Court of California, County of San Diego against a number of individuals and entities, including the Company, Dr. Frost, Steven Rubin, the Company's Executive Vice President-Administration, and an entity affiliated with Dr. Frost, based on the allegations raised in the SEC Complaint. The lawsuit seeks an award for actual and punitive damages, pre- and post-judgment interest; that the defendants be required to make full disclosure and accounting of their interests and transactions in plaintiff's securities; costs of the suit, and reasonable attorney's fees; and such other legal and equitable relief as the Court may deem proper under the circumstances. The Company, Dr. Frost, Mr. Rubin and the Frost-affiliated entity have filed a motion to quash the complaint for lack of personal jurisdiction, which remains pending. The Company believes the allegations against the Company, Dr. Frost and Mr. Rubin are without merit and intends to vigorously defend against the claims.

On April 5, 2019, former shareholders of Claros Diagnostics, Inc. filed a complaint in the Chancery Court of Delaware against the Company, alleging among other things, that the Company breached the Agreement and Plan of Merger dated October 13, 2011 by and among the Company, Claros Merger Subsidiary, LLC and Claros Diagnostics, Inc. (the "Merger Agreement"): (i) by failing to make a milestone payment of $2.375 million (payable in OPKO Common Stock) upon obtaining FDA approval of the Claros PSA test; and (ii) by repudiating its obligations to make additional future milestone payments as required under the Merger Agreement. In January 2021, the Company and the shareholder representative entered into a settlement agreement providing, among other things, that it pay the shareholders $1.1875 million, which amount is equal to half the initial milestone payable under the Merger Agreement. A Stipulation of Dismissal With Prejudice has been filed with the Court.

On or about February 3, 2021 BioReference received correspondence from the US Department of Labor ("US DOL") stating that it would be conducting a Wage and Hour investigation for the Genpath division for the span of 2019 and 2020 and was seeking records related to same including gross sales, employee roster information, comprehensive payroll and time-log records, and 1099 forms and contract records for independent contractors and subcontractors. On February 15, 2021, BioReference received a Subpoena from the NJ Department of Labor ("NJ DOL") seeking similar information for the time time period as the US DOL inquiry for BioReference, as well as information related to unemployment and disability taxes,

workmen's compensation, and records related to earned sick leave, and financial information. It is uncertain at this time whether the two matters are interrelated and the Company can express no opinion as to the likelihood of an unfavorable outcome or range of potential loss regarding this matter. BioReference is currently gathering the requested information.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

PART II

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

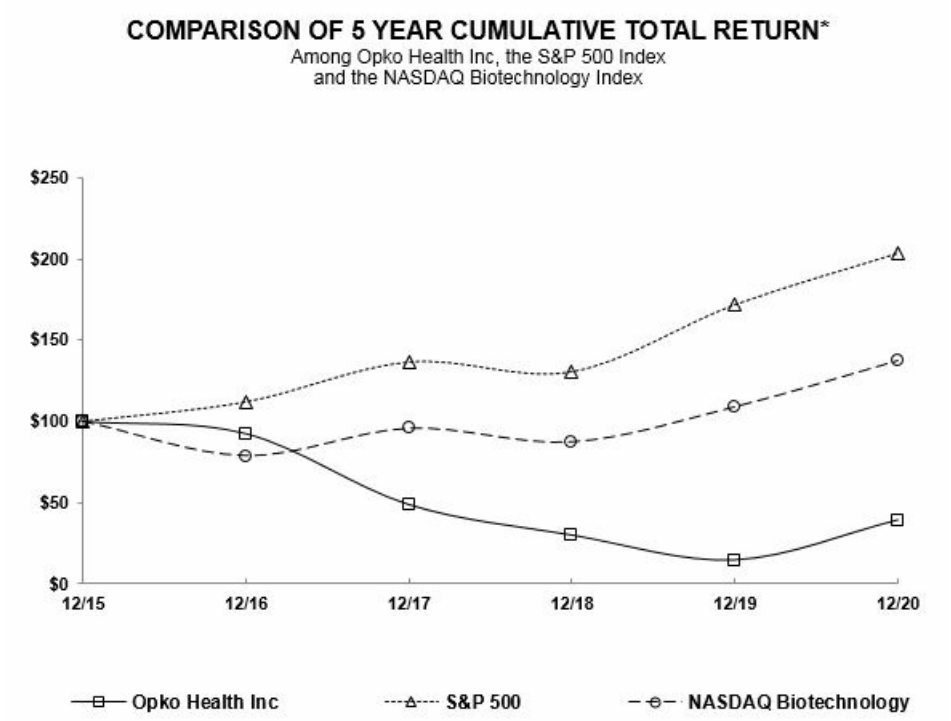
Our Common Stock is traded publicly on the NASDAQ Stock Market ("NASDAQ") and the Tel Aviv Stock Exchange under the symbol "OPK".

As of February 8, 2021, there were approximately 402 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 2021. We repurchased no shares of Common Stock during the fourth quarter of the year ended December 31, 2020.

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, 2015 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.



	12/31/2015	12/31/2016	12/31/2017	12/31/2018	12/31/2019	12/31/2020
OPKO Health, Inc.	$ 100.00	$ 92.54	$ 48.76	$ 29.95	$ 14.63	$ 39.30
S&P 500	100.00	111.96	136.40	130.42	171.49	203.04
NASDAQ Biotechnology	100.00	78.65	95.67	87.19	109.08	137.90

Recent Sales of Unregistered Securities

All recent sales of unregistered securities were previously reported in a Current Report on Form 8-K or Quarterly Report on Form 10-Q.

ITEM 6. Selected Financial Data.

Not applicable.

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

This Annual Report on Form 10-K contains 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 and prospects. You can identify forward-looking statements by the fact that these statements do not relate 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 except as required by applicable law. We intend that all forward-looking statements be subject to the safe harbor provisions of PSLRA. These forward-looking statements reflect our views only as of the date they are made.

OVERVIEW

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, Inc. ("BioReference"), one of the nation's largest full service laboratories with a core genetic testing business and an almost 300-person sales and marketing team focused on driving growth and leveraging new products, including the *4Kscore* test. Our pharmaceutical business features *Rayaldee*, a, U.S. Food and Drug Administration ("FDA") approved treatment for secondary hyperparathyroidism ("SHPT") in adults with stage 3 or 4 chronic kidney disease ("CKD") and vitamin D insufficiency (launched in November 2016) and a pipeline of products in various stages of development. Our leading product in development is hGH-CTP (Somatrogon), a once-weekly human growth hormone for which we have partnered with Pfizer Inc. ("Pfizer"). We have submitted the initial Biologics License Application ("BLA") with FDA for approval of Somatrogon in the U.S. as well as a New Drug Application with the Ministry of Health, Labour and Welfare in Japan. We are incorporated in Delaware, and our principal executive offices are located in leased offices in Miami, Florida.

Through BioReference, we provide laboratory testing services, primarily to customers in the larger metropolitan areas in New York, New Jersey, Florida, Texas, Maryland, California, Pennsylvania, Delaware, Washington, DC, Illinois and Massachusetts, as well as to customers in a number of other states. We offer a comprehensive test menu of clinical diagnostics for blood, urine and tissue analysis. This includes hematology, clinical chemistry, immunoassay, infectious diseases, serology, hormones, and toxicology assays, as well as Pap smear, anatomic pathology (biopsies) and other types of tissue analysis. We market our laboratory testing services directly to physicians, geneticists, hospitals, clinics, correctional and other health facilities.

We operate established pharmaceutical platforms in Ireland, Chile, Spain, 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. In addition, we have a development and commercial supply pharmaceutical company and a global supply chain operation and holding company in Ireland. We 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.

RECENT DEVELOPMENTS

In January 2021, we announced that the FDA had accepted for filing the initial BLA for Somatrogon, a long-acting human growth hormone that is intended to be administered once-weekly for the treatment of pediatric patients with growth hormone deficiency ("GHD"). The target Prescription Drug User Fee Act (PDUFA) action date for decision by the FDA is in October 2021.

In December, 2020, we announced the appointment of Roger Medel, M.D. as an independent member of our Board of Directors, effective December 18, 2020. With this appointment, we have 11 Directors, including seven independent Directors.

RESULTS OF OPERATIONS

Impact of COVID-19

As the disease caused by SARS-CoV-2, a novel strain of coronavirus, COVID-19 continues to spread and severely impact the economy of the U.S. and other countries around the world, we are committed to being a part of the coordinated public and private sector response to this unprecedented challenge. In response to the COVID-19 pandemic, BioReference is accepting specimens from U.S. healthcare providers, clinics and health and hospital systems for two types of COVID-19 testing, diagnostic molecular testing and serology antibody testing, which is intended to promote earlier diagnosis of the coronavirus, assess a patient's immune response to the virus and aid in limiting the spread of infection.

We have put preparedness plans in place at our facilities to maintain continuity of operations, while also taking steps to keep our employees and customers healthy and safe. In line with recommendations to reduce large gatherings and increase social distancing, we have, where practical, transitioned many office-based employees to a remote work environment.

Revenue from services for the year ended December 31, 2020 increased by $545.8 million as compared to 2019, due to COVID-19 testing volumes; however we are unable to predict how long demand will continue for our COVID-19 related testing, or whether pricing and reimbursement policies for testing will sustain, and accordingly, the sustainability of our COVID-19 testing volumes is uncertain. Additionally, beginning in March 2020, BioReference experienced, and continues to experience, a decline in routine clinical and genomics testing volumes due to the COVID-19 pandemic. Excluding COVID-19 test volumes, for the year ended December 31, 2020, volumes in our diagnostics segment declined 17% as compared to volumes for the year ended December 31, 2019. Additionally, sales of *Rayaldee* have not increased in accordance with its expected growth trajectory as a result of challenges in onboarding new patients due to the COVID-19 pandemic. Federal, state and local governmental policies and initiatives designed to reduce the transmission of COVID-19 have resulted in, among other things, a significant reduction in physician office visits, the cancellation of elective medical procedures, customers closing or severely curtailing their operations (voluntarily or in response to government orders), and the adoption of work-from-home or shelter-in-place policies. As stay at home orders and other restrictions have been lifted, we have seen our routine clinical and genomic testing volumes trending towards normalization with prior periods, however should stay at home orders or other restrictions be reenacted, we could see our routine testing levels decline. We also continue to see a substantial need for COVID-19 testing by our existing clients and expect new clients as infection rates for the virus continue to increase across the country.

In March 2020, in response to the COVID-19 pandemic, the Coronavirus Aid, Relief, and Economic Security (CARES) Act was signed into law. The CARES Act provides numerous tax provisions and other stimulus measures, including temporary changes regarding the prior and future utilization of net operating losses, temporary changes to the prior and future limitations on interest deductions, temporary suspension of certain payment requirements for the employer portion of Social Security taxes, technical corrections from prior tax legislation for tax depreciation of certain qualified improvement property, and the creation of certain payroll tax credits associated with the retention of employees.

We have received, or expect to receive a number of benefits under The CARES Act including, but not limited to:

- During the year ended December 31, 2020, we received approximately $14 million under The Centers for Medicare & Medicaid Services (CMS) Accelerated and Advance Payment Program, which provides accelerated payments to Medicare providers/suppliers working to provide treatment to patients and combat the COVID-19 pandemic, and such amounts advanced to us are loans which will be offset against future claims and must be repaid in 2021;
- We are eligible to defer depositing the employer's share of Social Security taxes for payments due from March 27, 2020 through December 31, 2020, interest-free and penalty-free;
- We received approximately $16.2 million during the year ended December 31, 2020 from the funds that were distributed to healthcare providers for related expenses or lost revenues that are attributable to the COVID-19 pandemic;
- U.S. Department of Health and Human Services (HHS), will provide claims reimbursement to healthcare providers generally at Medicare rates for testing uninsured patients; and
- Clinical laboratories are provided a one-year reprieve from the reporting requirements under the Protecting Access to Medicare Act ("PAMA") as well as a one-year delay of reimbursement rate reductions for clinical laboratory services provided under Medicare that were scheduled to take place in 2021.

In October 2020, the U.S. Department of Health & Human Services issued new reporting requirements for the CARES Act funding. Due to these new reporting requirements and various interpretations, there is a reasonable possibility that amounts recorded under CARES Act funding will change in future periods.

For The Years Ended December 31, 2020 and December 31, 2019

Our consolidated income (loss) from operations for the years ended December 31, 2020 and 2019 is as follows:

	For the years ended December 31,			
(In thousands)	2020	2019	Change	% Change
Revenues:				
Revenue from services	$ 1,262,242	$ 716,434	$ 545,808	76 %
Revenue from products	119,952	112,184	7,768	7 %
Revenue from transfer of intellectual property and other	53,219	73,317	(20,098)	(27)%
Total revenues	1,435,413	901,935	533,478	59 %
Costs and expenses:				
Cost of revenue	894,408	572,484	321,924	56 %
Selling, general and administrative	355,573	343,305	12,268	4 %
Research and development	75,316	117,870	(42,554)	(36)%
Contingent consideration	(3,989)	(14,854)	10,865	(73)%
Amortization of intangible assets	56,391	64,783	(8,392)	(13)%
Asset impairment charges	—	92,399	(92,399)	(100)%
Total costs and expenses	1,377,699	1,175,987	201,712	17 %
Income (loss) from operations	57,714	(274,052)	331,766	(121)%

We manage our operations in two reportable segments, pharmaceuticals and diagnostics. The pharmaceuticals segment consists of our pharmaceutical operations in Latin America, Ireland, Israel and Spain, *Rayaldee* product sales and our pharmaceutical research and development. The diagnostics segment primarily consists of our clinical and genetic laboratory operations through BioReference and GeneDx as well as our point-of-care operations. There are no significant inter-segment sales. We evaluate the performance of each segment based on operating profit or loss. The following presents the financial measures that management considers to be the most significant indicators of the Company's performance.

Diagnostics

	For the years ended December 31,			
(In thousands)	2020	2019	Change	% Change
Revenues				
Revenue from services	$ 1,262,242	$ 716,434	545,808	76 %
Revenue from transfer of intellectual property and other	16,240	—	16,240	100 %
Total revenues	1,278,482	716,434	562,048	78 %
Costs and expenses:				
Cost of revenue	823,927	510,857	313,070	61 %
Selling, general and administrative	266,488	242,020	24,468	10 %
Research and development	15,003	14,219	784	6 %
Contingent consideration	(2,066)	(8,401)	6,335	(75)%
Amortization of intangible assets	36,208	42,401	(6,193)	(15)%
Asset impairment charges	—	38,697	(38,697)	(100)%
Total costs and expenses	1,139,560	839,793	299,767	36 %
Income (loss) from operations	138,922	(123,359)	262,281	(213)%

Revenue. Revenue from services for the year ended December 31, 2020 increased by approximately $545.8 million compared to the year ended December 31, 2019, due to COVID-19 testing volumes. BioReference performed 0.8 million serology antibody tests and 10.1 million diagnostic molecular tests for COVID-19 during the year ended December 31, 2020, which represented 57% of total testing volume. Revenue attributable to tests for COVID-19 was partially offset by the negative impacts of:

- A reduction in clinical test volumes and genomic test volumes at BioReference resulted in decreased revenues of $99.5 million and $15.6 million, respectively, as compared to the year ended December 31, 2019. The decline in routine clinical and genomic testing volume reflects negative impacts from the COVID-19 pandemic, principally from referring physician office closures and stay-at-home guidance throughout states in which we predominately operate.
- A reduction in clinical test and genomic test reimbursement at BioReference of $10.2 million and $27.6 million, respectively, as compared to the year ended December 31, 2019. The lower reimbursement within our clinical business was primarily the result of the negative impact of the PAMA price reduction that went into effect January 1, 2020 combined with an overall shift in our test mix that was partially offset by increased reimbursement of our *4KScore* test. The lower reimbursement within our genomic business resulted from an increase in denial rates and changes to payor policy and procedural requirements.

Estimated collection amounts are subject to the complexities and ambiguities of billing, reimbursement regulations and claims processing, as well as considerations unique to Medicare and Medicaid programs, and require us to consider the potential for retroactive adjustments when estimating variable consideration in the recognition of revenue in the period the related services are rendered. Revenue from services for the year ended December 31, 2020 included $12.1 million related to the successful appeal of previously denied claims for the *4Kscore* test. In addition, the year ended December 31, 2020 included positive revenue adjustments recognized due to changes in estimates of implicit price concessions for performance obligations satisfied in prior periods of $0.3 million, and for the year ended December 31, 2019, revenue reductions of $24.8 million were recognized due to changes in estimates of implicit price concessions for performance obligations satisfied in prior periods.

The composition of Revenue from services by payor for the years ended December 31, 2020 and 2019 was as follows:

	For the years ended December 31,	
(In thousands)	2020	2019
Healthcare insurers	$ 483,643	$ 421,386
Government payers	90,288	115,711
Client payers	637,645	158,527
Patients	50,666	20,810
Total	$ 1,262,242	$ 716,434

Client payers include cities, states and companies for which BioReference provides COVID-19 testing services.

Revenue from the transfer of intellectual property and other for the year ended December 31, 2020 are the result of grants received under the CARES Act totaling $16.2 million.

Cost of revenue. Cost of revenue for the year ended December 31, 2020 increased $313.1 million compared to the year ended December 31, 2019. Cost of revenue increased primarily due to labor and material costs for COVID-19 testing and the significant volume of tests performed during the year ended December 31, 2020, partially offset by a decline in non-COVID testing volumes and to cost reduction initiatives leading to a 12.4% improvement in cost per patient encounter, inclusive of all volumes.

Selling, general and administrative expenses. Selling, general and administrative expenses for the years ended December 31, 2020 and 2019 were $266.5 million and $242.0 million, respectively. Selling, general and administrative expenses in our diagnostics segment increased primarily due to higher variable billing and compensation costs of $23.2 million from an increase in volume and collections during the year ended December 31, 2020 and $3.0 million in marketing costs and other administrative and marketing costs directly associated the COVID-19 PCR testing volumes. In comparison, the December 31, 2019 period included $12.6 million of expense related to the Department of Justice settlement. As a percentage of net revenue SG&A for the diagnostic segment decreased to 21% from 34%, for the years ended December 31, 2020 and 2019, respectively as a result of per requisition efficiencies and expense management during this recent period of rapid volume growth. Selling, general and administrative expenses for the diagnostics segment for the years ended December 31, 2020 and 2019 included equity-based compensation expense of $2.1 million and $2.2 million, respectively.

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

Research and Development Expenses	For the years ended December 31,	
	2020	2019
External expenses:		
PMA studies	$ 218	$ 774
Research and development employee-related expenses	9,317	7,320
Other internal research and development expenses	5,468	6,125
Total research and development expenses	$ 15,003	$ 14,219

Research and development for the diagnostic segment relates to the development of testing services for our clinical and genomics testing at BioReference and the development of the Claros Analyzer, a diagnostic instrument system to provide rapid, high performance blood test results in the point-of-care setting. The increase in research and development expenses for the year ended December 31, 2020 resulted primarily from an increased research and development expenses related to the development of clinical and genomics testing services.

Contingent consideration. Contingent consideration for the years ended December 31, 2020 and 2019 was $(2.1) million of expense and $8.4 million reversal of expense, respectively. Contingent consideration for the years ended December 31, 2020 and 2019 was attributable to changes in assumptions regarding the timing of achievement of future milestones for OPKO Diagnostics in both periods, and potential amounts payable to former stockholders of OPKO Diagnostics in connection therewith, pursuant to our acquisition agreement in October 2011.

Amortization of intangible assets. Amortization of intangible assets was $36.2 million and $42.4 million, respectively, for the years ended December 31, 2020 and 2019. Amortization expense reflects the amortization of acquired intangible assets with defined useful lives.

Asset impairment charges. Asset impairment charges were $38.7 million for the year ended December 31, 2019. Asset impairment charges for the year ended December 31, 2019 is primarily related to a goodwill impairment charge of $18.0 million to write the carrying amount of the OPKO Diagnostics reporting unit down to its estimated fair value, and an impairment charge of $20.7 million to write our intangible asset for the Claros Analyzer down to its estimated fair value. The asset impairment charges for the year ended December 31, 2019, resulted from liquidity constraints, longer than expected development timelines and changes in the competitive landscape, which resulted in changes to our estimates and assumptions of the expected future cash flows associated with the Claros Analyzer.

We believe that our estimates and assumptions in testing goodwill and other intangible assets are consistent with assumptions that marketplace participants would use in their estimates. However, if actual results are not consistent with our estimates and assumptions, including as a result of the COVID-19 global pandemic, we may be exposed to an impairment charge that could be material.

Pharmaceuticals

(In thousands)	For the years ended December 31, 2020	2019	Change	% Change
Revenues:				
Revenue from products	$ 119,952	$ 112,184	$ 7,768	7 %
Revenue from transfer of intellectual property and other	36,979	72,521	(35,542)	(49)%
Total revenues	156,931	184,705	(27,774)	(15)%
Costs and expenses:				
Cost of revenue	70,565	61,888	8,677	14 %
Selling, general and administrative	50,476	57,589	(7,113)	(12)%
Research and development	61,149	104,659	(43,510)	(42)%
Contingent consideration	(1,923)	(6,453)	4,530	(70)%
Amortization of intangible assets	20,183	22,382	(2,199)	(10)%
Asset impairment charges	—	53,702	(53,702)	(100)%
Total costs and expenses	200,450	293,767	(93,317)	(32)%
Loss from operations	(43,519)	(109,062)	65,543	(60)%

Revenue. The increase in revenue from products for the year ended December 31, 2020 compared to the year ended December 31, 2019 was primarily attributable to an increase in sales at OPKO Chile and an increase in sales of *Rayaldee.* Sales of *Rayaldee* were $36.8 million for the year ended December 31, 2020, as compared to $31.4 million for 2019. Revenue from transfer of intellectual property for the years ended December 31, 2020 and 2019 principally reflected $28.7 million and $66.8 million, respectively, of revenue related to the Pfizer Transaction. Revenue from transfer of intellectual property for the year ended December 31, 2020 also included a $3 million milestone payment triggered by the first marketing approval of *Rayaldee* in Europe.

Cost of revenue. Cost of revenue for the year ended December 31, 2020 increased $8.7 million compared to the year ended December 31, 2019. Cost of product revenue increased primarily due to an increase in sales at OPKO Chile and changes in product mix during the year ended December 31, 2020.

Selling, general and administrative expenses. Selling, general and administrative expenses for the years ended December 31, 2020 and 2019 were $50.5 million and $57.6 million, respectively. The decrease in selling, general and administrative expenses was primarily due to decreased expenses at our pharmaceutical subsidiaries and a decrease in equity-based compensation expense. Selling, general and administrative expenses for the pharmaceutical segment for the years ended December 31, 2020 and 2019 included equity-based compensation expense of $1.0 million and $2.0 million, respectively.

Research and development expenses. Research and development expenses for the years ended December 31, 2020 and 2019 were $61.1 million and $104.7 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 for phase 3 clinical trials for drug approval and premarket approval for diagnostics tests, if any. Internal expenses include employee-related expenses such as salaries, benefits and equity-based compensation expense. Other 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:

Research and Development Expenses	For the years ended December 31,	
	2020	2019
External expenses:		
Manufacturing expense for biological products	$ 5,326	$ 38,592
Phase III studies	10,513	16,869
Post-marketing studies	1,270	2,019
Earlier-stage programs	14,811	21,201
Research and development employee-related expenses	21,931	22,023
Other internal research and development expenses	9,440	8,813
Third-party grants and funding from collaboration agreements	(2,142)	(4,858)
Total research and development expenses	$ 61,149	$ 104,659

The decrease in research and development expenses for the year ended December 31, 2020 was primarily due to a decrease in research and development expenses related to Somatrogon, a once-weekly human growth hormone injection for which we have partnered with Pfizer and successfully completed a phase 3 study in August 2019. Ongoing expenses for the Somatrogon program support open label extension studies that will continue until the market launch of Somatrogon in certain countries, as well as the preparation of applications for marketing approvals. Research and development expenses for the pharmaceutical segment for the years ended December 31, 2020 and 2019 included equity-based compensation expense of $1.6 million and $2.1 million, respectively.

Contingent consideration. Contingent consideration for the years ended December 31, 2020 and 2019 was $1.9 million and $6.5 million reversal of expense, respectively. Contingent consideration for the years ended December 31, 2020 and 2019 was primarily attributable to changes in assumptions regarding the timing of achievement of future milestones for OPKO Renal, and potential amounts payable to former stockholders of OPKO Renal in connection therewith, pursuant to our acquisition agreement in March 2013.

Amortization of intangible assets. Amortization of intangible assets was $20.2 million and $22.4 million, respectively, for the years ended December 31, 2020 and 2019. Amortization expense reflects the amortization of acquired intangible assets with defined useful lives. Our indefinite lived IPR&D assets will not be amortized until the underlying development programs are completed. Upon obtaining regulatory approval by the U.S. FDA, the IPR&D assets will be accounted for as a finite-lived intangible asset and amortized on a straight-line basis over its estimated useful life.

Asset impairment charges. Asset impairment charges were $53.7 million for the year ended December 31, 2019. Asset impairment charges for the year ended December 31, 2019 were primarily related to an impairment charge of $44.8 million to write our IPR&D assets for OPK88003 (oxyntomodulin) and CURNA's platform technology for oligonucleotide therapeutics down to their estimated fair values, and a goodwill impairment charge of $8.2 million to write the carrying amount of the CURNA and Transition Therapeutics reporting units down to their estimated fair values. The Asset impairment charges for the year ended December 31, 2019, resulted from liquidity constraints, longer than expected development timelines and changes in the competitive landscape, which resulted in changes to our estimates and assumptions of the expected future cash flows associated with OPK88003 and CURNA's platform technology.

We believe that our estimates and assumptions in testing goodwill and other intangible assets, including IPR&D, for impairment are consistent with assumptions that marketplace participants would use in their estimates. However, if actual results are not consistent with our estimates and assumptions, including as a result of the COVID-19 global pandemic, we may be exposed to an impairment charge that could be material. If we are unable to successfully develop Somatrogon, or changes in projections and assumptions negatively impact our forecast of net cash flows, we may be exposed to a material impairment charge related to the IPR&D for Somatrogon.

Corporate

(In thousands)	For the years ended December 31, 2020	2019	Change	% Change
Revenues:				
Revenue from transfer of intellectual property and other	$ —	$ 796	(796)	(100)%
Total revenues	—	796	(796)	(100)%
Costs and expenses:				
Cost of revenue	(84)	(261)	177	(68)%
Selling, general and administrative	38,609	43,696	(5,087)	(12)%
Research and development	(836)	(1,008)	172	(17)%
Total costs and expenses	37,689	42,427	(4,738)	(11)%
Loss from operations	(37,689)	(41,631)	3,942	(9)%

Operating loss for our unallocated corporate operations for the years ended December 31, 2020 and 2019 was $37.7 million and $41.6 million, respectively, and principally reflects general and administrative expenses incurred in connection with our corporate operations. The decrease in operating loss for the year ended December 31, 2020 was primarily attributable to a decrease in legal fees incurred for the year ended December 31, 2020, as compared to the year ended December 31, 2019.

Other

Interest income. Interest income for the years ended December 31, 2020 and 2019 was not significant as our cash investment strategy emphasizes the security of the principal invested and fulfillment of liquidity needs.

Interest expense. Interest expense for the years ended December 31, 2020 and 2019 was $21.9 million and $21.5 million, respectively. Interest expense was principally related to interest incurred on our Senior Convertible Notes due 2025 (the "2025 Notes"), our 5% Convertible Promissory Notes (the "2023 Convertible Notes"), our 3.0% Senior Notes due 2033 (the "2033 Senior Notes"), and BioReference's outstanding debt under its credit facility.

Fair value changes of derivative instruments, net. Fair value changes of derivative instruments, net for the years ended December 31, 2020 and 2019, was $50 thousand and $174 thousand of income, respectively. Derivative income for the year ended December 31, 2020, was principally related to the change in fair value on foreign currency forward exchange contracts at OPKO Chile.

Other income (expense), net. Other income (expense), net for the years ended December 31, 2020 and 2019, was $12.7 million of income and $11.3 million of expense, respectively. Other income for the year ended December 31, 2020 primarily consisted of realized and unrealized gains recognized during the period on our investment in VBI Vaccines Inc. ("VBI"), offset by net unrealized losses recognized during the period on our investment in Eloxx Pharmaceuticals, Inc. ("Eloxx"). Other expense for the year ended December 31, 2019 primarily consisted of net unrealized losses recognized during the period on Eloxx and VBI.

Income tax provision. Our income tax provision for the years ended December 31, 2020 and 2019 was $17.6 million and $7.1 million, respectively, and reflects results using our expected effective tax rate. For the year ended December 31, 2020, the tax rate differed from the U.S. federal statutory rate of 21% primarily due to the relative mix in earnings and losses in the U.S. versus foreign tax jurisdictions, the impact of certain discrete tax events and operating results in tax jurisdictions that do not result in a tax benefit.

Loss from investments in investees. We have made investments in certain early stage companies that we perceive to have valuable proprietary technology and significant potential to create value for us as a shareholder or member. 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 report net losses. Loss from investments in investees was $0.5 million and $2.9 million for the years ended December 31, 2020 and 2019, respectively.

For The Years Ended December 31, 2019 and December 31, 2018

Our consolidated loss from operations for the years ended December 31, 2019 and 2018 is as follows:

	For the years ended December 31,			
(In thousands)	2019	2018	Change	% Change
Revenues:				
Revenue from services	$ 716,434	$ 813,248	$ (96,814)	(12)%
Revenue from products	112,184	107,112	5,072	5 %
Revenue from transfer of intellectual property and other	73,317	69,906	3,411	5 %
Total revenues	901,935	990,266	(88,331)	(9)%
Costs and expenses:				
Cost of revenue	572,484	604,636	(32,152)	(5)%
Selling, general and administrative	343,305	358,346	(15,041)	(4)%
Research and development	117,870	125,586	(7,716)	(6)%
Contingent consideration	(14,854)	(16,816)	1,962	(12)%
Amortization of intangible assets	64,783	67,933	(3,150)	(5)%
Asset impairment charges	92,399	21,778	70,621	324 %
Total costs and expenses	1,175,987	1,161,463	14,524	1 %
Loss from operations	(274,052)	(171,197)	(102,855)	60 %

Diagnostics

	For the years ended December 31,			
(In thousands)	2019	2018	Change	% Change
Revenues				
Revenue from services	$ 716,434	$ 813,248	(96,814)	(12)%
Total revenues	716,434	813,248	(96,814)	(12)%
Costs and expenses:				
Cost of revenue	510,857	546,305	(35,448)	(6)%
Selling, general and administrative	242,020	254,330	(12,310)	(5)%
Research and development	14,219	14,637	(418)	(3)%
Contingent consideration	(8,401)	(1,907)	(6,494)	341 %
Amortization of intangible assets	42,401	44,825	(2,424)	(5)%
Asset impairment charges	38,697	—	38,697	100 %
Total costs and expenses	839,793	858,190	(18,397)	(2)%
Loss from operations	(123,359)	(44,942)	(78,417)	174 %

Revenue from services for the year ended December 31, 2019 decreased approximately $96.8 million compared to the year ended December 31, 2018. Revenue from services for the year ended December 31, 2019 was negatively affected by $49.2 million of decreased reimbursement for our clinical testing and by $21.2 million from our genomics testing, as a result of an increase in denial rates and changes to payor pricing, policy and procedural requirements, the impact of PAMA, and a decline in *4Kscore* revenue due to the non-coverage decision issued by Novitas, which became effective on March 21, 2019. Subsequent to the effective date of the non-coverage determination, in November 2019, Novitas issued its final LCD for Medicare payments for the *4Kscore* test, effective December 30, 2019. Under the final LCD, Medicare will reimburse the test for patients who meet defined criteria.

Revenue from services for the year ended December 31, 2019 was also negatively affected by $13.8 million as a result of a reduction in clinical test volumes, which was offset by higher genomics testing volume of $13.0 million.

Estimated collection amounts are subject to the complexities and ambiguities of billing, reimbursement regulations and claims processing, as well as considerations unique to Medicare and Medicaid programs, and require us to consider the potential for retroactive adjustments when estimating variable consideration in the recognition of revenue in the period the related services are rendered. For the years ended December 31, 2019 and 2018, we recognized revenue reductions due to

changes in estimates of implicit price concessions for performance obligations satisfied in prior periods of $24.8 million and $22.8 million, respectively.

We may have an obligation to reimburse Medicare, Medicaid, and third-party payors for overpayments regardless of fault. We have periodically identified and reported overpayments, reimbursed payors for overpayments and taken what we believe to be appropriate corrective action. Settlements with third-party payors for retroactive adjustments due to audits, reviews or investigations are considered variable consideration and are included in the determination of the estimated transaction price for providing services. These settlements are estimated based on the terms of the payment agreement with the payor, correspondence from the payor and our historical settlement activity, including an assessment of the probability a significant reversal of cumulative revenue recognized will occur when the uncertainty is subsequently resolved. Estimated settlements are adjusted in future periods as adjustments become known (that is, new information becomes available), or as years are settled or are no longer subject to such audits, reviews, and investigations. For the years ended December 31, 2019 and 2018, Revenue from services was reduced by approximately $2.6 million and $8.1 million, respectively, related to claims of overpayment.

The composition of Revenue from services by payor for the years ended December 31, 2019 and 2018 is as follows:

	For the years ended December 31,	
(In thousands)	2019	2018
Healthcare insurers	$ 421,386	$ 492,995
Government payors	115,711	150,851
Client payors	158,527	148,070
Patients	20,810	21,332
Total	$ 716,434	$ 813,248

Costs of revenue. Costs of revenue for the year ended December 31, 2019 decreased $35.4 million compared to 2018. Cost of service revenue decreased in 2019 primarily due to cost reduction initiatives resulting in per patient encounter efficiency gains at BioReference.

Selling, general and administrative expenses. Selling, general and administrative expenses for the years ended December 31, 2019 and 2018 were $242.0 million and $254.3 million, respectively. The decrease in selling, general and administrative expenses was primarily due to decreased expenses at BioReference due to enacting cost reduction initiatives, which were partially offset by $12.6 million of expenses incurred in connection with certain legal matters. Selling, general and administrative expenses for the years ended December 31, 2019 and 2018 included equity-based compensation expense of $2.2 million and $2.8 million, respectively.

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

Research and Development Expenses	For the years ended December 31,	
	2019	2018
External expenses:		
PMA studies	$ 774	$ —
Research and development employee-related expenses	7,320	7,725
Other internal research and development expenses	6,125	6,912
Total research and development expenses	$ 14,219	$ 14,637

Research and development for the diagnostic segment relates to the development of testing services for our clinical and genomics testing at BioReference and the development of the Claros Analyzer, a diagnostic instrument system to provide rapid, high performance blood test results in the point-of-care setting. Research and development expenses for the year ended December 31, 2019 were consistent with research and development expenses for the year ended December 31, 2018.

Contingent consideration. Contingent consideration for the years ended December 31, 2019 and 2018 was $8.4 million and $1.9 million reversal of expense, respectively. Contingent consideration for the years ended December 31, 2019 and 2018 was attributable to changes in assumptions regarding the timing of achievement of future milestones for OPKO Diagnostics in

both periods, and potential amounts payable to former stockholders of OPKO Diagnostics in connection therewith, pursuant to our acquisition agreement in October 2011.

Amortization of intangible assets. Amortization of intangible assets was $42.4 million and $44.8 million, respectively, for the years ended December 31, 2019 and 2018. Amortization expense reflects the amortization of acquired intangible assets with defined useful lives.

Asset impairment charges. Asset impairment charges were $38.7 million for the year ended December 31, 2019. Asset impairment charges for the year ended December 31, 2019 is primarily related to a goodwill impairment charge of $18.0 million to write the carrying amount of the OPKO Diagnostics reporting unit down to its estimated fair value, and an impairment charge of $20.7 million to write our intangible asset for the Claros Analyzer down to its estimated fair value. The Asset impairment charges for the year ended December 31, 2019, resulted from liquidity constraints, longer than expected development timelines and changes in the competitive landscape, which resulted in changes to our estimates and assumptions of the expected future cash flows associated with the Claros Analyzer.

We believe that our estimates and assumptions in testing goodwill and other intangible assets are consistent with assumptions that marketplace participants would use in their estimates. However, if actual results are not consistent with our estimates and assumptions, we may be exposed to an impairment charge that could be material.

Pharmaceuticals

	For the years ended December 31,			
(In thousands)	2019	2018	Change	% Change
Revenues:				
Revenue from products	$ 112,184	$ 107,112	$ 5,072	5 %
Revenue from transfer of intellectual property and other	72,521	69,906	2,615	4 %
Total revenues	184,705	177,018	7,687	4 %
Costs and expenses:				
Cost of revenue	61,888	58,794	3,094	5 %
Selling, general and administrative	57,589	58,789	(1,200)	(2)%
Research and development	104,659	112,099	(7,440)	(7)%
Contingent consideration	(6,453)	(14,909)	8,456	(57)%
Amortization of intangible assets	22,382	23,108	(726)	(3)%
Asset impairment charges	53,702	21,778	31,924	147 %
Total costs and expenses	293,767	259,659	34,108	13 %
Loss from operations	(109,062)	(82,641)	(26,421)	32 %

Revenue. The increase in Revenue from products for 2019 as compared to 2018 was primarily attributable to an increase in sales of *Rayaldee* of $31.4 million for the year ended December 31, 2019, compared to $20.3 million for the year ended December 31, 2018, which was partially offset by a decrease in revenue at OPKO Chile. The increase in Revenue from transfer of intellectual property was primarily attributable to an increase in revenue related to the Pfizer Transaction of $66.8 million for the year ended December 31, 2019, as compared to $60.0 million for the year ended December 31, 2018, which was partially offset by $2.0 million of revenue from a milestone payment from our licensee VFMCRP in 2018.

Costs of revenue. Cost of revenue increased primarily due to an increase in sales of *Rayaldee* in 2019 and changes in the product mix of items sold during the period.

Selling, general and administrative expenses. Selling, general and administrative expenses for the years ended December 31, 2019 and 2018 were $57.6 million and $58.8 million, respectively. The decrease in selling, general and administrative expenses was primarily due to a decrease in equity-based compensation expense. Selling, general and administrative expenses for the years ended December 31, 2019 and 2018 included equity-based compensation expense of $2.0 million and $4.4 million, respectively.

Research and development expenses. Research and development expenses for the years ended December 31, 2019 and 2018 were $104.7 million and $112.1 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 for phase 3 clinical trials for drug approval and PMAs for diagnostics tests, if any. Internal expenses include employee-related expenses such as salaries, benefits and equity-based compensation expense. Other 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,	
	2019	2018
External expenses:		
Manufacturing expense for biological products	$ 38,592	$ 28,245
Phase III studies	16,869	23,759
Post-marketing studies	2,019	1,403
Earlier-stage programs	21,201	33,957
Research and development employee-related expenses	22,023	24,947
Other internal research and development expenses	8,813	5,731
Third-party grants and funding from collaboration agreements	(4,858)	(5,943)
Total research and development expenses	$ 104,659	$ 112,099

The decrease in research and development expenses for the year ended December 31, 2019 was primarily due to a decrease in research and development expenses related to OPK88004, a selective androgen receptor modulator which we are exploring for various potential applications. In addition, for the years ended December 31, 2019 and 2018, we recorded, as an offset to research and development expenses, $3.7 million and $5.2 million, respectively, related to research and development tax credits recognized in Ireland. Research and development expenses for the years ended December 31, 2019 and 2018 included equity-based compensation expenses of $2.1 million and $3.5 million, respectively. We expect our research and development expenses to increase as we continue to expand our research and development of potential future products.

Contingent consideration. Contingent consideration for the years ended December 31, 2019 and 2018 was $6.5 million and $14.9 million reversal of expense, respectively. Contingent consideration for the years ended December 31, 2019 and 2018 was primarily attributable to changes in assumptions regarding the timing of achievement of future milestones for OPKO Renal, and potential amounts payable to former stockholders of OPKO Renal in connection therewith, pursuant to our acquisition agreement in March 2013.

Amortization of intangible assets. Amortization of intangible assets was $22.4 million and $23.1 million, respectively, for the years ended December 31, 2019 and 2018. Amortization expense reflects the amortization of acquired intangible assets with defined useful lives. Our indefinite lived IPR&D assets will not be amortized until the underlying development programs are completed. Upon obtaining regulatory approval by the U.S. FDA, the IPR&D assets will be accounted for as a finite-lived intangible asset and amortized on a straight-line basis over its estimated useful life.

Asset impairment charges. Asset impairment charges were $53.7 million and $21.8 million, respectively, for the years ended December 31, 2019 and 2018. Asset impairment charges for the year ended December 31, 2019 is primarily related to an impairment charge of $44.8 million to write our IPR&D assets for OPK88003 (oxyntomodulin) and CURNA's platform technology for oligonucleotide therapeutics down to their estimated fair values, and a goodwill impairment charge of $8.2 million to write the carrying amount of the CURNA and Transition Therapeutics reporting units down to their estimated fair values. The Asset impairment charges for the year ended December 31, 2019, resulted from liquidity constraints, longer than expected development timelines and changes in the competitive landscape, which resulted in changes to our estimates and assumptions of the expected future cash flows associated with OPK88003 and CURNA's platform technology. Asset impairment charges for the year ended December 31, 2018 is related to an impairment charge of $10.1 million to write our IPR&D assets for *Alpharen* and OPK88004 down to their estimated fair values and a goodwill impairment charge of $11.7 million to write the carrying amount of the FineTech reporting unit down to its estimated fair value.

We believe that our estimates and assumptions in testing goodwill and other intangible assets, including IPR&D, for impairment are consistent with assumptions that marketplace participants would use in their estimates. However, if actual results are not consistent with our estimates and assumptions, including as a result of the COVID-19 global pandemic, we may

be exposed to an impairment charge that could be material. If we are unable to successfully develop Somatrogon, or changes in projections and assumptions negatively impact our forecast of net cash flows, we may be exposed to a material impairment charge related to the IPR&D for Somatrogon.

Corporate

	For the years ended December 31,			
(In thousands)	2019	2018	Change	% Change
Revenues:				
Revenue from transfer of intellectual property and other	$ 796	$ —	796	100 %
Total revenues	796	—	796	100 %
Costs and expenses:				
Cost of revenue	(261)	(463)	202	(44)%
Selling, general and administrative	43,696	45,227	(1,531)	(3)%
Research and development	(1,008)	(1,150)	142	(12)%
Total costs and expenses	42,427	43,614	(1,187)	(3)%
Loss from operations	(41,631)	(43,614)	1,983	(5)%

Operating loss for our unallocated corporate operations for the years ended December 31, 2019 and 2018 was $41.6 million and $43.6 million, respectively, and principally reflects general and administrative expenses incurred in connection with our corporate operations.

Other

Interest income. Interest income for the years ended December 31, 2019 and 2018, was not significant as our cash investment strategy emphasizes the security of the principal invested and fulfillment of liquidity needs.

Interest expense. Interest expense for the years ended December 31, 2019 and 2018, was $21.5 million and $11.9 million, respectively. Interest expense was principally related to interest incurred on the 2025 Notes, the 2023 Convertible Notes, the 2033 Senior Notes, and BioReference's outstanding debt under its credit facility. The increase in interest expense for the year ended December 31, 2019 was primarily due to interest incurred on the 2025 Notes and 2023 Convertible Notes.

Fair value changes of derivative instruments, net. Fair value changes of derivative instruments, net for the years ended December 31, 2019 and 2018, were $0.2 million and $3.0 million of income, respectively. Derivative income for the year ended December 31, 2018 principally related to the change in fair value of warrants to purchase additional shares of Neovasc.

Other income and (expense), net. Other income and (expense), net for the years ended December 31, 2019 and 2018, was $11.3 million of expense and $1.5 million of income, respectively. Other expense for the year ended December 31, 2019 primarily consisted of net unrealized losses recognized during the period on our investments in Eloxx Pharmaceuticals, Inc. and VBI Vaccines Inc. Other income for the year ended December 31, 2018 primarily consisted of net unrealized gains recognized during the period on equity securities.

Income tax benefit (provision). Our income tax benefit (provision) for the years ended December 31, 2019 and 2018 was $(7.1) million, and $38.7 million, respectively. For the year ended December 31, 2019, our effective tax rate differed from the U.S. federal statutory rate of 21% primarily due to the relative mix in earnings and losses in the U.S. versus foreign tax jurisdictions, the impact of certain discrete tax events and operating results in tax jurisdictions that do not result in a tax benefit. The income tax benefit for the year ended December 31, 2018 included benefits related to discrete events which did not recur during 2019.

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 or member. 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 report a net loss. Loss from investments in investees was $2.9 million and $14.5 million for the years ended December 31, 2019 and 2018, respectively.

LIQUIDITY AND CAPITAL RESOURCES

At December 31, 2020, we had cash and cash equivalents of approximately $72.2 million. Cash provided by operations of $39.5 million for year ended December 31, 2020 principally reflects cash generated by our diagnostics segment due to the positive impact of COVID-19 testing volumes, which was partially offset by general and administrative expenses related to our corporate operations and research and development activities. Cash used in investing activities for the year ended December 31, 2020 primarily reflects capital expenditures of $33.7 million, which was partially offset by proceeds from sales of equity securities of $15.1 million. Cash used in financing activities of $35.1 million primarily reflects net repayments on our lines of credit. We have not generated sustained positive cash flow sufficient to offset our operating and other expenses, and our primary sources of cash have been from the public and private placement of equity, the issuance of the 2033 Senior Notes, 2023 Convertible Notes and 2025 Notes and credit facilities available to us. However, as a result of the significant increase in testing volumes resulting from the COVID-19 pandemic, and if our routine clinical and genomic testing volumes continue to trend towards normalization with prior periods, we anticipate generating positive cash flow from operations. We are unable to predict how long the demand will continue for our COVID-19 related testing, whether pricing and reimbursement policies for testing will sustain, or whether further restrictions will be placed on elective procedures or if stay at home orders will be reinstated and accordingly, the sustainability of the cash flow is uncertain.

On February 25, 2020, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to provide us with an unsecured line of credit in the amount of $100 million. Borrowings under this line of credit bear interest at a rate of 11% per annum and may be repaid and reborrowed at any time. The credit agreement includes various customary remedies for the lender following an event of default, including the acceleration of repayment of outstanding amounts under this line of credit. This line of credit matures on February 25, 2025. As of December 31, 2020, no funds were borrowed under this line of credit.

On October 29, 2019, we issued 50 million shares of our Common Stock at a price of $1.50 per share in an underwritten public offering, resulting in net proceeds to the Company of approximately $70 million, after deducting underwriting commissions and offering expenses. In November 2019, pursuant to an option the Company granted the underwriters, we issued an additional 4,227,749 shares of Common Stock at $1.50 per share, resulting in proceeds of approximately $6 million after deducting underwriting commissions.

In February 2019, we issued $200.0 million aggregate principal amount of the 2025 Notes in an underwritten public offering. The 2025 Notes bear interest at a rate of 4.50% per year, payable semiannually in arrears on February 15 and August 15 of each year. The notes mature on February 15, 2025, unless earlier repurchased, redeemed or converted.

Holders may convert their 2025 Notes into shares of Common Stock at their option at any time prior to the close of business on the business day immediately preceding November 15, 2024 only under the following circumstances: (1) during any calendar quarter commencing after the calendar quarter ending on March 31, 2019 (and only during such calendar quarter), if the last reported sale price of our Common Stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; (2) during the five business day period after any five consecutive trading day period (the "measurement period") in which the trading price per $1,000 principal amount of 2025 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our Common Stock and the conversion rate on each such trading day; (3) if we call any or all of the 2025 Notes for redemption, at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date; or (4) upon the occurrence of specified corporate events set forth in the indenture governing the 2025 Notes. On or after November 15, 2024, until the close of business on the business day immediately preceding the maturity date, holders of the 2025 Notes may convert their notes at any time, regardless of the foregoing circumstances. Upon conversion, we will pay or deliver, as the case may be, cash, shares of our Common Stock, or a combination of cash and shares of our Common Stock, at our election.

The current conversion rate for the 2025 Notes is 236.7424 shares of Common Stock per $1,000 principal amount of 2025 Notes (equivalent to a conversion price of approximately $4.22 per share of Common Stock). The conversion rate for the 2025 Notes is subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest.

On February 1, 2019, holders of our 2033 Senior Notes tendered to us approximately $28.8 million aggregate principal amount of such notes pursuant to such holders' option to require us to repurchase the 2033 Senior Notes as set forth in the indenture, following which repurchase only $3.0 million aggregate principal amount of the 2033 Senior Notes remained outstanding. Holders of the remaining $3.0 million principal amount of the 2033 Senior Notes may require us to repurchase such notes for 100% of their principal amount, plus accrued and unpaid interest, on February 1, 2023, on February 1, 2028, or following the occurrence of a fundamental change as defined in the indenture governing the 2033 Senior Notes.

As of December 31, 2020, the total commitments under our Credit Agreement (as defined below) with CB and our lines of credit with financial institutions in Chile and Spain were $87.7 million, of which $23.0 million was drawn as of December 31, 2020. At December 31, 2020, the weighted average interest rate on these lines of credit was approximately 4.9%. These lines of credit are short-term and are used primarily as a source of working capital. The highest aggregate principal balance at any time outstanding during the year ended December 31, 2020, was $66.5 million. We intend to continue to draw on 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.

In November 2015, BioReference and certain of its subsidiaries entered into a credit agreement with CB, as lender and administrative agent, as amended (the "Credit Agreement"). The Credit Agreement provides for a $75.0 million secured revolving credit facility and includes a $20.0 million sub-facility for swingline loans and a $20.0 million sub-facility for the issuance of letters of credit. The Credit Agreement matures on November 5, 2021 and is guaranteed by all of BioReference's domestic subsidiaries. The Credit Agreement is also secured by substantially all assets of BioReference and its domestic subsidiaries, as well as a non-recourse pledge by us of our equity interest in BioReference. Availability under the Credit Agreement is based on a borrowing base composed of eligible accounts receivables of BioReference and certain of its subsidiaries, as specified therein. As of December 31, 2020, $57.6 million remained available for borrowing under the Credit Agreement.

In February 2018, in a transaction exempt from registration under the Securities Act, we issued the 2023 Convertible Notes in the aggregate principal amount of $55.0 million maturing in February 2023. Each holder of a 2023 Convertible Note has the option, from time to time, to convert all or any portion of the outstanding principal balance of such 2023 Convertible Note, together with accrued and unpaid interest thereon, into shares of our Common Stock, par value $0.01 per share, at a conversion price of $5.00 per share of Common Stock. We may redeem all or any part of the then issued and outstanding 2023 Convertible Notes, together with accrued and unpaid interest thereon upon no fewer than 30 days, and no more than 60 days, notice to the holders. The 2023 Convertible Notes contain customary events of default and representations and warranties of OPKO.

On October 12, 2017, EirGen, our wholly-owned subsidiary, and JT entered into the JT Agreement granting JT the exclusive rights for the development and commercialization of *Rayaldee* in Japan. The license grant to JT covers the therapeutic and preventative use of *Rayaldee* 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. In connection with the transaction, OPKO received an initial upfront payment of $6 million, and OPKO received another $6 million upon the initiation of OPKO's phase 2 study for *Rayaldee* in dialysis patients in the U.S. in September 2018. 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 sales of *Rayaldee* 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.

In May 2016, EirGen, our wholly-owned subsidiary, partnered with VFMCRP through the VFMCRP Agreement for the development and commercialization of*Rayaldee* in the VFMCRP Territory. The license to VFMCRP potentially covers all therapeutic and prophylactic uses of the product in human patients, provided that initially the license is for the use of the product for the treatment or prevention of SHPT related to patients with CKD and vitamin D insufficiency/deficiency ("VFMCRP Initial Indication"). Effective May 5, 2020, we entered into the VFMCRP Amendment, pursuant to which the parties agreed to exclude Mexico, South Korea, the Middle East and all of the countries of Africa from the VFMCRP Territory. In addition, the parties agreed to certain amendments to the milestone structure and to reduce minimum royalties payable.

We have received non-refundable and non-creditable payments of $55 million to date and are eligible to receive up to an additional $227 million pursuant to the terms of the VFMCRP Amendment upon the achievement of certain regulatory and sales-based milestones tied to sales and reimbursement levels. In addition, we are eligible to receive tiered 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.

As part of the arrangement, the companies will share responsibility for the conduct of trials specified within an agreed-upon development plan, with each company leading certain activities within the plan. For the initial development plan, the companies have agreed to certain cost sharing arrangements. VFMCRP will be responsible for all other development costs that VFMCRP considers necessary to develop the product for the VFMCRP Initial Indication in the VFMCRP Territory except as otherwise provided in the VFMCRP Agreement. EirGen also granted to VFMCRP an option to acquire an exclusive license to use, import, offer for sale, sell, distribute and commercialize the product in the U.S. for treatment of SHPT in dialysis patients

with stage 5 CKD and vitamin D insufficiency (the "Dialysis Indication"). Upon exercise of the Option, VFMCRP will reimburse EirGen for all of the development costs incurred by EirGen with respect to the product for the Dialysis Indication in the U.S. VFMCRP would also pay EirGen up to an additional aggregate amount of $555 million upon the achievement of certain milestones and would be obligated to pay 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.

In June 2020, we announced that the Japan phase 3 clinical trial met its primary and secondary objectives, and demonstrated that the efficacy and safety of Somatrogon administered weekly was comparable to GENOTROPIN® for injection administered once-daily as measured by annual height velocity after 12 months of treatment in treatment-naïve Japanese pre-pubertal children with GHD. In October 2019, we and Pfizer announced that the global phase 3 trial evaluating Somatrogon (hGH-CTP) dosed once-weekly in prepubertal children with GHD met its primary endpoint of non-inferiority to daily Genotropin® (somatropin) for injection, as measured by annual height velocity at 12 months.

In 2014, Pfizer and OPKO entered into a worldwide agreement for the development and commercialization of our long-acting Somatrogon 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. In May 2020, we entered into a Restated Agreement with Pfizer which was effective as of January 1, 2020, pursuant to which the parties agreed to share all costs for Manufacturing Activities, as defined in the Restated Agreement, for developing a licensed product for the three indications included in the Agreement. Under the terms of the agreements with Pfizer, we received non-refundable and non-creditable upfront payments of $295 million in 2015 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 Somatrogon worldwide. In addition, we are eligible to receive initial tiered royalty payments associated with the commercialization of Somatrogon for Adult GHD with percentage rates ranging from the high teens to mid-twenties. Upon the launch of Somatrogon for Pediatric GHD in certain major markets, the royalties will transition to regional, tiered gross profit sharing for both Somatrogon and Pfizer's Genotropin®.

In January 2021, we announced that the FDA has accepted for filing the initial BLA for Somatrogon for the treatment of pediatric patients with GHD. The target PDUFA action date for decision by the FDA is in October 2021. In January 2021 we also announced the submission of a New Drug Application to the Ministry of Health, Labour, and Welfare in Japan for Somatrogon for the treatment of pediatric patients with GHD.

In connection with our acquisitions of CURNA, OPKO Diagnostics and OPKO Renal, we agreed to pay future consideration to the sellers upon the achievement of certain events, including 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 $125.0 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.

We believe that the cash and cash equivalents on hand at December 31, 2020, cash from operations 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, and the timing of those requirements, will depend on a number of factors, including the impact of the COVID-19 pandemic on our business, the approval and success of our products in development, particularly our long acting Somatrogon for which we have submitted for approval in the U.S. and Japan and expect to submit for approval in the Europe shortly, the commercial success of *Rayaldee*, including the launch of *Rayaldee* by Vifor expected later in 2021, BioReference's financial performance, 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, our success in developing markets for our product candidates and results of government investigations, payor claims, and legal proceedings that may arise, including, without limitation class action and derivative litigation to which we are subject, and our ability to obtain insurance coverage for such claims. We have not generated sustained positive cash flow and 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 or reduce our marketing or sales efforts or cease operations.

Additionally, the rapid development and fluidity of the COVID-19 pandemic makes it very difficult to predict its ultimate impact on our business, results of operations and liquidity. The pandemic presents a significant uncertainty that could materially and adversely affect our results of operations, financial condition and cash flows, including due to a continued negative impact on non-COVID-related diagnostics testing services provided by BioReference in our diagnostics segment, notwithstanding that our results of operations have been positively impacted by our provision of COVID-19 testing services.

Further, deteriorating economic conditions globally have resulted in a challenging capital raising environment, which could materially limit our access to capital, whether through the issuance and sale of our common stock, debt securities or otherwise, as well as through bank facilities and lines of credit. Events resulting from the effects of COVID-19 could negatively impact our ability to comply with certain covenants in the Credit Agreement or require that we pursue alternative financing. We can provide no assurance that any such alternative financing, if required, could be obtained on acceptable terms or at all. The combination of potential disruptions to our business resulting from COVID-19 together with and volatile credit and capital markets could adversely impact our future liquidity, which could have an adverse effect on our business and results of operations. We will continue to monitor and assess the impact COVID-19 may have on our business and financial results.

The following table provides information as of December 31, 2020, with respect to the amounts and timing of our known contractual obligation payments due by period.

Contractual obligations (In thousands)	2021	2022	2023	2024	2025	Thereafter	Total
Open purchase orders	$ 342,103	$ 49	$ —	$ —	$ —	$ —	$ 342,152
Operating leases	9,028	7,687	6,193	4,195	2,445	9,240	38,788
Capital leases	2,428	1,422	835	503	70	—	5,258
Convertible Notes	—	—	58,050	—	156,163	—	214,213
Mortgages and other debts payable	1,031	807	597	500	94	—	3,029
Lines of credit	22,954	—	—	—	—	—	22,954
Interest commitments	296	286	13,972	260	36,852	—	51,666
Total	$ 377,840	$ 10,251	$ 79,647	$ 5,458	$ 195,624	$ 9,240	$ 678,060

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 seven years and are payable in either shares of our Common Stock or cash, at our option, and that may aggregate up to $144.1 million.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

Use of estimates. The preparation of financial statements in conformity with accounting principles generally accepted in the U.S. (“GAAP”) 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 significantly from these estimates.

Goodwill and intangible assets. Goodwill and other intangible assets, including IPR&D, acquired in business combinations, licensing and other transactions at December 31, 2020 and 2019, was $1.7 billion and $1.8 billion, respectively.

Assets acquired and liabilities assumed in business combinations, licensing and other transactions are generally 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. At acquisition, we generally determine 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.

Subsequent to acquisition, goodwill and indefinite lived intangible assets are tested at least annually as of October 1 for impairment, or when events or changes in circumstances indicate it is more likely than not that the carrying amount of such assets may not be recoverable. Our annual assessment may consist of a qualitative or quantitative analysis to determine

whether it is more likely than not that its fair value exceeds the carrying value. When performing qualitative analysis, the factors we consider include our share price, our financial performance compared to budgets, long-term financial plans, the timing and cost of development plans, macroeconomic, industry and market conditions as well as the excess of fair value over the carrying value of net assets from the annual impairment test previously performed.

When performing quantitative analysis, we use a combination of income and market valuation methods and may weigh the outcomes of valuation approaches when estimating fair value. Inputs and assumptions used to determine fair value are determined from a market participant view, which might be different than our specific views. The valuation process is complex and requires significant input and judgment using internal and external sources. Market approaches depend on the availability of guideline companies and representative transactions. When using the income approach, complex and judgmental matters applicable to the valuation process may include the following:

- Estimated useful life – The asset life expected to contribute meaningful cash flows is determined after considering expected regulatory approval dates (if unapproved), exclusivity periods and other legal, regulatory or contractual provisions.
- Projections – Future revenues are estimated after considering many factors such as historical results, market opportunity, pricing, sales trajectories to peak sales levels, competitive environment and product evolution. Future costs and expenses are estimated after considering historical factors such as the timing and level of development costs to obtain regulatory approvals, maintain or further enhance the product. For IPR&D projects, 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. In determining the tax rate, we consider the jurisdiction in which the intellectual property is held and the location of the research and manufacturing infrastructure.
- 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 Company specific technical, legal, regulatory, or economic barriers to entry.

Goodwill was $680.6 million and $671.9 million, respectively, at December 31, 2020 and 2019. Estimating the fair value of a reporting unit for goodwill impairment is highly sensitive to changes in projections and assumptions and changes in 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, potential changes in these assumptions may impact the estimated fair value of a reporting unit and result in an impairment if the fair value of such reporting unit is less than its carrying value.

Net intangible assets other than goodwill were $1.1 billion, including IPR&D of $590.2 million, at both December 31, 2020 and 2019. Intangible assets are highly vulnerable to impairment charges, particularly newly acquired assets for recently launched products and IPR&D. 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 may occur in future periods. Estimating the fair value of IPR&D for potential impairment is highly sensitive to changes in projections and assumptions and changes in assumptions could potentially lead to impairment.

Upon obtaining regulatory approval, IPR&D assets are 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. Finite lived intangible assets are tested for impairment when events or changes in circumstances indicate it is more likely than not that the carrying amount of such assets may not be recoverable. The testing includes a comparison of the carrying amount of the asset to its estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated undiscounted future cash flows, then an impairment charge is recognized for the amount by which the carrying amount of the asset exceeds the fair value of the asset.

Impairment charges for the year ended December 31, 2019 were $92.4 million and consist of a goodwill impairment charge of $26.2 million to write the carrying amount of the OPKO Diagnostics, CURNA and Transition Therapeutics reporting units down to their estimated fair value, an impairment charge of $44.8 million to write our IPR&D assets for OPK88003 and CURNA's platform technology for oligonucleotide therapeutics down to their estimated fair value, and an impairment charge of $20.7 million to write our intangible asset for the Claros Analyzer down to its estimated fair value as a result of our testing. These impairment charges for the year ended December 31, 2019, resulted from liquidity constraints, longer than expected

development timelines and changes in the competitive landscape, which resulted in changes to our estimates and assumptions of the expected future cash flows of the reporting units focused on the development of the Claros Analyzer, OPK88003 and CURNA's platform technology. No impairment charges were recognized for the year ended December 31, 2020.

We recorded a goodwill impairment charge of $11.7 million in Asset impairment charges in our Consolidated Statement of Operations for the year ended December 31, 2018 to write the carrying amount of the FineTech reporting unit down to its estimated fair value. We also recorded an impairment charge of $10.1 million in Asset impairment charges in our Consolidated Statement of Operations for the year ended December 31, 2018 to write our IPR&D assets for *Alpharen* and OPK88004 down to their estimated fair value as a result of our testing.

We believe that our estimates and assumptions are reasonable and otherwise consistent with assumptions that marketplace participants would use in their estimates of fair value. However, if future results are not consistent with our estimates and assumptions, including as a result of the COVID-19 global pandemic, then we may be exposed to an impairment charge, which could be material.

We amortize intangible assets with definite lives on a straight-line basis over their estimated useful lives, ranging from 3 to 20 years. 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 $56.4 million and $64.8 million for the years ended December 31, 2020 and 2019, respectively.

Revenue recognition. We generate revenues from services, products and intellectual property as follows:

Revenue from services. Revenue for laboratory services is recognized at the time test results are reported, which approximates when services are provided and the performance obligations are satisfied. Services are provided to patients covered by various third-party payor programs including various managed care organizations, as well as the Medicare and Medicaid programs. Billings for services are included in revenue net of allowances for contractual discounts, allowances for differences between the amounts billed and estimated program payment amounts, and implicit price concessions provided to uninsured patients which are all elements of variable consideration.

The following are descriptions of our payors for laboratory services:

Healthcare Insurers. Reimbursements from healthcare insurers are based on negotiated fee-for-service schedules. Revenues consist of amounts billed, net of contractual allowances for differences between amounts billed and the estimated consideration we expect to receive from such payors, which considers historical denial and collection experience and the terms of our contractual arrangements. Adjustments to the allowances, based on actual receipts from the third-party payors, are recorded upon settlement.

Government Payors. Reimbursements from government payors are based on fee-for-service schedules set by governmental authorities, including traditional Medicare and Medicaid. Revenues consist of amounts billed, net of contractual allowances for differences between amounts billed and the estimated consideration we expect to receive from such payors, which considers historical denial and collection experience and the terms of our contractual arrangements. Adjustments to the allowances, based on actual receipts from the government payors, are recorded upon settlement.

Client Payors. Client payors include physicians, hospitals, employers, and other institutions for which services are performed on a wholesale basis, and are billed and recognized as revenue based on negotiated fee schedules.

Patients. Uninsured patients are billed based on established patient fee schedules or fees negotiated with physicians on behalf of their patients. Insured patients (including amounts for coinsurance and deductible responsibilities) are billed based on fees negotiated with healthcare insurers. Collection of billings from patients is subject to credit risk and ability of the patients to pay. Revenues consist of amounts billed net of discounts provided to uninsured patients in accordance with our policies and implicit price concessions. Implicit price concessions represent differences between amounts billed and the estimated consideration that we expect to receive from patients, which considers historical collection experience and other factors including current market conditions. Adjustments to the estimated allowances, based on actual receipts from the patients, are recorded upon settlement.

The complexities and ambiguities of billing, reimbursement regulations and claims processing, as well as considerations unique to Medicare and Medicaid programs, require us to estimate the potential for retroactive adjustments as an element of variable consideration in the recognition of revenue in the period the related services are rendered. Actual amounts are adjusted in the period those adjustments become known. For the year ended December 31, 2020, positive revenue adjustments due to changes in estimates of implicit price concessions for performance obligations satisfied in prior periods of $0.3 million were recognized. For the years ended December 31, 2019 and 2018, revenue reductions due to changes in estimates of implicit price

concessions for performance obligations satisfied in prior periods of $24.8 million and $22.8 million, respectively, were recognized

Third-party payors, including government programs, may decide to deny payment or recoup payments for testing they contend were improperly billed or not medically necessary, against their coverage determinations, or for which they believe they have otherwise overpaid (including as a result of their own error), and we may be required to refund payments already received. Our revenues may be subject to retroactive adjustment as a result of these factors among others, including without limitation, differing interpretations of billing and coding guidance and changes by government agencies and payors in interpretations, requirements, and "conditions of participation" in various programs. We have processed requests for recoupment from third-party payors in the ordinary course of our business, and it is likely that we will continue to do so in the future. If a third-party payor denies payment for testing or recoups money from us in a later period, reimbursement for our testing could decline.

As an integral part of our billing compliance program, we periodically assess our billing and coding practices, respond to payor audits on a routine basis, and investigate reported failures or suspected failures to comply with federal and state healthcare reimbursement requirements, as well as overpayment claims which may arise from time to time without fault on the part of the Company. We may have an obligation to reimburse Medicare, Medicaid, and third-party payors for overpayments regardless of fault. We have periodically identified and reported overpayments, reimbursed payors for overpayments and taken appropriate corrective action.

Settlements with third-party payors for retroactive adjustments due to audits, reviews or investigations are also considered variable consideration and are included in the determination of the estimated transaction price for providing services. These settlements are estimated based on the terms of the payment agreement with the payor, correspondence from the payor and our historical settlement activity, including an assessment of the probability a significant reversal of cumulative revenue recognized will occur when the uncertainty is subsequently resolved. Estimated settlements are adjusted in future periods as adjustments become known (that is, new information becomes available), or as years are settled or are no longer subject to such audits, reviews, and investigations.

Revenue from products. We recognize revenue from product sales when a customer obtains control of promised goods or services. The amount of revenue that is recorded reflects the consideration that we expect to receive in exchange for those goods or services. 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 our evaluation of specific factors that may increase or decrease the risk of product returns. Product revenues are recorded net of estimated rebates, chargebacks, discounts, co-pay assistance and other deductions (collectively, "Sales Deductions") as well as estimated product returns which are all elements of variable consideration. Allowances are recorded as a reduction of revenue at the time product revenues are recognized. The actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect Revenue from products in the period such variances become known.

Rayaldee is distributed in the U.S. principally through the retail pharmacy channel, which initiates with the largest wholesalers in the U.S. (collectively, "*Rayaldee* Customers"). In addition to distribution agreements with *Rayaldee* Customers, we have entered into arrangements with many healthcare providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of *Rayaldee.*

We recognize revenue for shipments of *Rayaldee* at the time of delivery to customers after estimating Sales Deductions and product returns as elements of variable consideration utilizing historical information and market research projections. For the years ended December 31, 2020, 2019 and 2018, we recognized $36.8 million, $31.4 million and 20.3 million in net product revenue from sales of *Rayaldee.*

Taxes collected from customers related to revenues from services and revenues from products are excluded from revenues.

Revenue from intellectual property. We recognize revenues from the transfer of intellectual property generated through license, development, collaboration and/or commercialization agreements. The terms of these agreements typically include payment to us for one or more of the following: non-refundable, up-front license fees; development and commercialization milestone payments; funding of research and/or development activities; and royalties on sales of licensed products. Revenue is recognized upon satisfaction of a performance obligation by transferring control of a good or service to the customer.

For research, development and/or commercialization agreements that result in revenues, we identify all material performance obligations, which may include a license to intellectual property and know-how, and research and development activities. In order to determine the transaction price, in addition to any upfront payment, we estimate the amount of variable

consideration at the outset of the contract either utilizing the expected value or most likely amount method, depending on the facts and circumstances relative to the contract. We constrain (reduce) our estimates of variable consideration such that it is probable that a significant reversal of previously recognized revenue will not occur throughout the life of the contract. When determining if variable consideration should be constrained, we consider whether there are factors outside of our control that could result in a significant reversal of revenue. In making these assessments, we consider the likelihood and magnitude of a potential reversal of revenue. These estimates are re-assessed each reporting period as required.

Upfront License Fees: If a license to our intellectual property is determined to be functional intellectual property distinct from the other performance obligations identified in the arrangement, we recognize revenue from nonrefundable, upfront license fees based on the relative value prescribed to the license compared to the total value of the arrangement. The revenue is recognized when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are not distinct from other obligations identified in the arrangement, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If the combined performance obligation is satisfied over time, we apply an appropriate method of measuring progress for purposes of recognizing revenue from nonrefundable, upfront license fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Development and Regulatory Milestone Payments: Depending on facts and circumstances, we may conclude that it is appropriate to include the milestone in the estimated transaction price or that it is appropriate to fully constrain the milestone. A milestone payment is included in the transaction price in the reporting period that we conclude that it is probable that recording revenue in the period will not result in a significant reversal in amounts recognized in future periods. We may record revenues from certain milestones in a reporting period before the milestone is achieved if we conclude that achievement of the milestone is probable and that recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. We record a corresponding contract asset when this conclusion is reached. Milestone payments that have been fully constrained are not included in the transaction price to date. These milestones remain fully constrained until we conclude that achievement of the milestone is probable and that recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. We re-evaluate the probability of achievement of such development milestones and any related constraint each reporting period. We adjust our estimate of the overall transaction price, including the amount of revenue recorded, if necessary.

Research and Development Activities: If we are entitled to reimbursement from our customers for specified research and development expenses, we account for them as separate performance obligations if distinct. We also determine whether the research and development funding would result in revenues or an offset to research and development expenses in accordance with provisions of gross or net revenue presentation. The corresponding revenues or offset to research and development expenses are recognized as the related performance obligations are satisfied.

Sales-based Milestone and Royalty Payments: Our customers may be required to pay us sales-based milestone payments or royalties on future sales of commercial products. We recognize revenues related to sales-based milestone and royalty payments upon the later to occur of (i) achievement of the customer's underlying sales or (ii) satisfaction of any performance obligation(s) related to these sales, in each case assuming the license to our intellectual property is deemed to be the predominant item to which the sales-based milestones and/or royalties relate.

Other Potential Products and Services: Arrangements may include an option for license rights, future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's election. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations at the inception of the contract and revenue is recognized only if the option is exercised and products or services are subsequently delivered or when the rights expire. If the promise is based on market terms and not considered a material right, the option is accounted for if and when exercised. If we are entitled to additional payments when the licensee exercises these options, any additional payments are generally recorded in license or other revenues when the licensee obtains control of the goods, which is upon delivery.

For the years ended December 31, 2020, 2019 and 2018 we recorded $53.2 million, $73.3 million and $69.9 million of revenue from the transfer of intellectual property and other, respectively. For the year ended December 31, 2020 and 2019, revenue from the transfer of intellectual property and other included $28.7 million and $66.8 million related to the Pfizer Transaction. In addition, revenue from the transfer of intellectual property and other for the year ended December 31, 2020 included $16.2 million of grants received by BioReference under the CARES Act and a $3 million milestone payment triggered by the first marketing approval of *Rayaldee* in Europe. For the year ended December 31, 2018, revenue from the transfer of intellectual property included $60.0 million related to the Pfizer Transaction and $2.0 million related to a milestone payment from our licensee, Vifor Fresenius Medical Care Renal Pharma Ltd ("VFMCRP"). Refer to Note 16.

Contract liabilities relate to cash consideration that OPKO receives in advance of satisfying the related performance obligations. Changes in the contractual liabilities balance for the years ended December 31, 2020 are as follows:

(In thousands)		
Balance at December 31, 2019	$	21,767
Balance at December 31, 2020		16,378
Revenue recognized in the period from:		
Amounts included in contracts liability at the beginning of the period		19,048

The contract liability balance at December 31, 2020 related primarily to accelerated payments received as part of the CARES Act.

Concentration of credit risk and allowance for doubtful accounts Financial instruments that potentially subject us to concentrations of credit risk consist primarily of accounts receivable. Substantially all of our accounts receivable are with either companies in the health care industry or patients. However, credit risk is limited due to the number of our clients as well as their dispersion across many different geographic regions.

While we have receivables due from federal and state governmental agencies, we do not believe that such receivables represent a credit risk since the related healthcare programs are funded by federal and state governments, and payment is primarily dependent upon submitting appropriate documentation. At December 31, 2020 and 2019, receivable balances (net of explicit and implicit price concessions) from Medicare and Medicaid were 6% and 6%, respectively, of our consolidated Accounts receivable, net. At December 31, 2020, receivable balances (net of explicit and implicit price concessions) due directly from states, cities and other municipalities, specifically related to our real-time reverse-transcription polymerase chain reaction (real-time RT-PCR) assay to detect COVID-19, were 6.3% of our consolidated accounts receivable, net.

The portion of our accounts receivable due from individual patients comprises the largest portion of credit risk. At December 31, 2020 and 2019, receivables due from patients represented approximately 0.7% and 2.5%, respectively, of our consolidated Accounts receivable, net.

We assess the collectability of accounts receivable balances by considering factors such as historical collection experience, customer credit worthiness, the age of accounts receivable balances, regulatory changes and current economic conditions and trends that may affect a customer's ability to pay. Actual results could differ from those estimates. The allowance for credit losses was $2.1 million and $1.9 million at December 31, 2020 and 2019, respectively. The credit loss expense for the years ended December 31, 2020 and 2019 was $0.2 million and $0.5 million, respectively.

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 for 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. Valuation allowances on certain U.S. deferred tax assets and non-U.S. deferred tax assets are established, because realization of these tax benefits through future taxable income does not meet the more-likely-than-not threshold.

On December 22, 2017, the 2017 Tax Cuts and Jobs Act (the "Tax Act") was enacted into law and the new legislation contains several key tax provisions, including a reduction of the corporate income tax rate from 35% to 21% effective January 1, 2018 and a one-time mandatory transition tax on accumulated foreign earnings, among others. We were required to recognize the effect of the tax law changes in the period of enactment, such as remeasuring our U.S. deferred tax assets and liabilities, as well as reassessing the net realizability of our deferred tax assets and liabilities.

Effective January 1, 2018, the Tax Act provides for a new global intangible low-taxed income ("GILTI") provision. Under the GILTI provision, certain foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets are included in U.S. taxable income. The Company currently estimates GILTI will be immaterial for the years ended December 31, 2020, 2019 and 2018, although interpretive guidance continues to be issued and future guidance may impact this analysis. The Company has not recorded any deferred taxes for future GILTI inclusions as any future inclusions are expected to be offset by net operating loss carryforwards in the U.S.

Equity-based compensation. We measure the cost of 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 Statements 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 cash flows from operations. 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." 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. The selection of assumptions is subject to significant judgment and future changes to our assumptions and estimates which may have a material impact on our Consolidated Financial Statements.

Inventories. Inventories are valued at the lower of cost and 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 and net realizable value. Inventories at our diagnostics segment consist primarily of purchased laboratory supplies, which is used in our testing laboratories. Inventory obsolescence for the years ended December 31, 2020 and 2019 was $4.4 million and $2.3 million, respectively.

Contingent consideration. Each period we revalue the contingent consideration obligations associated with certain prior acquisitions to their fair value and record increases in the fair value as contingent consideration expense and decreases in the fair value as a reduction in contingent consideration expense. 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.

RECENT ACCOUNTING PRONOUNCEMENTS

Recently adopted accounting pronouncements.

In June 2016, the FASB issued ASU No. 2016-13, "Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments," which amends the impairment model by requiring entities to use a forward-looking approach based on expected losses rather than incurred losses to estimate credit losses on certain types of financial instruments, including trade receivables. This may result in the earlier recognition of allowances for losses. The ASU is effective for public entities for fiscal years beginning after December 15, 2019, with early adoption permitted. The adoption of ASU 2016-13 on January 1, 2020, did not have a significant impact on our Consolidated Financial Statements.

Pending accounting pronouncements.

In August 2020, the FASB issued ASU No. 2020-06, "Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40)." ASU 2020-06 will simplify the accounting for convertible instruments by reducing the number of accounting models for convertible debt instruments and convertible preferred stock. The ASU is effective for public entities for fiscal years beginning after December 15, 2021, with early adoption permitted. We are currently evaluating the impact of this new guidance on our Consolidated Financial Statements.

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 portions 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 may be 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 and fair valued, respectively, at current spot rates, with gains and losses included in earnings.

Our derivative activities, which consist of foreign exchange forward contracts, are initiated to economically 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' respective 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 Statements 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. Our foreign exchange forward contracts primarily hedge exchange rates on the Chilean Peso to the U.S. dollar. If Chilean 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 interest rate risk relates to our cash and investments and to our borrowings. We generally maintain an investment portfolio of money market funds and marketable securities. 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, 2020, we had cash and cash equivalents of $72.2 million. The weighted average interest rate related to our cash and cash equivalents for the year ended December 31, 2020 was less than 1%. As of December 31, 2020, the principal outstanding balance under BioReference's Credit Agreement with JPMorgan Chase Bank, N.A. and our Chilean and Spanish credit lines was $23.0 million in the aggregate at a weighted average interest rate of approximately 4.9%.

Our $3.0 million aggregate principal amount of our 2033 Senior Notes has a fixed interest rate of 3%, our $55.0 million aggregate principal amount of our 2023 Convertible Notes has a fixed interest rate of 5%, and our $200.0 million aggregate principal amount of the 2025 Notes has a fixed interest rate of 4.50%, and therefore are 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 may 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.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of OPKO Health, Inc. and subsidiaries

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of OPKO Health, Inc. and subsidiaries (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations, comprehensive income (loss), shareholders' equity and cash flows for each of the three years in the period ended December 31, 2020, and the related notes and financial statement schedule included at Item 15(a)(1) (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, 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) (PCAOB), the Company's internal control over financial reporting as of December 31, 2020, 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 18, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Valuation of Goodwill for Rayaldee

Description of the Matter

At December 31, 2020, the Company's goodwill was $680.6 million, and goodwill assigned to the *Rayaldee* reporting unit was $93.4 million. As discussed in Note 2 to the consolidated financial statements, 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. To determine the estimated fair value of the *Rayaldee* reporting unit, management considers both market and income valuation approaches.

Auditing management's annual impairment test of goodwill included in the *Rayaldee* reporting unit was complex and highly judgmental due to the significant assumptions used in the determination of guideline companies, market transactions and market multiples, as well as the discount rate and revenue growth rates used to estimate future cash flows, which are affected by expectations about future market or economic conditions.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's annual goodwill impairment review process, including controls over management's review of the significant assumptions in the *Rayaldee* analysis described above.

To test the estimated fair value of the *Rayaldee* reporting unit, we performed audit procedures that included, among others, assessing methodologies and testing the significant assumptions discussed above and the underlying data used by the Company in its analysis. We compared the significant assumptions used by management to current industry and economic trends, changes to the Company's business model and other relevant factors. We involved valuation specialists to assist with assessing the methodologies and evaluating certain significant assumptions, such as the determination of guideline companies, market transactions, market multiples and the discount rate. We assessed the historical accuracy of management's projected financial information and performed sensitivity analyses on significant assumptions to evaluate the changes in the fair value that would result from changes in the assumptions.

Variable Consideration in Determining Revenue from Services

Description of the Matter

For the year ended December 31, 2020, the Company recorded revenue from services of $1,262.2 million. As discussed in Note 15 to the consolidated financial statements, revenue from services includes amounts due under third-party and government payer programs, net of estimates
for explicit and implicit price concessions and other elements of variable consideration. The Company estimates variable consideration by evaluating, among other factors, recent collections experience as well as changes in reimbursement regulations, claims processing and coverage determinations.

Auditing revenue from services is complex and highly judgmental due to the estimation required to measure the variable consideration. In particular, management applies judgment in evaluating whether changes in reimbursement regulations, claims processing and coverage determinations affect the estimate of the revenue management expects to be entitled to collect. This resulted in significant auditor judgment in the performance of our procedures.

How We Addressed the Matter in Our Audit	We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's variable consideration estimation process, including controls over management's review of collections experience and the evaluation of factors that would affect the amount of variable consideration described above. To test the estimate of variable consideration, we performed audit procedures that included, among others, assessing the methodology used and testing the underlying data used by the Company in its analysis. We compared the collection rates used by management to historical collection trends and evaluated whether changes in the regulatory environment or the Company's business model, customer base, mix of services and other factors would affect the estimate of variable consideration. We assessed the historical accuracy of management's estimate and performed sensitivity analyses to evaluate the changes in variable consideration that would result from changes in the expected collection rates used and the corresponding effect on revenue from services.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2007.

Miami, Florida
February 18, 2021

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of OPKO Health, Inc. and subsidiaries

Opinion on Internal Control over Financial Reporting

We have audited OPKO Health, Inc. and subsidiaries' internal control over financial reporting as of December 31, 2020, 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). In our opinion, OPKO Health, Inc, and subsidiaries (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2020 consolidated financial statements of the Company and our report dated February 18, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's 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 are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. 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.

Definition and Limitations of Internal Control Over Financial Reporting

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.

/s/ Ernst & Young LLP

Miami, Florida
February 18, 2021

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

	December 31,	
	2020	2019
ASSETS		
Current assets:		
Cash and cash equivalents	$ 72,211	$ 85,452
Accounts receivable, net	286,314	134,617
Inventory, net	132,341	53,434
Other current assets and prepaid expenses	32,313	50,542
Total current assets	523,179	324,045
Property, plant and equipment, net	140,554	127,111
Intangible assets, net	475,002	528,962
In-process research and development	590,200	590,200
Goodwill	680,602	671,940
Investments	15,731	20,746
Operating lease right-of-use assets	37,735	39,380
Other assets	10,060	6,888
Total assets	$ 2,473,063	$ 2,309,272
LIABILITIES AND EQUITY		
Current liabilities:		
Accounts payable	$ 100,883	$ 62,537
Accrued expenses	240,869	164,925
Current maturities of operating leases	9,028	12,038
Current portion of lines of credit and notes payable	24,703	9,619
Total current liabilities	375,483	249,119
Operating lease liabilities	29,760	27,665
Convertible notes	221,989	211,208
Deferred tax liabilities	137,208	118,717
Other long-term liabilities, principally contract liabilities, contingent consideration and lines of credit	37,072	87,804
Total long-term liabilities	426,029	445,394
Total liabilities	801,512	694,513
Equity:		
Common Stock - $ 0.01 par value, 1,000,000,000 shares authorized at December 31, 2020 and 2019, respectively; 670,585,576 and 670,378,701 shares issued at December 31, 2020 and 2019, respectively	6,706	6,704
Treasury Stock, - 549,907 shares at December 31, 2020 and 2019, respectively	(1,791)	(1,791)
Additional paid-in capital	3,152,694	3,142,993
Accumulated other comprehensive loss	(4,225)	(22,070)
Accumulated deficit	(1,481,833)	(1,511,077)
Total shareholders' equity	1,671,551	1,614,759
Total liabilities and equity	$ 2,473,063	$ 2,309,272

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

OPKO Health, Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share data)

	For the years ended December 31,		
	2020	2019	2018
Revenues:			
Revenue from services	$ 1,262,242	$ 716,434	$ 813,248
Revenue from products	119,952	112,184	107,112
Revenue from transfer of intellectual property and other	53,219	73,317	69,906
Total revenues	1,435,413	901,935	990,266
Costs and expenses:			
Cost of service revenue	823,899	511,206	546,654
Cost of product revenue	70,509	61,278	57,982
Selling, general and administrative	355,573	343,305	358,346
Research and development	75,316	117,870	125,586
Contingent consideration	(3,989)	(14,854)	(16,816)
Amortization of intangible assets	56,391	64,783	67,933
Asset impairment charges	—	92,399	21,778
Total costs and expenses	1,377,699	1,175,987	1,161,463
Operating income (loss)	57,714	(274,052)	(171,197)
Other income and (expense), net:			
Interest income	152	1,710	1,240
Interest expense	(21,934)	(21,516)	(11,890)
Fair value changes of derivative instruments, net	50	174	3,043
Other income (expense), net	12,701	(11,281)	1,535
Other income and (expense), net	(9,031)	(30,913)	(6,072)
Income (loss) before income taxes and investment losses	48,683	(304,965)	(177,269)
Income tax benefit (provision)	(17,617)	(7,060)	38,726
Net income (loss) before investment losses	31,066	(312,025)	(138,543)
Loss from investments in investees	(480)	(2,900)	(14,497)
Net income (loss)	$ 30,586	$ (314,925)	$ (153,040)
Income (loss) per share basic and diluted:			
Income (loss) per share	$ 0.05	$ (0.53)	$ (0.27)
Weighted average number of common shares outstanding, basic and diluted	640,655,290	595,454,394	563,143,663

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

OPKO Health, Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(In thousands)

	For the years ended December 31,		
	2020	2019	2018
Net income (loss)	$ 30,586	$ (314,925)	$ (153,040)
Other comprehensive income (loss), net of tax:			
Change in foreign currency translation and other comprehensive income (loss)	17,845	(1,939)	(14,727)
Investments:			
Reclassification adjustments due to adoption of ASU 2016-01	—	—	(4,876)
Comprehensive income (loss)	$ 48,431	$ (316,864)	$ (172,643)

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

OPKO Health, Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF EQUITY
(In thousands, except share and per share data)
For the years ended December 31, 2020, 2019, 2018

	Common Stock		Treasury		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total
	Shares	Dollars	Shares	Dollars				
Balance at December 31, 2017	560,023,745	$ 5,600	(549,907)	$ (1,791)	$ 2,889,256	$ (528)	$ (1,048,914)	$ 1,843,623
Equity-based compensation expense	—	—	—	—	21,761	—	—	21,761
Exercise of Common Stock options and warrants	353,677	4	—	—	1,170	—	—	1,174
Adoption of ASU 2016-01	—	—	—	—	—	(4,876)	4,876	—
Private placement	26,504,298	265	—	—	92,235	—	—	92,500
Net loss	—	—	—	—	—	—	(153,040)	(153,040)
Other comprehensive loss	—	—	—	—	—	(14,727)	—	(14,727)
Balance at December 31, 2018	586,881,720	$ 5,869	(549,907)	$ (1,791)	$ 3,004,422	$ (20,131)	$ (1,197,078)	$ 1,791,291

	Common Stock		Treasury		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total
	Shares	Dollars	Shares	Dollars				
Balance at December 31, 2018	586,881,720	$ 5,869	(549,907)	$ (1,791)	$ 3,004,422	$ (20,131)	$ (1,197,078)	$ 1,791,291
Equity-based compensation expense	—	—	—	—	13,421	—	—	13,421
Exercise of Common Stock options and warrants	19,232	—	—	—	(3)	—	—	(3)
Adoption of ASU 2018-07	—	—	—	—	(926)	—	926	—
2025 convertible notes including share lending agreement	29,250,000	293	—	—	50,559	—	—	50,852
Sale of common stock	54,227,749	542	—	—	75,520	—	—	76,062
Net loss	—	—	—	—	—	—	(314,925)	(314,925)
Other comprehensive loss	—	—	—	—	—	(1,939)	—	(1,939)
Balance at December 31, 2019	670,378,701	$ 6,704	(549,907)	$ (1,791)	$ 3,142,993	$ (22,070)	$ (1,511,077)	$ 1,614,759

	Common Stock		Treasury		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total
	Shares	Dollars	Shares	Dollars				
Balance at December 31, 2019	670,378,701	$ 6,704	(549,907)	$ (1,791)	$ 3,142,993	$ (22,070)	$ (1,511,077)	$ 1,614,759
Equity-based compensation expense	—	—	—	—	8,947	—	—	8,947
Exercise of Common Stock options and warrants	206,875	2	—	—	754	—	—	756
Adoption of ASC 326	—	—	—	—	—	—	(1,342)	(1,342)
Net income	—	—	—	—	—	—	30,586	30,586
Other comprehensive loss	—	—	—	—	—	17,845	—	17,845
Balance at December 31, 2020	670,585,576	$ 6,706	(549,907)	$ (1,791)	$ 3,152,694	$ (4,225)	$ (1,481,833)	$ 1,671,551

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

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

	For the years ended December 31,		
	2020	2019	2018
Cash flows from operating activities:			
Net income (loss)	$ 30,586	$ (314,925)	$ (153,040)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Depreciation and amortization	85,362	93,807	97,344
Non-cash interest	9,994	8,731	4,903
Amortization of deferred financing costs	847	995	187
Losses from investments in investees	480	2,900	14,497
Equity-based compensation – employees and non-employees	8,947	13,421	21,761
Asset impairment charges	—	92,399	21,778
Realized loss (gain) on disposal of fixed assets and sales of equity securities and other	(10,681)	739	46
Change in fair value of equity securities and derivative instruments and other	(101)	8,748	(6,524)
Change in fair value of contingent consideration	(3,989)	(14,854)	(16,816)
Deferred income tax provision (benefit)	15,640	4,324	(35,133)
Changes in assets and liabilities, net of the effects of acquisitions:			
Accounts receivable, net	(150,437)	7,376	20,397
Inventory, net	(77,642)	(12,133)	4,590
Other current assets and prepaid expenses	20,504	(11,486)	2,276
Other assets	(447)	409	(69)
Accounts payable	37,159	15,636	(26,083)
Foreign currency measurement	(3,185)	(71)	294
Contract liabilities	(5,389)	(69,302)	(61,264)
Accrued expenses and other liabilities	81,828	764	1,715
Net cash provided by (used in) operating activities	39,476	(172,522)	(109,141)
Cash flows from investing activities:			
Investments in investees	—	(1,200)	(1,000)
Proceeds from sale of investments	15,110	—	1,516
Proceeds from the sale of property, plant and equipment	245	671	1,223
Capital expenditures	(33,682)	(12,741)	(27,858)
Net cash used in investing activities	(18,327)	(13,270)	(26,119)
Cash flows from financing activities:			
Issuance of common stock	—	76,062	92,500
Issuance of 2023 Convertible Notes, including to related parties	—	200,293	55,000
Debt issuance costs	—	(7,762)	—
Proceeds from the exercise of Common Stock options and warrants	756	(3)	1,174
Borrowings on lines of credit	1,107,866	294,780	26,917
Repayments of lines of credit	(1,143,698)	(359,322)	(34,681)
Redemption of 2033 Senior Notes	—	(28,800)	—
Net cash (used in) provided by financing activities	(35,076)	175,248	140,910
Effect of exchange rate changes on cash and cash equivalents	686	(477)	(676)
Net increase (decrease) in cash and cash equivalents	(13,241)	(11,021)	4,974
Cash and cash equivalents at beginning of period	85,452	96,473	91,499
Cash and cash equivalents at end of period	$ 72,211	$ 85,452	$ 96,473
SUPPLEMENTAL INFORMATION:			
Interest paid	$ 10,908	$ 11,873	$ 2,076
Income taxes paid, net of refunds	$ (903)	$ 2,667	$ (1,410)
Operating lease right-of-use assets due to adoption of ASU No. 2016-02	$ —	$ 39,380	$ —
Operating lease liabilities due to adoption of ASU No. 2016-02	$ —	$ 39,703	$ —
Non-cash financing:			
Shares issued upon the conversion of:			
Common Stock options and warrants, surrendered in net exercise	$ —	$ 20	$ 806

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

Note 1 Business and Organization

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, Inc. ("BioReference"), one of the nation's largest full service laboratories with a core genetic testing business and an almost 300-person sales and marketing team focused on driving growth and leveraging new products, including the *4Kscore* test. Our pharmaceutical business features *Rayaldee*, an FDA-approved treatment for secondary hyperparathyroidism ("SHPT") in adults with stage 3 or 4 chronic kidney disease ("CKD") and vitamin D insufficiency (launched in November 2016) and a pipeline of products in various stages of development. Our leading product in development is Somatrogon (hGH-CTP), a once-weekly human growth hormone for which we have partnered with Pfizer Inc. ("Pfizer") and successfully completed a phase 3 study in August 2019, and for which the FDA has accepted the initial BLA for filing and we have submitted a New Drug Application (an "NDA") with the Ministry of Health, Labour and Welfare in Japan. We are incorporated in Delaware, and our principal executive offices are located in leased offices in Miami, Florida.

Through BioReference, we provide laboratory testing services, primarily to customers in the larger metropolitan areas in New York, New Jersey, Florida, Texas, Maryland, California, Pennsylvania, Delaware, Washington, DC, Illinois and Massachusetts, as well as to customers in a number of other states. We offer a comprehensive test menu of clinical diagnostics for blood, urine and tissue analysis. This includes hematology, clinical chemistry, immunoassay, infectious diseases, serology, hormones, and toxicology assays, as well as Pap smear, anatomic pathology (biopsies) and other types of tissue analysis. We market our laboratory testing services directly to physicians, geneticists, hospitals, clinics, correctional and other health facilities.

We operate established pharmaceutical platforms in Ireland, Chile, Spain, 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. In addition, we have a development and commercial supply pharmaceutical company and a global supply chain operation and holding company in Ireland. 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.

Our research and development activities are primarily performed at facilities in Woburn, MA, Waterford, Ireland, Kiryat Gat, Israel, and Barcelona, Spain.

Note 2 Impact of COVID-19

As the disease caused by SARS-CoV-2, a novel strain of coronavirus, COVID-19 continues to spread and severely impact the economy of the U.S. and other countries around the world, we are committed to being a part of the coordinated public and private sector response to this unprecedented challenge. In response to the COVID-19 pandemic, BioReference is accepting specimens from U.S. healthcare providers, clinics and health and hospital systems for two types of COVID-19 testing, diagnostic molecular testing and serology antibody testing, which is intended to promote earlier diagnosis of the coronavirus, assess a patient's immune response to the virus and aid in limiting the spread of infection.

We have put preparedness plans in place at our facilities to maintain continuity of operations, while also taking steps to keep our employees and customers healthy and safe. In line with recommendations to reduce large gatherings and increase social distancing, we have, where practical, transitioned many office-based employees to a remote work environment.

Revenue from services for the year ended December 31, 2020 increased by $45.8 million as compared to 2019 due to COVID-19 testing volumes; however we are unable to predict how long the demand will continue for our COVID-19 related testing, or whether pricing and reimbursement policies for testing will sustain, and accordingly, the sustainability of our COVID-19 testing volumes is uncertain. Additionally, beginning in March 2020, BioReference experienced, and continues to experience, a decline in routine clinical and genomics testing volumes due to the COVID-19 pandemic. Excluding COVID-19 test volumes, for the year ended December 31, 2020, volumes in our diagnostics segment declined 17% as compared to volumes for the year ended December 31, 2019. Additionally, sales of *Rayaldee* have not increased in accordance with its expected growth trajectory as a result of challenges in onboarding new patients due to the COVID-19 pandemic. Federal, state and local governmental policies and initiatives designed to reduce the transmission of COVID-19 have resulted in, among other things, a significant reduction in physician office visits, the cancellation of elective medical procedures, customers closing or severely curtailing their operations (voluntarily or in response to government orders), and the adoption of work-from-home or shelter-in-place policies. As stay at home orders and other restrictions have been lifted, we have seen our routine clinical and genomic testing volumes trending towards normalization with prior periods; however should stay at home orders or other

restrictions be reenacted, we could see our routine testing levels decline. We also continue to see a substantial need for COVID-19 testing by our existing clients and expect new clients as infection rates for the virus continue to increase across the country.

In March 2020, in response to the COVID-19 pandemic, the Coronavirus Aid, Relief, and Economic Security (CARES) Act was signed into law. The CARES Act provides numerous tax provisions and other stimulus measures, including temporary changes regarding the prior and future utilization of net operating losses, temporary changes to the prior and future limitations on interest deductions, temporary suspension of certain payment requirements for the employer portion of Social Security taxes, technical corrections from prior tax legislation for tax depreciation of certain qualified improvement property, and the creation of certain payroll tax credits associated with the retention of employees.

We have received, or expect to receive a number of benefits under the CARES Act including, but not limited to:

- During the year ended December 31, 2020, we received approximately $14 million under The Centers for Medicare & Medicaid Services (CMS) Accelerated and Advance Payment Program, which provides accelerated payments to Medicare providers/suppliers working to provide treatment to patients and combat the COVID-19 pandemic, and such amounts advanced to us are loans which will be offset against future claims and must be repaid in 2021;
- We are eligible to defer depositing the employer's share of Social Security taxes for payments due from March 27, 2020 through December 31, 2020, interest-free and penalty-free;
- We received approximately $16.2 million during the year ended December 31, 2020 from the funds that were distributed to healthcare providers for related expenses or lost revenues that are attributable to the COVID-19 pandemic;
- U.S. Department of Health and Human Services (HHS), will provide claims reimbursement to healthcare providers generally at Medicare rates for testing uninsured patients; and
- Clinical laboratories are provided a one-year reprieve from the reporting requirements under the Protecting Access to Medicare Act ("PAMA") as well as a one-year delay of reimbursement rate reductions for clinical laboratory services provided under Medicare that were scheduled to take place in 2021.

In October 2020, the U.S. Department of Health & Human Services issued new reporting requirements for the CARES Act funding. Due to these new reporting requirements and various interpretations, there is a reasonable possibility that amounts recorded under CARES Act funding will change in future periods.

Note 3 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.

Principles of consolidation. The accompanying Consolidated Financial Statements include the accounts of OPKO Health, Inc. and of our wholly-owned subsidiaries. All intercompany accounts and transactions are eliminated in consolidation.

Use of estimates. The preparation of financial statements in conformity with GAAP 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 significantly from these 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 and 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 and net realizable value. Inventories at our diagnostics segment consist primarily of purchased laboratory supplies, which is used in our testing laboratories. Inventory obsolescence expense for the years ended December 31, 2020 and 2019 was $4.4 million and $2.3 million, respectively.

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.

Goodwill and intangible assets. Goodwill represents the difference between the purchase price and the estimated fair value of the net assets acquired accounted for by the acquisition method of accounting. Refer to Note 6. Goodwill, in-process research and development ("IPR&D") and other intangible assets acquired in business combinations, licensing and other transactions at December 31, 2020 and 2019, was $1.7 billion and $1.8 billion, respectively.

Assets acquired and liabilities assumed in business combinations, licensing and other transactions are generally 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. At acquisition, we generally determine the fair value of intangible assets, including IPR&D, using the "income method."

Subsequent to acquisition, goodwill and indefinite lived intangible assets are tested at least annually as of October 1 for impairment, or when events or changes in circumstances indicate it is more likely than not that the carrying amount of such assets may not be recoverable.

Goodwill was $680.6 million and $671.9 million, respectively, at December 31, 2020 and 2019. Estimating the fair value of a reporting unit for goodwill impairment is highly sensitive to changes in projections and assumptions and changes in 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, potential changes in these assumptions may impact the estimated fair value of a reporting unit and result in an impairment if the fair value of such reporting unit is less than its carrying value.

Net intangible assets other than goodwill were $1.1 billion, including IPR&D of $590.2 million, at both December 31, 2020 and 2019. Intangible assets are highly vulnerable to impairment charges, particularly newly acquired assets for recently launched products and IPR&D. 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 may occur in future periods. Estimating the fair value of IPR&D for potential impairment is highly sensitive to changes in projections and assumptions and changes in assumptions could potentially lead to impairment.

Upon obtaining regulatory approval, IPR&D assets are 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. Finite lived intangible assets are tested for impairment when events or changes in circumstances indicate it is more likely than not that the carrying amount of such assets may not be recoverable. The testing includes a comparison of the carrying amount of the asset to its estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated undiscounted future cash flows, then an impairment charge is recognized for the amount by which the carrying amount of the asset exceeds the fair value of the asset.

Impairment charges for the year ended December 31, 2019 were $92.4 million and consisted of a goodwill impairment charge of $26.2 million to write the carrying amount of the OPKO Diagnostics, CURNA and Transition Therapeutics reporting units down to their estimated fair value, an impairment charge of $44.8 million to write our IPR&D assets for OPK88003 and CURNA's platform technology for oligonucleotide therapeutics down to their estimated fair value, and an impairment charge of $20.7 million to write our intangible asset for the Claros Analyzer down to its estimated fair value as a result of our testing. These impairment charges for the year ended December 31, 2019, resulted from liquidity constraints, longer than expected development timelines and changes in the competitive landscape, which resulted in changes to our estimates and assumptions of the expected future cash flows of the reporting units focused on the development of the Claros Analyzer, OPK88003 and CURNA's platform technology.

We recorded a goodwill impairment charge of $11.7 million in Asset impairment charges in our Consolidated Statement of Operations for the year ended December 31, 2018 to write the carrying amount of the FineTech reporting unit down to its estimated fair value. We recorded an impairment charge of $10.1 million in Asset impairment charges in our Consolidated Statement of Operations for the year ended December 31, 2018 to write our IPR&D assets for *Alpharen* and OPK88004 down to their estimated fair value as a result of our testing.

We believe that our estimates and assumptions are reasonable and otherwise consistent with assumptions that marketplace participants would use in their estimates of fair value. However, if future results are not consistent with our estimates and assumptions, including as a result of the COVID-19 global pandemic, then we may be exposed to an impairment charge, which could be material.

We amortize intangible assets with definite lives on a straight-line basis over their estimated useful lives, ranging from3 to 20 years. 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 $56.4 million, $64.8 million and $67.9 million for the years ended December 31, 2020, 2019 and 2018, respectively. Amortization expense from operations for our intangible assets is expected to be $50.6 million, $50.3 million, $47.5 million, $44.4 million and $42.9 million for the years ended December 31, 2021, 2022, 2023, 2024 and 2025, respectively.

Fair value measurements. The carrying amounts of our cash and cash equivalents, accounts receivable, accounts payable and short-term debt approximate their fair value due to the short-term maturities of these instruments. Investments that are considered equity securities as of December 31, 2020 and 2019 are predominately carried at fair value. Our debt under the credit agreement with JPMorgan Chase Bank, N.A. approximates fair value due to the variable rate of interest applicable to such debt.

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 19.

Contingent consideration. Each period we revalue the contingent consideration obligations associated with certain prior acquisitions to their fair value and record increases in the fair value as contingent consideration expense and decreases in the fair value as a reduction in contingent consideration expense. 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, 2020 and 2019, our foreign currency forward contracts held to economically hedge 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 20.

Property, plant and equipment. Property, plant and equipment are recorded at cost or fair value if acquired in a business combination. Depreciation is provided using the straight-line method over the estimated useful lives of the assets and includes amortization expense for assets capitalized under finance leases. The estimated useful lives by asset class are as follows: software - 3 years, machinery, medical and other equipment - 5-8 years, furniture and fixtures - 5-12 years, leasehold improvements - the lesser of their useful life or the lease term, buildings and improvements - 10-40 years, and automobiles - 3-5 years. Expenditures for repairs and maintenance are charged to expense as incurred. Depreciation expense was $29.0 million, $29.0 million and $29.4 million for the years ended December 31, 2020, 2019 and 2018, respectively. Assets held under finance leases are included within Property, plant and equipment, net in our Consolidated Balance Sheets and are amortized over the shorter of their useful lives or the expected term of their related leases.

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 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 for 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. Valuation allowances on certain U.S. deferred tax assets and non-U.S. deferred tax assets are established, because realization of these tax benefits through future taxable income does not meet the more-likely-than-not threshold.

On December 22, 2017, the Tax Act was enacted into law and the new legislation contains several key tax provisions, including a reduction of the corporate income tax rate from 35% to 21% effective January 1, 2018 and a one-time mandatory transition tax on accumulated foreign earnings, among others. We were required to recognize the effect of the tax law changes in the period of enactment, such as remeasuring our U.S. deferred tax assets and liabilities, as well as reassessing the net realizability of our deferred tax assets and liabilities.

Effective January 1, 2018, the Tax Act provides for a new GILTI provision. Under the GILTI provision, certain foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets are included in U.S. taxable income. The Company currently estimates GILTI will be immaterial for the years ended December 31, 2020, 2019 and 2018, although interpretive guidance continues to be issued and future guidance may impact this analysis. The Company has not recorded any deferred taxes for future GILTI inclusions as any future inclusions are expected to be treated as a period expense and offset by net operating loss carryforwards in the U.S.

We operate in various countries and tax jurisdictions globally. For the year ended December 31, 2020, the tax rate differed from the U.S. federal statutory rate of 21% primarily due to the valuation allowance against certain U.S. and non-U.S. deferred tax assets, the relative mix in earnings and losses in the U.S. versus foreign tax jurisdictions, and the impact of certain discrete tax events and operating results in tax jurisdictions that do not result in a tax benefit.

Included in Other long-term liabilities is an accrual of $2.9 million related to uncertain tax positions involving income recognition. We recognize that local tax law is inherently complex and the local taxing authorities may not agree with certain tax positions taken. In connection with an examination of a 2014 and 2015 tax return in a foreign jurisdiction, the taxing authority has issued an initial income tax assessment of approximately $66 million (including interest). We are protesting this assessment as we believe that it is without technical merit. We expect to exhaust all administrative and judicial remedies necessary to resolve the matter, which could be a lengthy process. There can be no assurance that this matter will be resolved in our favor, and an adverse outcome, or any future tax examinations involving similar assertions, could have a material effect on our financial condition, results of operations and cash flows.

Revenue recognition. We recognize revenue when a customer obtains control of promised goods or services in accordance with Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* ("Topic 606"). The amount of revenue that is recorded reflects the consideration that we expect to receive in exchange for those goods or services. We apply the following five-step model in order to determine this amount: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation.

We apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, we review the contract to determine which performance obligations we must deliver and which of these performance obligations are distinct. We recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when the performance obligation is satisfied or as it is satisfied. For a complete discussion of accounting for Revenues from services, Revenues from products and Revenue from transfer of intellectual property and other, refer to Note 15.

Concentration of credit risk and allowance for doubtful accounts Financial instruments that potentially subject us to concentrations of credit risk consist primarily of accounts receivable. Substantially all of our accounts receivable are with either companies in the health care industry or patients. However, credit risk is limited due to the number of our clients as well as their dispersion across many different geographic regions.

While we have receivables due from federal and state governmental agencies, we do not believe that such receivables represent a credit risk since the related healthcare programs are funded by federal and state governments, and payment is primarily dependent upon submitting appropriate documentation. At December 31, 2020 and 2019, receivable balances (net of explicit and implicit price concessions) from Medicare and Medicaid were 6% and 6%, respectively, of our consolidated Accounts receivable, net. At December 31, 2020, receivable balances (net of explicit and implicit price concessions) due directly from states, cities and other municipalities, specifically related to our real-time reverse-transcription polymerase chain reaction (real-time RT-PCR) assay to detect COVID-19, were 6.3% of our consolidated accounts receivable, net.

The portion of our accounts receivable due from individual patients comprises the largest portion of credit risk. At December 31, 2020 and 2019, receivables due from patients represent approximately 0.7% and 2.5%, respectively, of our consolidated Accounts receivable, net.

We assess the collectability of accounts receivable balances by considering factors such as historical collection experience, customer credit worthiness, the age of accounts receivable balances, regulatory changes and current economic conditions and trends that may affect a customer's ability to pay. Actual results could differ from those estimates. The allowance for credit losses was $2.1 million and $1.9 million at December 31, 2020 and 2019, respectively. The credit loss expense for the years ended December 31, 2020 and 2019 was $0.2 million and $0.5 million, respectively.

Equity-based compensation. We measure the cost of 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 cash flows from operations. During the years ended December 31, 2020, 2019 and 2018, we recorded $8.9 million, $13.4 million and $21.8 million, respectively, of equity-based compensation expense.

Research and development expenses. Research and development expenses include external and internal expenses. 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 equity-based compensation expense. Other 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.

Research and development expense includes costs for in-process research and development projects acquired in 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 estimated 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 manage our operations in two reportable segments, pharmaceutical and diagnostics. The pharmaceutical segment consists of our pharmaceutical operations in Chile, Mexico, Ireland, Israel and Spain, *Rayaldee* product sales and our pharmaceutical research and development. The diagnostics segment primarily consists of clinical laboratory operations through BioReference and point-of-care 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 or income taxes. Refer to Note 18.

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 Statement of Operations.

Foreign currency translation. The financial statements of certain of our foreign operations are measured using the local currency as the functional currency. The local currency assets and liabilities are generally translated at the rate of exchange to the U.S. dollar on the balance sheet date and the local currency revenues and expenses are translated at average rates of exchange to the U.S. dollar during the reporting periods. Foreign currency transaction gains (losses) have been reflected as a component of Other income (expense), net within the Consolidated Statement of Operations and foreign currency translation gains (losses) have been included as a component of the Consolidated Statement of Comprehensive Income (Loss). During the years ended December 31, 2020, 2019 and 2018, we recorded $1.6 million, $0.4 million and $1.9 million, respectively of transaction gains (losses).

Variable interest entities. The consolidation of a variable interest entity ("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 5.

Investments. We have made strategic investments in development stage and emerging companies. We record these investments as equity method investments or as equity securities 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 5. For investments classified as equity securities, we record changes in their fair value as Other income (expense) in our Consolidated Statement of Operations based on their closing price per share at the end of each reporting period, unless the equity security does not have a readily determinable fair value. Refer to Note 5.

Recently adopted accounting pronouncements.

In June 2016, the FASB issued ASU No. 2016-13, "Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments," which amends the impairment model by requiring entities to use a forward-looking approach based on expected losses rather than incurred losses to estimate credit losses on certain types of financial instruments, including trade receivables. This may result in the earlier recognition of allowances for losses. The ASU is effective for public entities for fiscal years beginning after December 15, 2019, with early adoption permitted. The adoption of ASU 2016-13 on January 1, 2020, did not have a significant impact on our Consolidated Financial Statements.

Pending accounting pronouncements.

In August 2020, the FASB issued ASU No. 2020-06, "Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40)." ASU 2020-06 will simplify the accounting for convertible instruments by reducing the number of accounting models for convertible debt instruments and convertible preferred stock. The ASU is effective for public entities for fiscal years beginning after December 15, 2021, with early adoption permitted. We are currently evaluating the impact of this new guidance on our Consolidated Financial Statements.

Note 4 Income (loss) Per Share

Basic income (loss) per share is computed by dividing our net income (loss) by the weighted average number of shares of our common stock par value $0.01 per share ("Common Stock") outstanding during the period. Shares of Common Stock outstanding under the share lending arrangement entered into in conjunction with the 2025 Notes (as defined in Note 7) are excluded from the calculation of basic and diluted earnings per share because the borrower of the shares is required under the share lending arrangement to refund any dividends paid on the shares lent. Refer to Note 7. For diluted earnings per share, the dilutive impact of stock options and warrants is determined by applying the "treasury stock" method. The dilutive impact of the 2033 Senior Notes, the 2023 Convertible Notes and the 2025 Notes (each, as defined and discussed in Note 7) has been considered using the "if converted" method. For periods in which their effect would be antidilutive, no effect is given to outstanding options, warrants or the potentially dilutive shares issuable pursuant to the 2033 Senior Notes, the 2023 Convertible Notes and the 2025 Notes in the dilutive computation.

A total of 70,029,480, 67,765,380 and 16,568,520 potential shares of Common Stock have been excluded from the calculation of diluted net income (loss) per share for the years ended December 31, 2020, 2019 and 2018, respectively, because their inclusion would be antidilutive. A full presentation of diluted earnings per share has not been provided because the required adjustments to the numerator and denominator resulted in diluted earnings per share equivalent to basic earnings per share.

During the year ended December 31, 2020, an aggregate of 206,875 options and warrants to purchase shares of our Common Stock were exercised, resulting in the issuance of 206,875 shares of Common Stock. Of the 206,875 Common Stock options and Common Stock warrants exercised, 0 shares of Common Stock were surrendered in lieu of a cash payment via the net exercise feature of the applicable option and warrant agreements.

During the year ended December 31, 2019, an aggregate of 24,877 options and warrants to purchase shares of our Common Stock were exercised, resulting in the issuance of 19,232 shares of Common Stock. Of the 24,877 Common Stock options and Common Stock warrants exercised, 5,645 shares of Common Stock were surrendered in lieu of a cash payment via the net exercise feature of the applicable option and warrant agreements.

During the year ended December 31, 2018, an aggregate of 540,000 options and warrants to purchase shares of our Common Stock were exercised, resulting in the issuance of 353,677 shares of Common Stock. Of the 540,000 Common Stock options and Common Stock warrants exercised, 186,323 shares of Common Stock were surrendered in lieu of a cash payment via the net exercise feature of the applicable option and warrant agreements.

Note 5 Investments

Investments

The following table reflects the accounting method, carrying value and underlying equity in net assets of our unconsolidated investments as of December 31, 2020 and 2019:

(in thousands)	As of December 31, 2020		As of December 31, 2019	
Investment type	Investment Carrying Value	Underlying Equity in Net Assets	Investment Carrying Value	Underlying Equity in Net Assets
Equity method investments	$ 426	$ 2,252	$ 826	$ 9,931
Variable interest entity, equity method	1,060	9	894	—
Equity securities	14,136		18,870	
Equity securities with no readily determinable fair value	35		36	
Warrants and options	74		120	
Total carrying value of investments	$ 15,731		$ 20,746	

Equity method investments

Our equity method investments consist of investments in Pharmsynthez (ownership9%), Cocrystal Pharma, Inc. ("COCP") (4%), Non-Invasive Monitoring Systems, Inc. ("NIMS") (1%), Neovasc Inc. ("Neovasc") (1%), InCellDx, Inc. ("InCellDx") (29%), BioCardia, Inc. ("BioCardia") (2%), and Xenetic Biosciences, Inc. ("Xenetic") (3%). The aggregate total assets, liabilities, and net losses of our equity method investees as of and for the year ended December 31, 2020 were $90.9 million, $28.4 million, and $75.4 million, respectively. The aggregate total assets, liabilities, and net losses of our equity method investees as of and for the year ended December 31, 2019 was $191.5 million, $58.4 million, and $62.9 million, respectively. We have determined that we and/or our related parties can significantly influence the control of our equity method investments through our board representation and/or voting power. Accordingly, we account for our investment in these entities under the equity method and record our proportionate share of their respective losses in Loss from investments in investees in our Consolidated Statement of Operations. Included in Loss from investments in investees for the year ended December 31, 2018 is a charge of $2.9 million to write our investment in InCellDx, Inc. down to its fair value as of December 31, 2018. The aggregate value of our equity method investments based on the quoted market price of their respective shares of common stock and the number of shares held by us as of December 31, 2020 and 2019 was $7.5 million and 6.0 million, respectively.

Investments in Equity securities

Our equity securities consist of investments in Phio Pharmaceuticals ("Phio") (0.01%), VBI Vaccines Inc. ("VBI") (1%), ChromaDex Corporation (0.1%), MabVax Therapeutics Holdings, Inc. ("MabVax") (1%), and Eloxx Pharmaceuticals, Inc. ("Eloxx") (3%). We have determined that our ownership, along with that of our related parties, does not provide us with significant influence over the operations of these investments. Accordingly, we account for our investment in these entities as equity securities, and we record changes in the fair value of these investments in Other income (expense) each reporting period when they have readily determinable fair value. Equity securities without a readily determinable fair value are adjusted to fair value when there is an observable price change. Net gains and losses on our equity securities for the year ended December 31, 2020, 2019 and 2018 are as follows:

	For the year ended December 31		
(in thousands)	2020	2019	2018
Equity Securities:			
Net gains and losses recognized during the period on equity securities	$ 10,376	$ (7,443)	$ 2,752
Less: Net gains and losses realized during the period on equity securities	(10,324)	—	113
Unrealized net gains and losses recognized during the period on equity securities still held at the reporting date	$ 52	$ (7,443)	$ 2,865

Sales of investments

Gains (losses) included in earnings from sales of our investments are 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 equity securities, we hold options to purchase 47 thousand additional shares of BioCardia, all of which were vested as of December 31, 2020, and 33 thousand, 0.7 million, 40 thousand and 404 warrants to purchase additional shares of COCP, InCellDx, Inc., Xenetic and Phio, 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 Statement of Operations. We also recorded the fair value of the options and warrants in Investments, net in our Consolidated Balance Sheet. See further discussion of the Company's options and warrants in Note 19 and Note 20.

Investments in variable interest entities

We have determined that we hold variable interests in Detect Genomix, LLC ("Detect Genomix") 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.

In August 2020, GeneDx, Inc., a subsidiary of BioReference, announced that it had entered into an agreement with Pediatrix Medical Group ("Pediatrix"), a provider of maternal-fetal, and pediatric medical and surgical subspecialty physician services, to offer genomic sequencing to support clinical diagnosis in neonatal intensive care units staffed by Pediatrix's affiliated neonatologists. The offering is planned to include whole exome and whole genome sequencing and genomic support services under the brand Detect Genomix.

Our initial capital investment in Detect Genomix was $245,000 for which we received a 49% ownership interest in Detect Genomix. We are required to make additional capital contributions to Detect Genomix in accordance with our percentage interests if Detect Genomix is unable to generate positive cash flow from operations or is unable to obtain alternative financing. We have not made any other investments in or loans to Detect Genomix through December 31, 2020.

In order to determine the primary beneficiary of Detect Genomix, we evaluated our investment to identify if we had the power to direct the activities that most significantly impact the economic performance of Detect Genomix. Based on the capital structure, governing documents and overall business operations of Detect Genomix, we determined that, while a VIE, we do not have the power to direct the activities that most significantly impact Detect Genomix's economic performance. We determined, however, that we can significantly influence control of Detect Genomix through our board representation and voting power. Therefore, we have the ability to exercise significant influence over Detect Genomix's operations and account for our investment in Detect Genomix under the equity method.

We own 1,260,000 shares of Zebra Series A-2 Preferred Stock and 900,000 shares of Zebra restricted common stock (ownership 29% at December 31, 2020 and 2019). 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 parties' investment to identify if we had the power to direct the activities that most significantly impact the economic performance of Zebra. 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 and have no obligation to fund expected losses. We did determine, however, that we can significantly influence control of Zebra through our board representation and voting power. Therefore, we have the ability to exercise significant influence over Zebra's operations and account for our investment in Zebra under the equity method.

Note 6 Composition of Certain Financial Statement Captions

(In thousands)	For the years ended December 31, 2020	2019
Accounts receivable, net		
Accounts receivable	$ 288,369	$ 136,551
Less: allowance for doubtful accounts	(2,055)	(1,934)
	$ 286,314	$ 134,617
Inventories, net		
Consumable supplies	$ 86,779	$ 23,005
Finished products	36,831	25,142
Work in-process	5,268	3,238
Raw materials	5,784	4,586
Less: inventory reserve	(2,321)	(2,537)
	$ 132,341	$ 53,434
Other current assets and prepaid expenses		
Taxes recoverable	$ 13,440	$ 19,808
Other receivables	2,502	3,262
Prepaid supplies	7,259	8,147
Prepaid insurance	3,803	3,486
Other	5,309	15,839
	$ 32,313	$ 50,542
Property, plant and equipment, net:		
Machinery, medical and other equipment	$ 193,152	$ 165,501
Leasehold improvements	40,742	33,606
Furniture and fixtures	13,547	12,631
Automobiles and aircraft	10,537	10,029
Software	14,726	13,861
Building	21,848	18,462
Land	2,602	2,422
Construction in process	8,169	7,044
Less: accumulated depreciation	(164,769)	(136,445)
	$ 140,554	$ 127,111
Intangible assets, net:		
Customer relationships	$ 448,751	$ 445,408
Technologies	296,623	296,246
Trade names	49,820	49,786
Covenants not to compete	16,334	16,318
Licenses	5,766	5,766
Product registrations	8,025	7,578
Other	6,513	6,094
Less: accumulated amortization	(356,830)	(298,234)
	$ 475,002	$ 528,962

(In thousands)	For the years ended December 31, 2020	2019
Accrued expenses:		
Inventory received but not invoiced	$ 72,160	$ 13,751
Employee benefits	43,300	33,671
Contract liabilities	15,783	19,196
Commitments and contingencies	15,454	38,635
Clinical trials	7,112	8,122
Professional fees	4,985	1,333
Finance leases short-term	2,453	2,743
Contingent consideration	1,188	2,375
Other	78,434	45,099
	$ 240,869	$ 164,925
Other long-term liabilities:		
Line of credit	$ —	$ 44,749
Contract liabilities	595	2,571
Contingent consideration	4,507	7,308
Finance leases long-term	2,805	4,046
Mortgages and other debts payable	3,837	3,906
Other	25,328	25,224
	$ 37,072	$ 87,804

Our intangible assets and goodwill relate principally to our completed acquisitions of OPKO Renal, OPKO Biologics, EirGen Pharma Limited ("EirGen") and BioReference. We amortize intangible assets with definite lives on a straight-line basis over their estimated useful lives. The estimated useful lives by asset class are as follows: technologies - 7-17 years, customer relationships - 7-20 years, product registrations - 7-10 years, covenants not to compete - 5 years, trade names - 5-10 years, other 9-13 years. 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 any jurisdiction in which we operate.

The changes in value of the intangible assets and goodwill during the year ended December 31, 2020 are primarily due to foreign currency fluctuations between the Chilean Peso, the Euro and the Shekel against the U.S. dollar. The changes in value of the intangible assets and goodwill during the year ended December 31, 2019 are primarily due to an impairment charge of $44.8 million to write our IPR&D assets for OPK88003 and CURNA's platform technology for oligonucleotide therapeutics down to their estimated fair value, a goodwill impairment charge of $26.2 million to write the carrying amount of the OPKO Diagnostics, CURNA and Transition Therapeutics reporting units down to their estimated fair value, and an impairment charge of $20.7 million to write our intangible asset for the Claros Analyzer down to its estimated fair value. The changes in value of the intangible assets during the year ended December 31, 2018 are primarily due to an impairment charge of $10.1 million to write our IPR&D assets for *Alpharen* and OPK88004 down to their estimated fair value. The changes in value of our intangible assets and goodwill for the years ended December 31, 2019 and 2018 were also affected by foreign currency fluctuations between the Chilean Peso, the Euro and the Shekel against the U.S. dollar.

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	Ending balance
2020				
Allowance for doubtful accounts	$ (1,934)	(232)	111	$ (2,055)
Inventory reserve	$ (2,537)	(4,387)	4,603	$ (2,321)
Tax valuation allowance	$ (193,256)	(110,070)	—	$ (303,326)
2019				
Allowance for doubtful accounts	$ (1,758)	(469)	293	$ (1,934)
Inventory reserve	$ (2,956)	(2,349)	2,768	$ (2,537)
Tax valuation allowance	$ (154,916)	(38,340)	—	$ (193,256)

The following table summarizes the changes in Goodwill by reporting unit during the years ended December 31, 2020 and 2019.

	2020					2019				
(In thousands)	Gross goodwill at January 1	Cumulative impairment at January 1	Goodwill impairment	Foreign exchange and other	Balance at December 31st	Gross goodwill at January 1	Cumulative impairment at January 1	Goodwill impairment	Foreign exchange and other	Balance at December 31
Pharmaceuticals										
CURNA	$ 4,827	$ (4,827)	$ —	$ —	$ —	$ 4,827	$ —	$ (4,827)	$ —	$ —
Rayaldee	85,605	—	—	7,813	93,418	87,314	—	—	(1,709)	85,605
FineTech	11,698	(11,698)	—	—	—	11,698	(11,698)	—	—	—
OPKO Biologics	139,784	—	—	—	139,784	139,784	—	—	—	139,784
OPKO Chile	4,348	—	—	157	4,505	4,614	—	—	(266)	4,348
OPKO Health Europe	7,394	—	—	692	8,086	7,546	—	—	(152)	7,394
OPKO Mexico	100	(100)	—	—	—	100	(100)	—	—	—
Transition Therapeutics	3,421	(3,421)	—	—	—	3,322	—	(3,421)	99	—
Diagnostics										
BioReference	434,809	—	—	—	434,809	434,809	—	—	—	434,809
OPKO Diagnostics	17,977	(17,977)	—	—	—	17,977	—	(17,977)	—	—
	$ 709,963	$ (38,023)	$ —	$ 8,662	$ 680,602	$ 711,991	$ (11,798)	$ (26,225)	$ (2,028)	$ 671,940

Note 7 Debt

As of December 31, 2020 and 2019, our debt consists of the following:

(In thousands)	For the years ended December 31, 2020	2019
2025 Notes	$ 156,163	$ 148,140
2023 Convertible Notes	62,776	60,018
2033 Senior Notes	3,050	3,050
JP Morgan Chase	7,057	44,750
Chilean and Spanish lines of credit	15,897	7,327
Current portion of notes payable	1,749	2,292
Long term portion of notes payable	4,513	4,723
Total	$ 251,205	$ 270,300
Balance sheet captions		
Convertible Notes	$ 221,989	$ 211,208
Current portion of lines of credit and notes payable	24,703	9,619
JP Morgan Chase and LT notes payable included in long-term liabilities	4,513	49,473
Total	$ 251,205	$ 270,300

On February 25, 2020, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to provide us with an unsecured line of credit in the amount of $100 million. Borrowings under the line of credit will bear interest at a rate of 11% per annum and may be repaid and reborrowed at any time. The credit agreement includes various customary remedies for the lender following an event of default, including the acceleration of repayment of outstanding amounts under line of credit. The line of credit matures on February 25, 2025. The line of credit also calls for a commitment fee equal to 0.25% per annum of the unused portion of the line. As of December 31, 2020, no funds were borrowed under the line of credit.

In February 2019, we issued $200.0 million aggregate principal amount of Senior Convertible Notes due 2025 (the "2025 Notes") in an underwritten public offering. The 2025 Notes bear interest at a rate of 4.50% per year, payable semiannually in arrears on February 15 and August 15 of each year. The 2025 Notes mature on February 15, 2025, unless earlier repurchased, redeemed or converted.

Holders may convert their 2025 Notes into shares of Common Stock at their option at any time prior to the close of business on the business day immediately preceding November 15, 2024 only under the following circumstances: (1) during any calendar quarter commencing after the calendar quarter ended March 31, 2019 (and only during such calendar quarter), if the last reported sale price of our Common Stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; (2) during the five business day period after any five consecutive trading day period (the "measurement period") in which the trading price per $1,000 principal amount of 2025 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our Common Stock and the conversion rate on each such trading day; (3) if we call any or all of the 2025 Notes for redemption, at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date; or (4) upon the occurrence of specified corporate events set forth in the indenture governing the 2025 Notes. On or after November 15, 2024, until the close of business on the business day immediately preceding the maturity date, holders of the 2025 Notes may convert their notes at any time, regardless of the foregoing conditions. Upon conversion, we will pay or deliver, as the case may be, cash, shares of our Common Stock, or a combination of cash and shares of our Common Stock, at our election.

The initial and current conversion rate for the 2025 Notes is 236.7424 shares of Common Stock per $1,000 principal amount of 2025 Notes (equivalent to a conversion price of approximately $4.22 per share of Common Stock). The conversion rate for the 2025 Notes is subject to adjustment in certain events, but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date of the 2025 Notes or if we deliver a notice of redemption, in certain circumstances the indenture governing the 2025 Notes requires an increase in the conversion rate of the 2025 Notes for a holder who elects to convert its notes in connection with such a corporate event or notice of redemption, as the case may be.

We may not redeem the 2025 Notes prior to February 15, 2022. We may redeem for cash any or all of the notes, at our option, on or after February 15, 2022, if the last reported sale price of our Common Stock has been at least 130% of the then current conversion price for the notes for at least 20 trading days (whether or not consecutive) during any 30 consecutive

trading day period (including the last trading day of such period) ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. No sinking fund is provided for the 2025 Notes.

If we undergo a fundamental change, as defined in the indenture governing the 2025 Notes, prior to the maturity date of the 2025 Notes, holders may require us to repurchase for cash all or any portion of their notes at a repurchase price equal to 100% of the principal amount of the notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. The 2025 Notes are our senior unsecured obligations and rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the 2025 Notes; equal in right of payment to any of our existing and future liabilities that are not so subordinated; effectively junior in right of payment to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of our current or future subsidiaries.

In conjunction with the issuance of the 2025 Notes, we agreed to loan up to30,000,000 shares of our Common Stock to affiliates of the underwriter in order to assist investors in the 2025 Notes to hedge their position. As of December 31, 2020 and 2019, a total of 29,250,000 shares were issued under the share lending arrangement. We will not receive any of the proceeds from the sale of the borrowed shares, but we received a one-time nominal fee of $0.3 million for the newly issued shares. Shares of our Common Stock outstanding under the share lending arrangement are excluded from the calculation of basic and diluted earnings per share. See Note 4.

As required by ASC 470-20, “Debt with Conversion and Other Options,” we calculated the equity component of the 2025 Notes, taking into account both the fair value of the conversion option and the fair value of the share lending arrangement. The equity component was valued at $52.6 million at issue date and this amount was recorded as Additional paid-in capital, which resulted in a discount on the 2025 Notes. The discount is being amortized to Interest expense over the term of the 2025 Notes, which results in an effective interest rate on the 2025 Notes of 11.2%.

The following table sets forth information related to the 2025 Notes which is included in our Consolidated Balance Sheet as of December 31, 2020:

(In thousands)	2025 Senior Notes	Discount	Debt Issuance Costs	Total
Balance at December 31, 2019	$ 200,000	$ (46,774)	$ (5,086)	$ 148,140
Amortization of debt discount and debt issuance costs	—	7,237	786	8,023
Balance at December 31, 2020	$ 200,000	$ (39,537)	$ (4,300)	$ 156,163

On November 8, 2018, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to provide us with an unsecured line of credit in the aggregate principal amount of $60 million. The credit agreement was terminated on or around February 20, 2019 and we repaid the $28.8 million outstanding thereunder from the proceeds of the 2025 Notes offering.

In February 2018, we issued a series of5% Convertible Promissory Notes (the “2023 Convertible Notes”) in the aggregate principal amount of $55.0 million. The 2023 Convertible Notes mature 5 years from the date of issuance. Each holder of a 2023 Convertible Note has the option, from time to time, to convert all or any portion of the outstanding principal balance of such 2023 Convertible Note, together with accrued and unpaid interest thereon, into shares of our Common Stock at a conversion price of $5.00 per share of Common Stock. We may redeem all or any part of the then issued and outstanding 2023 Convertible Notes, together with accrued and unpaid interest thereon, pro rata among the holders, upon no fewer than 30 days, and no more than 60 days, notice to the holders. The 2023 Convertible Notes contain customary events of default and representations and warranties of OPKO.

Purchasers of the 2023 Convertible Notes included an affiliate of Dr. Phillip Frost, M.D., our Chairman and Chief Executive Officer, and Dr. Jane H. Hsiao, Ph.D., MBA, our Vice-Chairman and Chief Technical Officer.

In January 2013, we entered into note purchase agreements with respect to the issuance and sale of our3.0% Senior Notes due 2033 (the “2033 Senior Notes”) in a private placement exempt from registration under the Securities Act. We issued the 2033 Senior Notes on January 30, 2013. The 2033 Senior Notes, which totaled $175.0 million in original principal amount, bear interest at the rate of 3.0% per year, payable semiannually on February 1 and August 1 of each year. The 2033 Senior Notes mature on February 1, 2033, unless earlier repurchased, redeemed or converted. Upon a fundamental change as defined in the indenture, 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 related fundamental change repurchase date.

From 2013 to 2016, holders of the 2033 Senior Notes converted $143.2 million in aggregate principal amount into an aggregate of 21,539,873 shares of Common Stock. On February 1, 2019, approximately $28.8 million aggregate principal amount of 2033 Senior Notes were tendered by holders pursuant to such holders' option to require us to repurchase the 2033 Senior Notes as set forth in the indenture, governing the 2033 Senior Notes, following which repurchase only $3.0 million aggregate principal amount of the 2033 Senior Notes remained outstanding. Holders of the remaining $3.0 million principal amount of the 2033 Senior Notes may require us to repurchase such notes for 100% of their principal amount, plus accrued and unpaid interest, on February 1, 2023, on February 1, 2028, or following the occurrence of a fundamental change as described above.

The terms of the 2033 Senior Notes, include, among others: (i) rights to convert the notes 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 determined that these specific terms were embedded derivatives. 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 concluded that the embedded derivatives within the 2033 Senior Notes met these criteria and, as such, were valued separate and apart from the 2033 Senior Notes and recorded at fair value each reporting period.

For accounting and financial reporting purposes, we combined these embedded derivatives and valued them together as one unit of accounting. In 2017, certain terms of the embedded derivatives expired pursuant to the original agreement and the embedded derivatives no longer met the criteria to be separated from the host contract and, as a result, the embedded derivatives were no longer required to be valued separate and apart from the 2033 Senior Notes and were reclassified to additional paid in capital.

In November 2015, BioReference and certain of its subsidiaries entered into a credit agreement, as amended from time to time, with JPMorgan Chase Bank, N.A. ("CB"), as lender and administrative agent, as amended (the "Credit Agreement"). The Credit Agreement provides for a $75.0 million secured revolving credit facility and includes a $20.0 million sub-facility for swingline loans and a $20.0 million sub-facility for the issuance of letters of credit. The Credit Agreement matures on November 5, 2021 and is guaranteed by all of BioReference's domestic subsidiaries. The Credit Agreement is also secured by substantially all assets of BioReference and its domestic subsidiaries, as well as a non-recourse pledge by us of our equity interest in BioReference. Availability under the Credit Agreement is based on a borrowing base comprised of eligible accounts receivables of BioReference and certain of its subsidiaries, as specified therein. As of December 31, 2020, $57.6 million remained available for borrowing under the Credit Agreement. Principal under the Credit Agreement is due upon maturity on November 5, 2021.

At BioReference's option, borrowings under the Credit Agreement (other than swingline loans) will bear interest at (i) the CB floating rate (defined as the higher of (a) the prime rate and (b) the LIBOR rate (adjusted for statutory reserve requirements for Eurocurrency liabilities) for an interest period of one month plus 2.50%) plus an applicable margin of 0.35% for the first 12 months and 0.50% thereafter or (ii) the LIBOR rate (adjusted for statutory reserve requirements for Eurocurrency liabilities) plus an applicable margin of 1.35% for the first 12 months and 1.50% thereafter. Swingline loans will bear interest at the CB floating rate plus the applicable margin. The Credit Agreement also calls for other customary fees and charges, including an unused commitment fee of 0.25% of the lending commitments.

As of December 31, 2020 and 2019, $7.1 million and $44.7 million, respectively, was outstanding under the Credit Agreement.

The Credit Agreement contains customary covenants and restrictions, including, without limitation, covenants that require BioReference and its subsidiaries to maintain a minimum fixed charge coverage ratio if availability under the new credit facility falls below a specified amount and to comply with laws and restrictions on the ability of BioReference and its subsidiaries to incur additional indebtedness or to pay dividends and make certain other distributions to the Company, subject to certain exceptions as specified therein. Failure to comply with these covenants would constitute an event of default under the Credit Agreement, notwithstanding the ability of BioReference to meet its debt service obligations. The Credit Agreement also includes various customary remedies for the lenders following an event of default, including the acceleration of repayment of outstanding amounts under the Credit Agreement and execution upon the collateral securing obligations under the Credit Agreement. Substantially all the assets of BioReference and its subsidiaries are restricted from sale, transfer, lease, disposal or

distributions to the Company, subject to certain exceptions. As of December 31, 2020, BioReference and its subsidiaries had net assets of approximately $1.0 billion, which included goodwill of $434.8 million and intangible assets of $329.5 million.

In addition to the Credit Agreement with CB, we had line of credit agreements witheleven other financial institutions as of December 31, 2020 and 2019 in the U.S., 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 BioReference, Chilean and Spanish lines of credit:

(Dollars in thousands)			Balance Outstanding	
Lender	Interest rate on borrowings at December 31, 2020	Credit line capacity	December 31, 2020	December 31, 2019
JP Morgan Chase	3.75%	$ 75,000	$ 7,057	$ 44,750
Itau Bank	5.50%	1,810	2,353	472
Bank of Chile	6.60%	3,800	1,494	851
BICE Bank	5.50%	2,500	1,166	1,429
BBVA Bank	5.50%	3,250	—	11
Security Bank	5.50%	262	262	588
Estado Bank	5.50%	3,500	2,127	1,365
Santander Bank	5.50%	4,500	3,025	1,943
Scotiabank	5.00%	1,829	1,829	668
Corpbanca	5.00%	3,641	3,641	—
Banco De Sabadell	1.75%	613	—	—
Banco Bilbao Vizcaya	1.70%	368	—	—
Santander Bank	1.82%	613	—	—
Total		$ 101,686	$ 22,954	$ 52,077

At December 31, 2020 and 2019, the weighted average interest rate on our lines of credit was approximately4.9% and 4.0%, respectively.

At December 31, 2020 and 2019, we had notes payable and other debt (excluding the 2033 Senior Notes, the 2023 Convertible Notes, the 2025 Notes, the Credit Agreement and amounts outstanding under lines of credit described above) as follows:

(In thousands)	December 31, 2020	December 31, 2019
Current portion of notes payable	$ 1,749	$ 2,292
Other long-term liabilities	4,513	4,723
Total	$ 6,262	$ 7,015

The notes and other debt mature at various dates ranging from 2021 through 2024 bearing variable interest rates from0.7% up to 3.8%. The weighted average interest rate on the notes and other debt was 2.9% and 2.7% on December 31, 2020 and 2019. The notes are partially secured by our office space in Barcelona.

Note 8 Shareholders' Equity

Our authorized capital stock consists of1,000,000,000 shares of Common Stock, par value $0.01 per share, and 10,000,000 shares of Preferred Stock, par value $0.01 per share.

Sales of Common Stock

On October 29, 2019, we issued50 million shares of our Common Stock at a price of $1.50 per share in an underwritten public offering (the "Offering"), resulting in net proceeds to the Company of approximately $70 million, after deducting underwriting commissions and offering expenses. In November 2019, pursuant to an option the Company granted the underwriters, we issued an additional 4,227,749 shares at $1.50 per share, less underwriting discounts and commissions, resulting in net proceeds of approximately $6 million. Drs. Frost and Hsiao and Mr. Steven Rubin, members of OPKO's senior management purchased an aggregate of 2,415,000 shares in the Offering.

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 exempt from registration under the Securities Act an aggregate of approximately 26.5 million shares of Common Stock at a purchase price of $3.49 per share, which was the closing bid price per share of Common Stock on the NASDAQ Global Select Market ("NASDAQ") on such date, for an aggregate purchase price of $92.5 million. Investors in the offering included an affiliate of Dr. Phillip Frost, our Chairman and Chief Executive Officer ($70 million), and Dr. Jane Hsiao, our Vice Chairman and Chief Technical Officer ($2 million).

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.

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 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, 500,000 shares and 2,000,000 shares were designated Series A Preferred Stock, Series C Preferred Stock and Series D Preferred Stock, respectively. As of December 31, 2020 and 2019, there were no shares of Series A Preferred Stock, Series C Preferred Stock or Series D Preferred Stock issued or outstanding.

Note 9 Accumulated Other Comprehensive Income (Loss)

For the year ended December 31, 2020, changes in Accumulated other comprehensive income (loss), net of tax, were as follows:

(In thousands)	Foreign currency translation
Balance at December 31, 2019	$ (22,070)
Other comprehensive income	17,845
Balance at December 31, 2020	$ (4,225)

For the year ended December 31, 2019, changes in Accumulated other comprehensive income, net of tax, were as follows:

(In thousands)	Foreign currency translation
Balance at December 31, 2018	$ (20,131)
Other comprehensive loss	(1,939)
Balance at December 31, 2019	$ (22,070)

Note 10 Equity-Based Compensation

We maintain three equity-based incentive compensation plans, the 2016 Equity Incentive Plan, the 2007 Equity 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 2016 Equity Incentive Plan

are exercisable for a period of up to 10 years from the date of grant. 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 the Modigene Plan 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 cash flows from operations. There were no excess tax benefits for the years ended December 31, 2020, 2019, and 2018.

Valuation and Expense Information

We recorded equity-based compensation expense of $8.9 million, $13.4 million and $21.8 million for the years ended December 31, 2020, 2019, and 2018, respectively, all of which were reflected as operating expenses. Of the $8.9 million of equity based compensation expense recorded for the year ended December 31, 2020, $6.8 million was recorded as selling, general and administrative expenses, $1.8 million was recorded as research and development expenses and $0.3 million was recorded as a cost of revenue. Of the $13.4 million of equity based compensation expense recorded for the year ended December 31, 2019, $9.7 million was recorded as selling, general and administrative expense, $2.0 million was recorded as research and development expenses and $1.6 million was recorded as a cost of revenue. Of the $21.8 million of equity based compensation expense recorded for the year ended December 31, 2018, $14.7 million was recorded as selling, general and administrative expense, $4.2 million was recorded as research and development expenses and 2.8 million was recorded as cost of revenue.

As of December 31, 2020, there was $18.3 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 1.81 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. We account for forfeitures as they occur and apply the following assumptions in our Black-Scholes-Merton Model option-pricing formula:

	Year Ended December 31, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Expected term (in years)	4.0 - 10.0	3.0 - 10.0	3.0 - 10.0
Risk-free interest rate	0.16% - 1.41%	1.35% - 2.63%	2.32% - 3.09%
Expected volatility	56% - 76%	54% - 63%	40% - 54%
Expected dividend yield	0%	0%	0%

Expected Term: For the expected term of options grants, we used an estimate of the expected option life based on historical experience.

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 was based on the historical volatility of our Common Stock.

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, 2020, there were 20,879,993 shares of Common Stock reserved for issuance under our equity-based incentive plans. 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., OPKO Biologics and

BioReference, 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, 2020, 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, 2019	37,370,421	$ 8.01	6.00	$ —
Granted	9,362,500	$ 2.41		
Exercised	(206,875)	$ 3.66		
Forfeited	(1,002,500)	$ 4.22		
Expired	(6,935,625)	$ 9.78		
Outstanding at December 31, 2020	38,587,921	$ 6.45	6.78	$ 26,054
Vested and expected to vest at December 31, 2020	38,587,921	$ 6.45	6.78	$ 26,054
Exercisable at December 31, 2020	22,197,446	$ 9.15	5.26	$ 4,407

The total intrinsic value of stock options exercised for the years ended December 31, 2020, 2019, and 2018 was $0.4 million, $0.1 million and $0.5 million, respectively.

The weighted average grant date fair value of stock options granted for the years ended December 31, 2020, 2019, and 2018 was $1.39, $1.15, and $2.08, respectively. The total fair value of stock options vested during the years ended December 31, 2020, 2019, and 2018 was $10.6 million, $18.6 million and $25.8 million, respectively.

Note 11 Income Taxes

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

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

	For the years ended December 31,		
(In thousands)	2020	2019	2018
Current			
Federal	$ (234)	$ —	$ —
State	351	(89)	6,318
Foreign	(2,094)	(2,647)	(2,738)
	(1,977)	(2,736)	3,580
Deferred			
Federal	(254)	333	2,045
State	933	125	5,673
Foreign	(16,319)	(4,782)	27,428
	(15,640)	(4,324)	35,146
Total, net	$ (17,617)	$ (7,060)	$ 38,726

Deferred income tax assets and liabilities as of December 31, 2020 and 2019 are comprised of the following:

(In thousands)	December 31, 2020	December 31, 2019
Deferred income tax assets:		
Federal net operating loss	$ 90,032	$ 121,125
State net operating loss	54,074	64,648
Foreign net operating loss	17,452	32,162
Research and development expense	301	1,560
Tax credits	22,999	22,989
Stock options	26,683	30,640
Accruals	14,779	17,215
Equity investments	13,619	13,495
Bad debts	310	445
Lease liability	861	1,064
Foreign credits	9,819	9,909
Available-for-sale securities	2,473	2,478
Operating lease asset	9,842	10,204
Other	6,393	8,395
Deferred income tax assets	269,637	336,329
Deferred income tax liabilities:		
Intangible assets	(73,122)	(230,662)
Convertible debt	(10,462)	(12,219)
Operating lease liability	(9,842)	(10,204)
Fixed assets	(2,736)	(3,976)
Other	(2,082)	(2,130)
Deferred income tax liabilities	(98,244)	(259,191)
Net deferred income tax assets (liabilities)	171,393	77,138
Valuation allowance	(303,326)	(194,869)
Net deferred income tax liabilities	$ (131,933)	$ (117,731)

Note: Net deferred income tax liability balance includes $5.3 million recorded to Other Assets on the Consolidated Balance Sheet.

As of December 31, 2020, we have federal, state and foreign net operating loss carryforwards of approximately $538.7 million, $729.8 million and $78.6 million, respectively, that expire at various dates through 2040 unless indefinite in nature. As of December 31, 2020, we have research and development tax credit carryforwards of approximately $23.0 million that expire in varying amounts through 2040. As of each reporting date, management considers new evidence, both positive and negative, that could affect its view of the future realization of deferred tax assets. We have determined a valuation allowance is required against all of our net deferred tax assets that we do not expect to be utilized by the reversing of deferred income tax liabilities.

In 2020 we completed the transfer of certain assets to an OPKO affiliate. The transaction gave rise to a deferred tax asset of approximately $148.9 million. Realizability of a deferred tax asset ultimately depends on the existence of sufficient taxable income in the carryback and carryforward periods as permitted by tax law. The Company evaluated the realizability of the deferred tax asset as required by ASC 740-10-30-18. The Company has determined that the deferred tax asset is not more-likely-than-not to be realized as of December 31, 2020. As a result, the Company has recorded a full valuation allowance against the deferred tax asset.

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 Section 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. There is no current impact on these financial statements as a result of the annual limitation. This study did not conclude whether OPKO's predecessor, eXegenics, pre-merger NOLs were limited under Section 382. As such, of the $538.7 million of federal net operating loss carryforwards, at least approximately $47.4 million may not be able to be utilized.

During 2020, we conducted a study to determine whether any ownership changes occurred from 2009 through 2020. As a result, we have concluded that the annual utilization of our NOLs and tax credits is not subject to a limitation pursuant to Internal Revenue Code Section 382.

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 Nova Scotia 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. 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 2017. However, because we are carrying forward income tax attributes, such as net operating losses and tax credits from those years, these attributes can still be audited when utilized on returns filed in the future.

State: Under the statute of limitations applicable to most state income tax laws, we are no longer subject to state income tax examinations by tax authorities for years before 2016 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 2016.

Foreign: Under the statute of limitations applicable to our foreign operations, we are generally no longer subject to tax examination for years before 2015 in jurisdictions where we have filed income tax returns.

Tax Cuts and Jobs Act

On December 22, 2017, the 2017 Tax Act was enacted into law and the new legislation contains several key tax provisions, including a reduction of the corporate income tax rate from 35% to 21% effective January 1, 2018 and a one-time mandatory transition tax on accumulated foreign earnings, among others. We were required to recognize the effect of the tax law changes in the period of enactment, such as remeasuring our U.S. deferred tax assets and liabilities, as well as reassessing the net realizability of our deferred tax assets and liabilities.

Effective January 1, 2018, the Tax Act provides for a new GILTI provision. Under the GILTI provision, certain foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets are included in U.S. taxable income. The Company currently estimates GILTI will be immaterial for the year ended December 31, 2020, although interpretive guidance continues to be issued and future guidance may impact this analysis. The Company has not recorded any deferred taxes for future GILTI inclusions as any future inclusions are expected to be treated as a period expense and offset by net operating loss carryforwards in the U.S.

Unrecognized Tax Benefits

As of December 31, 2020, 2019, and 2018, the total amount of gross unrecognized tax benefits was approximately $14.0 million, $17.2 million, and $17.5 million, respectively. As of December 31, 2020, the total amount of unrecognized tax benefits that, if recognized, would affect our effective income tax rate was $(10.0) million. We account for any applicable interest and penalties on uncertain tax positions as a component of income tax expense and we recognized $(0.1) million and $(0.1) million of interest expense for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2019 and 2018, $(13.2) million and $(14.2) million of the unrecognized tax benefits, if recognized, would have affected our effective income tax rate. We believe it is reasonably possible that up to $1.5 million of unrecognized tax benefits may be recognized within the next twelve months, mainly due to an expected audit settlement.

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

	For the years ended December 31,		
(In thousands)	2020	2019	2018
Unrecognized tax benefits at beginning of period	$ 17,160	$ 17,513	$ 21,347
Gross increases – tax positions in current period	441	884	8,384
Gross decreases – tax positions in prior period	(244)	(298)	(7,597)
Gross decreases – settlements with taxing authorities	(2,770)	—	—
Lapse of Statute of Limitations	(633)	(939)	(4,621)
Unrecognized tax benefits at end of period	$ 13,954	$ 17,160	$ 17,513

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,		
	2020	2019	2018
Federal statutory rate	21.0 %	21.0 %	21.0 %
State income taxes, net of federal benefit	17.4 %	2.8 %	4.3 %
Foreign income tax	53.7 %	(6.6)%	(6.0)%
Income Tax Refunds	(0.6)%	— %	3.6 %
Research and development tax credits	(1.0)%	0.3 %	1.9 %
Non-Deductible components of Convertible Debt	— %	— %	(0.2)%
Valuation allowance	227.7 %	(17.9)%	(7.1)%
Rate change effect	11.4 %	0.4 %	8.1 %
Non-deductible items	5.2 %	(1.7)%	(3.9)%
Unrecognized tax benefits	(5.0)%	— %	(1.8)%
Impairments	— %	(1.6)%	— %
IPR&D benefit	(309.6)%	— %	— %
Stock options excess tax benefit	10.6 %	0.4 %	0.5 %
Imputed interest	2.5 %	0.5 %	0.6 %
Other	3.2 %	0.1 %	(0.8)%
Total	36.5 %	(2.3)%	20.2 %

Certain operations in Israel have been granted "Beneficiary Enterprise" status by the Israeli Income Tax Authority, which makes us eligible for tax benefits under the Israeli Law for Encouragement of Capital Investments, 1959. Under the terms of the Beneficiary Enterprise program, beneficiary income that is attributable to our operations in Kiryat Gat, Israel will be exempt from income tax through 2023. This tax incentive has an immaterial impact on our earnings per share for the year ended December 31, 2020.

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

	For the years ended December 31,		
(In thousands)	2020	2019	2018
Pre-tax income (loss):			
U.S.	$ 81,734	$ (236,544)	$ (132,102)
Foreign	(33,531)	(71,321)	(59,664)
Total	$ 48,203	$ (307,865)	$ (191,766)

Prior to the enactment of the Tax Act, the Company regularly determined certain foreign earnings to be indefinitely reinvested outside the U.S. Our intent is to permanently reinvest these funds outside the U.S. and our current plans do not demonstrate a need to repatriate cash to fund U.S. operations. However, if funds were repatriated, we would be required to accrue and pay applicable U.S. taxes (if any) and withholding taxes payable to foreign tax authorities.

Note 12 Related Party Transactions

In August 2020, we paid a $125,000 filing fee to the Federal Trade Commission (the “FTC”) in connection with filings made by us and Dr. Jane Hsiao, our Vice Chairman and Chief Technical Officer, under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (“HSR Act”) relating to her percentage equity ownership interest in OPKO and potential future purchases of our Common Stock.

In August 2020, Dr. Phillip Frost, our Chairman and Chief Executive Officer, paid a filing fee of $280,000 to the FTC under the HSR Act in connection with filings made by us and Dr. Frost, relating to his percentage equity ownership interest in OPKO and potential future purchases of our Common Stock. We reimbursed Dr. Frost for the HSR filing fee.

In August 2020, GeneDx, Inc., a subsidiary of BioReference, entered into an agreement with Mednax Services, Inc. (“Mednax Services”), a subsidiary of MEDNAX, Inc., (“MEDNAX”) pursuant to which the parties formed a joint venture under the brand Detect Genomix. GeneDx’s initial capital investment in Detect Genomix was $245,000 for which GeneDx received a 49% ownership interest in Detect Genomix, and Mednax Services contributed $255,000. Adam Logal, the

Company's CFO, is the chair and sits on the Board of Managers of the joint venture. Mednax Services provides administrative services to the joint venture pursuant to an administrative services agreement. GeneDx provides laboratory services to the joint venture. Dr. Roger Medel, a director of the Company as of December 18, 2020, is the former Chief Executive Officer of MEDNAX and Mednax Services. Dr. Medel continues to serve on the board of MEDNAX.

On February 25, 2020, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to provide us with an unsecured line of credit in the amount of $100 million. Borrowings under the line of credit will bear interest at a rate of 11% per annum and may be repaid and reborrowed at any time. The credit agreement includes various customary remedies for the lender following an event of default, including the acceleration of repayment of outstanding amounts under this line of credit. This line of credit matures on February 25, 2025. This line of credit also calls for a commitment fee equal to 0.25% per annum of the unused portion of the line. As of December 31, 2020, no funds were borrowed under this line of credit.

On October 29, 2019, we issued 50 million shares of our Common Stock at a price of $1.50 per share in an underwritten public offering (the "Offering"), resulting in net proceeds to the Company of approximately $70 million, after deducting underwriting commissions and offering expenses. In November 2019, pursuant to an option the Company granted the underwriters, we issued an additional 4,227,749 shares at the public offering price, less underwriting discounts and commissions, resulting in net proceeds to the Company of approximately $6 million. Drs. Frost and Hsiao and Mr. Steven Rubin, members of OPKO's senior management purchased an aggregate of 2,415,000 shares of Common Stock in the Offering.

On March 1, 2019, OPKO Pharmaceuticals, LLC entered into an assignment agreement with Xenetic Biosciences, Inc., as amended from time to time (the "Assignment Agreement"), pursuant to which Xenetic acquired all of OPKO Pharmaceuticals' right, title and interest in and to that certain Intellectual Property License Agreement (the "IP License Agreement"), entered into between The Scripps Research Institute and OPKO Pharmaceuticals, regarding certain patents for novel CAR T platform technology and through which the Scripps Research Institute granted an exclusive royalty-bearing license in exchange for royalties, subject to the terms of the IP License Agreement.

Under the Assignment Agreement and the IP License Agreement, Xenetic issued to OPKO Pharmaceuticals 164,062 shares of Xenetic common stock (the "OPKO Transaction Shares"). In connection with the Assignment Agreement, OPKO Pharmaceuticals entered into a voting agreement pursuant to which OPKO Pharmaceuticals agreed, among other things, to vote its shares in Xenetic in favor of the transactions contemplated by the Assignment Agreement, and a lock-up agreement with Xenetic which restricts OPKO Pharmaceuticals' sale or transfer of any of the OPKO Transaction Shares as provided therein and as otherwise required by law. The Assignment Agreement and the obligations thereunder took effect on July 19, 2019, after Xenetic satisfied certain closing conditions, including obtaining stockholder approval and securing certain financing.

The Company owns approximately 9% of Pharmsynthez, and Pharmsynthez is Xenetic's largest and controlling stockholder. Dr. Richard Lerner, a director of the Company, is a co-inventor of Xenetic's technology and received 31,240 shares of Xenetic upon the closing of the Xenetic transactions described above. Adam Logal, our Senior Vice President and Chief Financial Officer, is a director of Xenetic.

In March 2019, we paid the $125,000 filing fee to the FTC in connection with filings made by us and Dr. Jane Hsiao, our Vice Chairman and Chief Technical Officer, under the HSR Act relating to her purchases of Common Stock.

In February 2019, Dr. Phillip Frost, our Chairman and Chief Executive Officer, paid a filing fee of $280,000 to the FTC under the HSR Act in connection with filings made by us and Dr. Frost, relating to his purchases of Common Stock. We reimbursed Dr. Frost for the HSR filing fee.

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 an aggregate of approximately 26.5 million shares of our Common Stock at a purchase price of $3.49 per share, which was the closing bid price of our Common Stock on the NASDAQ on such date, for an aggregate purchase price of $92.5 million. The investors in the private placements included an affiliate of Dr. Frost ($70 million), and Dr. Hsiao ($2 million).

On November 8, 2018, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to provide us with an unsecured line of credit in the amount of $60 million. Borrowings under this line of credit bore interest at a rate of 10% per annum and could have been repaid and reborrowed at any time. The credit agreement included various customary remedies for the lender following an event of default, including the acceleration of repayment of outstanding amounts under this line of credit. This line of credit would have matured on November 8, 2023. We repaid approximately $28.8 million that was borrowed in 2019 and terminated this line of credit on or around February 20, 2019.

In February 2018, we issued the 2023 Convertible Notes in the aggregate principal amount of $55.0 million. Refer to Note 7. Purchasers of the 2023 Convertible Notes included Dr. Hsiao and an affiliate of Dr. Frost.

We hold investments in Zebra (ownership 29%), Neovasc (1%), ChromaDex Corporation (0%), MabVax (1%), COCP (4%), NIMS (1%), Eloxx (3%) and BioCardia (2%). These investments were considered related party transactions as a result of our executive management's ownership interests and/or board representation in these entities. See further discussion of our investments in Note 5.

In February 2018, we invested an additional $1.0 million in COCP for a convertible note, which was converted into 538,544 shares of its common stock in May 2018.

In November 2017, we invested an additional $3.0 million in Neovasc for 20,547 shares of its common stock, 20,547 Series A warrants, 20,547 Series B warrants and 8,221 Series C warrants, after adjusting for a 1-for-100 reverse stock split in 2018. In April 2018, we exercised our Series B warrants in a cashless exercise and received 10,690 shares of Neovasc common stock. In the first quarter of 2019, we exercised the Series C warrants for $1.2 million and exchanged the Series A warrants and received a total of 22,660 additional shares of Neovasc common stock.

In November 2016, we entered into a Pledge Agreement with the Museum of Science, Inc. and the Museum of Science Endowment Fund, Inc. pursuant to which we will contribute an aggregate of $1.0 million over a four-year period for constructing, equipping and the general operation of the Frost Science Museum. Dr. Frost and Mr. Richard Pfenniger serve on the Board of Trustees of the Frost Science Museum and Mr. Pfenniger is the Vice Chairman of the Board of Trustees.

We lease office space from Frost Real Estate Holdings, LLC ("Frost Holdings") in Miami, Florida, where our principal executive offices are located. Effective August 1, 2019, we entered into an amendment to our lease agreement with Frost Holdings. The lease, as amended, is for approximately 29,500 square feet of space. The lease provides for payments of approximately $89 thousand per month in the first year increasing annually to $101 thousand per month in the fifth year, plus applicable sales tax. The rent is inclusive of operating expenses, property taxes and parking.

BioReference purchases and uses certain products acquired from InCellDx, a company in which we hold a 29% minority interest.

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 for out-of-pocket operating costs for the use of the airplane by Dr. Frost or Company executives for Company-related business. We do not reimburse Dr. Frost for personal use of the airplane by Dr. Frost or any other executive. For the years ended December 31, 2020, 2019, and 2018, we recognized approximately $156 thousand, $328 thousand, and $238 thousand, respectively, for Company-related travel by Dr. Frost and other OPKO executives.

Note 13 Employee Benefit Plans

Effective January 1, 2007, the OPKO Health Savings and Retirement Plan (the "Plan") permits employees to contribute up to 100% 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 our plans, including predecessor plans for BioReference, were approximately $8.0 million, $8.3 million and $8.3 million for the years ended December 31, 2020, 2019, and 2018 respectively.

Note 14 Commitments and Contingencies

In connection with our acquisitions of CURNA, OPKO Diagnostics 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, 2020, we recorded $5.7 million as contingent consideration, with $1.2 million recorded within Accrued expenses and $4.5 million recorded within Other long-term liabilities in the accompanying Consolidated Balance Sheets. In January 2021, the Company settled the ongoing litigation with Claros Diagnostics, Inc. shareholders and, among other things, agreed to pay $1.2 million to the shareholders. Refer to Note 6.

As previously disclosed, on September 7, 2018, the Securities and Exchange Commission (the "SEC") filed a lawsuit in the Southern District of New York (the "SEC Complaint") against a number of individuals and entities (the "Defendants"), including the Company and its CEO and Chairman, Dr. Phillip Frost. The SEC alleged, among other things, that the Company (i) aided and abetted an illegal "pump and dump" scheme perpetrated by a number of the Defendants, and (ii) failed to file required Schedules 13D or 13G with the SEC. The Company and Dr. Frost entered into settlement agreements with the SEC that resolved the SEC Complaint against each of them. The settlement agreements were approved by the court in January 2019. Pursuant to the settlement, and without admitting or denying any of the allegations of the SEC Complaint, the Company is

enjoined from violating Section 13(d) of the Exchange Act and paid a $100,000 penalty. Liability under Section 13(d) can be established without any showing of wrongful intent or negligence.

Following the SEC's announcement of the SEC Complaint, we were named in several class action lawsuits, more than a dozen derivative suits, and other litigation relating to the allegations in the SEC Complaint among other matters. On June 26, 2020, The Amitim Funds, the lead plaintiff in the class action lawsuits, filed a Stipulation of Settlement in the Southern District of Florida of behalf of itself and the remainder of the class, which provides for the settlement of and release of the class action claims against the Company and Dr. Frost for $16.5 million. On September 4, 2020, an Order Preliminarily Approving Settlement was entered and a settlement hearing was held on December 15, 2020. The settlement remains subject to certain terms and conditions including court approval. Our insurance carriers have agreed to provide coverage for a significant portion of the currently contemplated settlement amounts in connection with the class action lawsuits.

The derivative suit was settled on November 2, 2020. The settlement amount of $3.1 million was paid by the individual defendants' insurance company.

In April 2017, the Civil Division of the United States Attorney's Office for the Southern District of New York (the "SDNY") informed BioReference that it believed that, from 2008 to 2012, BioReference had, in violation of the False Claims Act, improperly billed Medicare and TRICARE (both are federal government healthcare programs) for clinical laboratory services provided to hospital inpatient beneficiaries at certain hospitals. In April 2019, the SDNY also informed BioReference that it believed that BioReference provided physicians subsidies for electronic health record systems prior to 2012 that violated regulations adopted by HHS in 2006 which allowed laboratories to provide these donations under certain conditions. BioReference and the SDNY reached a settlement with respect to these matters and a final settlement and release, including BioReference's payment of an approximately $11.5 million settlement amount, was approved on September 22, 2020. The amount of related attorneys' fees is currently being negotiated.

On June 3, 2019, BioReference reported that Retrieval-Masters Creditors Bureau, Inc. d/b/a American Medical Collection Agency ("AMCA"), had notified BioReference about a data security incident involving AMCA (the "AMCA Incident"). AMCA informed BioReference that an unauthorized user had access to AMCA's system between August 1, 2018 and March 30, 2019. AMCA advised that AMCA's affected system may have included patient name, date of birth, address, phone, date of service, provider, and balance information, as well as credit card information, bank account information (but no passwords or security questions) and email addresses that were provided by the consumer to AMCA. AMCA advised BioReference that no Social Security Numbers were compromised, and BioReference provided no laboratory results or diagnostic information to AMCA. BioReference notified patients and provided notice to the Office of Civil Rights of the AMCA Incident. BioReference had been named in at least two class action lawsuits against AMCA and other defendants in connection with the AMCA Incident. In April 2020, the class action lawsuits against BioReference were dismissed without prejudice. The Office of Inspector General and Office for Civil Rights ("OCR") of the Department of Health and Human Services, as well as the attorney generals' offices from certain states have contacted BioReference to request additional information relating to the AMCA Incident. On June 22, 2020 the OCR advised us it was closing its file regarding the AHCA matter and no further action is required of BioReference with respect to this matter. The resolution with the OCR does not, however, foreclose continued inquiries from attorney generals' offices from other states. Accordingly, it is not possible at this time to estimate the amount of loss or range of loss, if any, that might result from adverse judgments, settlements, fines, penalties, or other resolution of these investigations based on the stage of these investigations, and the absence of specific allegations.

On October 11, 2019, GeneDx received a letter from the Centers for Medicare and Medicaid Services ("CMS"), notifying GeneDx of CMS' determination to suspend Medicare payments to GeneDx, which suspension became effective on September 27, 2019 (the "CMS Letter"). CMS advised that it suspended payments due to possible overpayments to GeneDx in connection with reimbursement claims for genetic testing services based on a diagnosis of family history of cancer, which testing CMS has alleged is not covered by Medicare under the applicable provisions of the Social Security Act on the basis that such testing is not reasonable and necessary for the diagnosis or treatment of illness or injury. CMS lifted the suspension on February 3, 2020, and issued an extrapolated overpayment finding of approximately $376,332, which GeneDx paid.

From time to time, we may receive inquiries, document requests, Civil Investigative Demands ("CIDs") or subpoenas from the Department of Justice, OCR, CMS, various payors and fiscal intermediaries, and other state and federal regulators regarding investigations, audits and reviews. In addition to the matters discussed in this note, we are currently responding to CIDs, subpoenas, payor audits, and document requests for various matters relating to our laboratory operations. Some pending or threatened proceedings against us may involve potentially substantial amounts as well as the possibility of civil, criminal, or administrative fines, penalties, or other sanctions, which could be material. Settlements of suits involving the types of issues that we routinely confront may require monetary payments as well as corporate integrity agreements. Additionally, qui tam or "whistleblower" actions initiated under the civil False Claims Act may be pending but placed under seal by the court to comply

with the False Claims Act's requirements for filing such suits. Also, from time to time, we may detect issues of non-compliance with federal healthcare laws pertaining to claims submission and reimbursement practices and/or financial relationships with physicians, among other things. We may avail ourselves of various mechanisms to address these issues, including participation in voluntary disclosure protocols. Participating in voluntary disclosure protocols can have the potential for significant settlement obligations or even enforcement action. The Company generally has cooperated, and intends to continue to cooperate, with appropriate regulatory authorities as and when investigations, audits and inquiries arise.

We are a party to other litigation in the ordinary course of business. While we cannot predict the ultimate outcome of legal matters, 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. It's reasonably possible the ultimate liability could exceed amounts currently estimated and we review established 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. Because of the high degree of judgment involved in establishing loss estimates, the ultimate outcome of such matters will differ from our estimates and such differences may be material to our business, financial condition, results of operations, and cash flows.

We have employment agreements with certain employees of BioReference which provide for compensation and certain other benefits and for severance payments under certain circumstances. During the years ended December 31, 2020, 2019 and 2018, we recognized $1.0 million, $3.0 million and $4.9 million, respectively, of severance costs pursuant to these employment agreements as a component of Selling, general and administrative expense.

At December 31, 2020, we were committed to make future purchases for inventory and other items in 2020 that occur in the ordinary course of business under various purchase arrangements with fixed purchase provisions aggregating approximately $342.2 million.

Note 15 Revenue Recognition

We generate revenues from services, products and intellectual property as follows:

Revenue from services

Revenue for laboratory services is recognized at the time test results are reported, which approximates when services are provided and the performance obligations are satisfied. Services are provided to patients covered by various third-party payor programs including various managed care organizations, as well as the Medicare and Medicaid programs. Billings for services are included in revenue net of allowances for contractual discounts, allowances for differences between the amounts billed and estimated program payment amounts, and implicit price concessions provided to uninsured patients which are all elements of variable consideration.

The following are descriptions of our payors for laboratory services:

Healthcare Insurers. Reimbursements from healthcare insurers are based on negotiated fee-for-service schedules. Revenues consist of amounts billed, net of contractual allowances for differences between amounts billed and the estimated consideration we expect to receive from such payors, which considers historical denial and collection experience and the terms of our contractual arrangements. Adjustments to the allowances, based on actual receipts from the third-party payors, are recorded upon settlement.

Government Payors. Reimbursements from government payors are based on fee-for-service schedules set by governmental authorities, including traditional Medicare and Medicaid. Revenues consist of amounts billed, net of contractual allowances for differences between amounts billed and the estimated consideration we expect to receive from such payors, which considers historical denial and collection experience and the terms of our contractual arrangements. Adjustments to the allowances, based on actual receipts from the government payors, are recorded upon settlement.

Client Payors. Client payors include physicians, hospitals, employers, and other institutions for which services are performed on a wholesale basis, and are billed and recognized as revenue based on negotiated fee schedules. Client payers also include cities, states and companies for which BioReference provides COVID-19 testing services.

Patients. Uninsured patients are billed based on established patient fee schedules or fees negotiated with physicians on behalf of their patients. Insured patients (including amounts for coinsurance and deductible responsibilities) are billed based on fees negotiated with healthcare insurers. Collection of billings from patients is subject to credit risk and ability of the patients to pay. Revenues consist of amounts billed net of discounts provided to uninsured patients in accordance with our policies and implicit price concessions. Implicit price concessions represent differences between amounts billed and the estimated

consideration that we expect to receive from patients, which considers historical collection experience and other factors including current market conditions. Adjustments to the estimated allowances, based on actual receipts from the patients, are recorded upon settlement.

The complexities and ambiguities of billing, reimbursement regulations and claims processing, as well as considerations unique to Medicare and Medicaid programs, require us to estimate the potential for retroactive adjustments as an element of variable consideration in the recognition of revenue in the period the related services are rendered. Actual amounts are adjusted in the period those adjustments become known. For the year ended December 31, 2020, positive revenue adjustments due to changes in estimates of implicit price concessions for performance obligations satisfied in prior periods of $0.3 million were recognized. For the years ended December 31, 2019 and 2018, revenue reductions due to changes in estimates of implicit price concessions for performance obligations satisfied in prior periods of $24.8 million and $22.8 million, respectively, were recognized.

Third-party payors, including government programs, may decide to deny payment or recoup payments for testing they contend were improperly billed or not medically necessary, against their coverage determinations, or for which they believe they have otherwise overpaid (including as a result of their own error), and we may be required to refund payments already received. Our revenues may be subject to retroactive adjustment as a result of these factors among others, including without limitation, differing interpretations of billing and coding guidance and changes by government agencies and payors in interpretations, requirements, and "conditions of participation" in various programs. We have processed requests for recoupment from third-party payors in the ordinary course of our business, and it is likely that we will continue to do so in the future. If a third-party payer denies payment for testing or recoups money from us in a later period, reimbursement for our testing could decline.

As an integral part of our billing compliance program, we periodically assess our billing and coding practices, respond to payor audits on a routine basis, and investigate reported failures or suspected failures to comply with federal and state healthcare reimbursement requirements, as well as overpayment claims which may arise from time to time without fault on the part of the Company. We may have an obligation to reimburse Medicare, Medicaid, and third-party payors for overpayments regardless of fault. We have periodically identified and reported overpayments, reimbursed payors for overpayments and taken appropriate corrective action.

Settlements with third-party payors for retroactive adjustments due to audits, reviews or investigations are also considered variable consideration and are included in the determination of the estimated transaction price for providing services. These settlements are estimated based on the terms of the payment agreement with the payor, correspondence from the payor and our historical settlement activity, including an assessment of the probability a significant reversal of cumulative revenue recognized will occur when the uncertainty is subsequently resolved. Estimated settlements are adjusted in future periods as adjustments become known (that is, new information becomes available), or as years are settled or are no longer subject to such audits, reviews, and investigations. As of December 31, 2020 and 2019, we have liabilities of approximately $14.9 million and $27.3 million within Accrued expenses and Other long-term liabilities related to reimbursements for payor overpayments.

The composition of Revenue from services by payor for the years ended December 31, 2020, 2019 and 2018 is as follows:

	For the years ended December 31,		
(In thousands)	2020	2019	2018
Healthcare insurers	$ 483,643	$ 421,386	$ 492,995
Government payors	90,288	115,711	150,851
Client payors	637,645	158,527	148,070
Patients	50,666	20,810	21,332
Total	$ 1,262,242	$ 716,434	$ 813,248

Revenue from products

We recognize revenue from product sales when a customer obtains control of promised goods or services. The amount of revenue that is recorded reflects the consideration that we expect to receive in exchange for those goods or services. 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 our evaluation of specific factors that may increase or decrease the risk of product returns. Product revenues are recorded net of estimated rebates, chargebacks, discounts, co-pay assistance and other deductions (collectively, "Sales Deductions") as well as estimated product returns which are all elements of variable consideration. Allowances are recorded as a reduction of revenue at the time product revenues are recognized. The actual

amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect Revenue from products in the period such variances become known.

Rayaldee is distributed in the U.S. principally through the retail pharmacy channel, which initiates with the largest wholesalers in the U.S. (collectively, "*Rayaldee* Customers"). In addition to distribution agreements with *Rayaldee* Customers, we have entered into arrangements with many healthcare providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of *Rayaldee.*

We recognize revenue for shipments of *Rayaldee* at the time of delivery to customers after estimating Sales Deductions and product returns as elements of variable consideration utilizing historical information and market research projections. For the years ended December 31, 2020, 2019 and 2018, we recognized $36.8 million, $31.4 million and $20.3 million in net product revenue from sales of *Rayaldee.*

The following table presents an analysis of product sales allowances and accruals as contract liabilities for the years ended December 31, 2020, 2019 and 2018:

(In thousands)	Chargebacks, discounts, rebates and fees	Governmental	Returns	Total
Balance at December 31, 2019	$ 3,194	$ 5,841	$ 2,751	$ 11,786
Provision related to current period sales	17,604	32,721	2,066	52,391
Credits or payments made	(18,466)	(32,750)	(1,224)	(52,440)
Balance at December 31, 2020	$ 2,332	$ 5,812	$ 3,593	$ 11,737
Total gross *Rayaldee* sales				$ 88,187
Provision for *Rayaldee* sales allowances and accruals as a percentage of gross *Rayaldee* sales				58 %

(In thousands)	Chargebacks, discounts, rebates and fees	Governmental	Returns	Total
Balance at December 31, 2018	$ 1,316	$ 2,090	$ 637	$ 4,043
Provision related to current period sales	13,723	25,106	3,699	42,528
Credits or payments made	(11,845)	(21,355)	(1,585)	(34,785)
Balance at December 31, 2019	$ 3,194	$ 5,841	$ 2,751	$ 11,786
Total gross *Rayaldee* sales				$ 73,965
Provision for *Rayaldee* sales allowances and accruals as a percentage of gross *Rayaldee* sales				57 %

(In thousands)	Chargebacks, discounts, rebates and fees	Governmental	Returns	Total
Balance at December 31, 2017	$ 233	$ 348	$ 437	$ 1,018
Provision related to current period sales	5,704	10,061	680	16,445
Credits or payments made	(4,621)	(8,319)	(480)	(13,420)
Balance at December 31, 2018	$ 1,316	$ 2,090	$ 637	$ 4,043
Total gross *Rayaldee* sales				$ 36,715
Provision for *Rayaldee* sales allowances and accruals as a percentage of gross *Rayaldee* sales				45 %

Taxes collected from customers related to revenues from services and revenues from products are excluded from revenues.

Revenue from intellectual property

We recognize revenues from the transfer of intellectual property generated through license, development, collaboration and/or commercialization agreements. The terms of these agreements typically include payment to us for one or more of the following: non-refundable, up-front license fees; development and commercialization milestone payments; funding of research and/or development activities; and royalties on sales of licensed products. Revenue is recognized upon satisfaction of a performance obligation by transferring control of a good or service to the customer.

For research, development and/or commercialization agreements that result in revenues, we identify all material performance obligations, which may include a license to intellectual property and know-how, and research and development activities. In order to determine the transaction price, in addition to any upfront payment, we estimate the amount of variable consideration at the outset of the contract either utilizing the expected value or most likely amount method, depending on the facts and circumstances relative to the contract. We constrain (reduce) our estimates of variable consideration such that it is probable that a significant reversal of previously recognized revenue will not occur throughout the life of the contract. When determining if variable consideration should be constrained, we consider whether there are factors outside of our control that could result in a significant reversal of revenue. In making these assessments, we consider the likelihood and magnitude of a potential reversal of revenue. These estimates are re-assessed each reporting period as required.

Upfront License Fees: If a license to our intellectual property is determined to be functional intellectual property distinct from the other performance obligations identified in the arrangement, we recognize revenue from nonrefundable, upfront license fees based on the relative value prescribed to the license compared to the total value of the arrangement. The revenue is recognized when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are not distinct from other obligations identified in the arrangement, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If the combined performance obligation is satisfied over time, we apply an appropriate method of measuring progress for purposes of recognizing revenue from nonrefundable, upfront license fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Development and Regulatory Milestone Payments: Depending on facts and circumstances, we may conclude that it is appropriate to include the milestone in the estimated transaction price or that it is appropriate to fully constrain the milestone. A milestone payment is included in the transaction price in the reporting period that we conclude that it is probable that recording revenue in the period will not result in a significant reversal in amounts recognized in future periods. We may record revenues from certain milestones in a reporting period before the milestone is achieved if we conclude that achievement of the milestone is probable and that recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. We record a corresponding contract asset when this conclusion is reached. Milestone payments that have been fully constrained are not included in the transaction price to date. These milestones remain fully constrained until we conclude that achievement of the milestone is probable and that recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. We re-evaluate the probability of achievement of such development milestones and any related constraint each reporting period. We adjust our estimate of the overall transaction price, including the amount of revenue recorded, if necessary.

Research and Development Activities: If we are entitled to reimbursement from our customers for specified research and development expenses, we account for them as separate performance obligations if distinct. We also determine whether the research and development funding would result in revenues or an offset to research and development expenses in accordance with provisions of gross or net revenue presentation. The corresponding revenues or offset to research and development expenses are recognized as the related performance obligations are satisfied.

Sales-based Milestone and Royalty Payments: Our customers may be required to pay us sales-based milestone payments or royalties on future sales of commercial products. We recognize revenues related to sales-based milestone and royalty payments upon the later to occur of (i) achievement of the customer's underlying sales or (ii) satisfaction of any performance obligation(s) related to these sales, in each case assuming the license to our intellectual property is deemed to be the predominant item to which the sales-based milestones and/or royalties relate.

Other Potential Products and Services: Arrangements may include an option for license rights, future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's election. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations at the inception of the contract and revenue is recognized only if the option is exercised and products or services are subsequently delivered or when the rights expire. If the promise is based on market terms and not considered a material right, the option is

accounted for if and when exercised. If we are entitled to additional payments when the licensee exercises these options, any additional payments are generally recorded in license or other revenues when the licensee obtains control of the goods, which is upon delivery.

For the years ended December 31, 2020, 2019 and 2018 we recorded $53.2 million, $73.3 million and $69.9 million of revenue from the transfer of intellectual property, respectively. For the year ended December 31, 2020 and 2019, revenue from the transfer of intellectual property included $28.7 million and $66.8 million related to the Pfizer Transaction. In addition, revenue from the transfer of intellectual property and other for the year ended December 31, 2020 included $16.2 million of grants received by BioReference under the CARES Act and a $3 million milestone payment triggered by the first marketing approval of *Rayaldee* in Europe. For the year ended December 31, 2018, revenue from the transfer of intellectual property included $60.0 million related to the Pfizer Transaction and $2.0 million related to a milestone payment from our licensee, Vifor Fresenius Medical Care Renal Pharma Ltd ("VFMCRP"). Refer to Note 16.

Contract liabilities relate to cash consideration that OPKO receives in advance of satisfying the related performance obligations. Changes in the contractual liabilities balance for the years ended December 31, 2020 are as follows:

(In thousands)		
Balance at December 31, 2019	$	21,767
Balance at December 31, 2020		16,378
Revenue recognized in the period from:		
Amounts included in contracts liability at the beginning of the period		19,048

The contract liability balance at December 31, 2020 related primarily to accelerated payments received as part of the CARES Act. Refer to Note 2.

Note 16 Strategic Alliances

Japan Tobacco Inc.

On October 12, 2017, EirGen, our wholly-owned subsidiary, and Japan Tobacco Inc. ("JT") entered into a Development and License Agreement (the "JT Agreement") 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 (the "JT Initial Indications"), as well as such additional indications as may be added to the scope of the license subject to the terms of the JT Agreement (the JT Additional Indications" and together with the JT Initial Indications, the "JT Field").

In connection with the license, OPKO received an initial upfront payment of $6 million and received another $6 million upon the initiation of OPKO's phase 2 study for *Rayaldee* in dialysis patients in the U.S. in September 2018 (the "Initial Consideration"). 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 is also entitled to receive tiered, double digit royalty payments at percentages ranging from low double digits to mid-teens on net sales of *Rayaldee* 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.

The JT Agreement provides for the following: (1) an exclusive license in the JT Territory in the JT Field for the development and commercialization of *Rayaldee*; and (2) at JT's option, EirGen will supply products to support the development, sale and commercialization of the products to JT in the JT Territory.

The Initial Consideration will be recognized over the performance period through 2021, when we anticipate completing the transfer of license materials specified in the JT Agreement and our performance obligation is complete. Payments received for regulatory, development and sales milestones are non-refundable. The milestones are payable if and when the associated milestone is achieved and will be recognized as revenue in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. To date, no revenue has been recognized related to these milestones.

Vifor Fresenius Medical Care Renal Pharma Ltd

In May 2016, EirGen and Vifor Fresenius Medical Care Renal Pharma Ltd ("VFMCRP"), entered into a Development and License Agreement (the "VFMCRP Agreement") for the development and commercialization of *Rayaldee* (the "Product") worldwide, except for (i) the U.S., (ii) any country in Central America or South America (excluding Mexico), (iii) Russia, (iv)

China, (v) Japan, (vi) Ukraine, (vii) Belorussia, (viii) Azerbaijan, (ix) Kazakhstan, and (x) Taiwan (the "VFMCRP Territory"). The license to VFMCRP potentially covers all therapeutic and prophylactic uses of the Product in human patients (the "VFMCRP Field"), provided that initially the license is for the use of the Product for the treatment or prevention of SHPT related to patients with CKD and vitamin D insufficiency/deficiency (the "VFMCRP Initial Indication").

Effective May 5, 2020, we entered into an amendment to the VFMCRP Agreement (the "VFMCRP Amendment"), pursuant to which the parties agreed to exclude Mexico, South Korea, the Middle East and all of the countries of Africa from the VFMCRP Territory. In addition, the parties agreed to certain amendments to the milestone structure and to reduce minimum royalties payable. As revised, the Company has received a $3 million payment triggered by the first marketing approval of *Rayaldee* in Europe and is eligible to receive up to an additional $17 million in regulatory milestones and $210 million in milestone payments tied to launch, pricing and sales of *Rayaldee*, and tiered, double-digit royalties.

Under the terms of the VFMCRP Agreement, as amended, EirGen granted to VFMCRP an exclusive license in the VFMCRP Territory in the VFMCRP Field to use certain EirGen patents and technology to make, have made, use, sell, offer for sale, and import Products and to develop, commercialize, have commercialized, and otherwise exploit the Product. EirGen received a non-refundable and non-creditable initial payment of $50 million, which was recognized in Revenue from the transfer of intellectual property and other in our Consolidated Statement of Operations in 2016. EirGen also received a $2.0 million payment triggered by the approval of *Rayaldee* in Canada for the treatment of SHPT in adults with stage 3 or 4 CKD and vitamin D insufficiency in July 2018 and a $3 million payment triggered by the first marketing approval of *Rayaldee* in Europe. EirGen is also eligible to receive up to an additional $17 million in Regulatory Milestones and $210 million in Sales Milestones tied to launch, pricing and sales of *Rayaldee*, and will receive tiered 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 the commencement of sales of the Product within the VFMCRP Territory and in the VFMCRP Field.

We plan to share responsibility with VFMCRP for the conduct of trials specified within an agreed-upon development plan, with each company leading certain activities within the plan. EirGen will lead the manufacturing activities within and outside the VFMCRP Territory and the commercialization activities outside the VFMCRP Territory and outside the VFMCRP Field in the VFMCRP Territory and VFMCRP will lead the commercialization activities in the VFMCRP Territory and the VFMCRP Field. For the initial development plan, the companies have agreed to certain cost sharing arrangements. VFMCRP will be responsible for all other development costs that VFMCRP considers necessary to develop the Product for the use of the Product for the VFMCRP Initial Indication in the VFMCRP Territory in the VFMCRP Field except as otherwise provided in the VFMCRP Agreement. The first of the clinical studies provided for in the development activities commenced in September 2018.

In connection with the VFMCRP Agreement, the parties entered into a letter agreement pursuant to which EirGen granted to VFMCRP an exclusive option (the "Option") to acquire an exclusive license under certain EirGen patents and technology to use, import, offer for sale, sell, distribute and commercialize the Product in the U.S. solely for the treatment of SHPT in dialysis patients with CKD and vitamin D insufficiency (the "Dialysis Indication"). Upon exercise of the Option, VFMCRP will reimburse EirGen for all of the development costs incurred by EirGen with respect to the Product for the Dialysis Indication in the U.S. VFMCRP would also pay EirGen up to an additional aggregate amount of $555 million of sales-based milestones upon the achievement of certain milestones and would be obligated to pay royalties at percentage rates that range from the mid-teens to the mid-twenties on sales of the Product in the U.S. for the Dialysis Indication. To date, VFMCRP has not exercised its option.

Payments received for Regulatory Milestones and Sales Milestones are non-refundable. The Regulatory Milestones are payable if and when VFMCRP obtains approval from certain regulatory authorities and will be recognized as revenue in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. We account for the Sales Milestones as royalties and Sales Milestones payments will be recognized as revenue in the period in which the associated milestone is achieved or sales occur, assuming all other revenue recognition criteria are met.

Pfizer Inc.

In December 2014, we entered into an exclusive worldwide agreement (the "Pfizer Agreement") with Pfizer for the development and commercialization of our long-acting Somatrogon (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 (the "Pfizer Transaction").

In May 2020, we entered into an Amended and Restated Development and Commercialization License Agreement (the "Restated Agreement") with Pfizer, effective January 1, 2020, pursuant to which the parties agreed, among other things, to share all costs for Manufacturing Activities, as defined in the Restated Agreement, for developing a licensed product for the three indications included in the Restated Agreement.

On October 21, 2019, we and Pfizer announced that the global phase 3 trial evaluating Somatrogon dosed once-weekly in prepubertal children with GHD met its primary endpoint of non-inferiority to daily Genotropin® (somatropin) for injection, as measured by annual height velocity at 12 months.

Under the terms of the Pfizer Transaction, as restated, we received non-refundable and non-creditable upfront payments of $295.0 million and are eligible to receive up to an additional $275.0 million upon the achievement of certain regulatory milestones. Pfizer received the exclusive license to commercialize Somatrogon worldwide. In addition, we are eligible to receive initial tiered royalty payments associated with the commercialization of Somatrogon for adult GHD with percentage rates ranging from the high teens to mid-twenties. Upon the launch of Somatrogon for pediatric GHD in certain major markets, the royalties will transition to regional, tiered gross profit sharing for both Somatrogon and Pfizer's Genotropin®.

The agreement with Pfizer will remain in effect until the last sale of the licensed product, unless earlier terminated as permitted under the Pfizer Agreement. In addition to termination rights for material breach and bankruptcy, Pfizer is permitted to terminate the Pfizer Agreement in its entirety, or with respect to one or more world regions, without cause after a specified notice period. If the Pfizer Agreement is terminated by us for Pfizer's uncured material breach, or by Pfizer without cause, provision has been made for transition of product and product responsibilities to us for the terminated regions, as well as continued supply of product by Pfizer or transfer of supply to us in order to support the terminated regions.

We recognized the non-refundable $295.0 million upfront payments as revenue as the research and development services were completed and as of December 31, 2020, we had no contract liabilities related to the Pfizer Transaction.

The Pfizer Transaction includes milestone payments of $275.0 million upon the achievement of certain milestones. The milestones range from $20.0 million to $90.0 million each and are based on achievement of regulatory approval in the U.S. and regulatory approval and price approval in other major markets. The milestone payments will be recognized as revenue in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. To date, no revenue has been recognized related to the achievement of the milestones.

Pharmsynthez

In April 2013, we entered into a series of concurrent transactions with Pharmsynthez, a Russian pharmaceutical company traded on the Moscow Stock Exchange pursuant to which we acquired an equity method investment in Pharmsynthez (ownership 9%). We also granted rights to certain technologies in the Russian Federation, Ukraine, Belarus, Azerbaijan and Kazakhstan (the "Pharmsynthez Territories") to Pharmsynthez and agreed to perform certain development activities. We will receive from Pharmsynthez royalties on net sales of products incorporating the technologies in the Pharmsynthez Territories, as well as a percentage of any sublicense income from third parties for the technologies in the Pharmsynthez Territories.

Other

We have completed strategic deals with numerous institutions and commercial partners. In connection with these 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.

Note 17 Leases

We have operating leases for office space, laboratory operations, research and development facilities, manufacturing locations, warehouses and certain equipment. We determine if a contract contains a lease at inception or modification of a contract. Our leases generally do not provide an implicit interest rate, and we therefore use our incremental borrowing rate as the discount rate when measuring operating lease liabilities. The incremental borrowing rate represents an estimate of the interest rate we would incur at lease commencement to borrow an amount equal to the lease payments on a collateralized basis over the term of the lease within a particular currency environment. We used the incremental borrowing rates as of January 1, 2019 for operating leases that commenced prior to that date. Many of our leases contain rental escalation, renewal options and/or termination options that are factored into our determination of lease payments as appropriate. Variable lease payment amounts that cannot be determined at the commencement of the lease are not included in the right-to-use assets or liabilities.

We elected the use of permitted practical expedients of not recording leases on our Consolidated Balance Sheet when the leases have terms of 12 months or less, and we elected not to separate nonlease components from lease components and instead account for each separate lease component and the nonlease components associated with that lease component as a single lease component.

The following table presents the lease balances within the Consolidated Balance Sheet as of December 31, 2020:

(in thousands)	Classification on the Balance Sheet	December 31, 2020	December 31, 2019
Assets			
Operating lease assets	Operating lease right-of-use assets	$ 37,735	$ 39,380
Finance lease assets	Property, plant and equipment, net	5,258	6,789
Liabilities			
Current			
Operating lease liabilities	Current maturities of operating leases	9,028	12,038
Accrued expenses	Current maturities of finance leases	2,453	2,743
Long-term			
Operating lease liabilities	Operating lease liabilities	29,760	27,665
Other long-term liabilities	Finance lease liabilities	$ 2,805	$ 4,046
Weighted average remaining lease term			
Operating leases		5.4 years	5.6 years
Finance leases		2.3 years	2.6 years
Weighted average discount rate			
Operating leases		5.8 %	6.3 %
Finance leases		3.6 %	3.0 %

The following table reconciles the undiscounted future minimum lease payments (displayed by year and in the aggregate) under noncancelable operating leases with terms of more than one year to the total operating lease liabilities recognized on our Consolidated Balance Sheet as of December 31, 2020:

(in thousands)	Operating	Finance
2021	$ 9,176	$ 2,527
2022	8,232	1,475
2023	6,940	860
2024	5,003	511
2025	3,145	72
Thereafter	14,768	—
Total undiscounted future minimum lease payments	47,264	5,445
Less: Difference between lease payments and discounted lease liabilities	8,476	187
Total lease liabilities	$ 38,788	$ 5,258

Expense under operating leases and finance leases was $17.8 million and $3.0 million, respectively, for the year ended December 31, 2020, and includes $3.0 million of variable lease costs. Expense under operating leases and finance leases was $20.2 million and $3.1 million, respectively, for the year ended December 31, 2019, and includes $3.4 million of variable lease costs.Operating lease costs and finance lease costs are included within Operating loss in the Consolidated Statement of Operations. Short-term lease costs were not material.

Supplemental cash flow information is as follows:

(in thousands)	For the years ended December 31,	
	2020	2019
Operating cash out flows from operating leases	$ 17,440	$ 20,712
Operating cash out flows from finance leases	196	374
Financing cash out flows from finance leases	2,872	2,833
Total	$ 20,508	$ 23,919

Note 18 Segments

We manage our operations in two reportable segments, pharmaceuticals and diagnostics. The pharmaceuticals segment consists of our pharmaceutical operations in Chile, Mexico, Ireland, Israel and Spain, *Rayaldee* product sales and our pharmaceutical research and development. The diagnostics segment primarily consists of our clinical laboratory operations through BioReference and our point-of-care 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.

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

(In thousands)	For the years ended December 31, 2020	2019	2018
Revenue from services:			
Pharmaceutical	$ —	$ —	$ —
Diagnostics	1,262,242	716,434	813,248
Corporate	—	—	—
	$ 1,262,242	$ 716,434	$ 813,248
Revenue from products:			
Pharmaceutical	$ 119,952	$ 112,184	$ 107,112
Diagnostics	—	—	—
Corporate	—	—	—
	$ 119,952	$ 112,184	$ 107,112
Revenue from transfer of intellectual property and other:			
Pharmaceutical	$ 36,979	$ 72,521	$ 69,906
Diagnostics	16,240	—	—
Corporate	—	796	—
	$ 53,219	$ 73,317	$ 69,906
Operating income (loss):			
Pharmaceutical	$ (43,519)	$ (109,062)	$ (82,641)
Diagnostics	138,922	(123,359)	(44,942)
Corporate	(37,689)	(41,631)	(43,614)
	$ 57,714	$ (274,052)	$ (171,197)
Depreciation and amortization:			
Pharmaceutical	$ 29,001	$ 30,073	$ 28,007
Diagnostics	56,361	63,675	69,246
Corporate	—	59	91
	$ 85,362	$ 93,807	$ 97,344
Loss from investment in investees:			
Pharmaceutical	$ (480)	$ (2,900)	$ (10,822)
Diagnostics	—	—	(3,675)
Corporate	—	—	—
	$ (480)	$ (2,900)	$ (14,497)
Revenues:			
U.S.	$ 1,317,766	$ 751,099	$ 837,509
Ireland	43,920	81,170	78,102
Chile	44,153	33,642	41,216
Spain	16,932	18,747	18,195
Israel	4,251	8,769	9,479
Mexico	7,865	8,032	5,598
Other	526	476	167
	$ 1,435,413	$ 901,935	$ 990,266

(In thousands)	December 31, 2020	December 31, 2019
Assets:		
Pharmaceutical	$ 1,176,245	$ 1,174,639
Diagnostics	1,268,738	1,035,112
Corporate	28,080	99,521
	$ 2,473,063	$ 2,309,272
Goodwill:		
Pharmaceutical	$ 245,793	$ 237,131
Diagnostics	434,809	434,809
Corporate	—	—
	$ 680,602	$ 671,940

No customer represented more than 10% of our total consolidated revenue during the years ended December 31, 2020, 2019 and 2018. As of December 31, 2020 and 2019, no customer represented more than 10% of our accounts receivable balance.

The following table reconciles our Property, plant and equipment, net between U.S. and foreign jurisdictions:

(In thousands)	December 31, 2020	December 31, 2019
PP&E:		
U.S.	$ 73,564	$ 62,158
Foreign	66,990	64,953
Total	$ 140,554	$ 127,111

Note 19 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 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 are: 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.

As of December 31, 2020, we have equity securities (refer to Note 5), forward foreign currency exchange contracts for inventory purchases (refer to Note 20) and contingent consideration related to the acquisitions of CURNA, OPKO Diagnostics 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 BioCardia, we record the related BioCardia options at fair value as well as the warrants from COCP, InCellDx, Inc., Xenetic and Phio.

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

	Fair value measurements as of December 31, 2020			
(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:				
Equity securities	$ 14,136	$ —	$ —	$ 14,136
Common stock options/warrants	—	74	—	74
Total assets	$ 14,136	$ 74	$ —	$ 14,210
Liabilities:				
Forward Contracts	$ —	$ 1,040	$ —	1,040
Contingent consideration:	—	—	5,695	5,695
Total liabilities	$ —	$ 1,040	$ 5,695	$ 6,735

	Fair value measurements as of December 31, 2019			
(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:				
Equity securities	$ 18,870	$ —	$ —	$ 18,870
Common stock options/warrants	—	120	—	120
Forward contracts	—	133	—	133
Total assets	$ 18,870	$ 253	$ —	$ 19,123
Liabilities:				
Contingent consideration:	$ —	$ —	$ 9,683	$ 9,683
Total liabilities	$ —	$ —	$ 9,683	$ 9,683

The carrying amount and estimated fair value of our 2025 Notes, as well as the applicable fair value hierarchy tiers, are contained in the table below. The fair value of the 2025 Notes is determined using inputs other than quoted prices in active markets that are directly observable.

	December 31, 2020				
(In thousands)	Carrying Value	Total Fair Value	Level 1	Level 2	Level 3
2025 Notes	$ 156,163	$ 254,000	$ —	$ 254,000	$ —

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, 2020 and 2019, the carrying value of our other financial instrument assets approximates their fair value due to their short-term nature or variable rate of interest.

The following tables reconcile the beginning and ending balances of our Level 3 assets and liabilities as of December 31, 2020 and 2019:

(In thousands)	December 31, 2020 Contingent consideration
Balance at December 31, 2019	$ 9,683
Total gains for the period:	
Included in results of operations	(3,989)
Balance at December 31, 2020	$ 5,694

(In thousands)	December 31, 2019 Contingent consideration
Balance at December 31, 2018	$ 24,537
Total gains for the period:	
Included in results of operations	(14,854)
Balance at December 31, 2019	$ 9,683

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 and OPKO Renal transactions. As of December 31, 2020, of the $5.7 million of contingent consideration, $1.2 million is recorded in Accrued expenses and $4.5 million is recorded in Other long-term liabilities. As of December 31, 2019, of the $9.7 million of contingent consideration, $2.4 million is recorded in Accrued expenses and $7.3 million is recorded in Other long-term liabilities.

Note 20 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, 2020	December 31, 2019
Derivative financial instruments:			
Common stock options/warrants	Investments, net	$ 74	$ 120
Forward contracts	Unrealized gains on forward contracts are recorded in Other current assets and prepaid expenses. Unrealized (losses) on forward contracts are recorded in Accrued expenses.	$ (1,040)	$ 133

We enter into foreign currency forward exchange contracts with respect to 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, 2020 and 2019, 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 Statement of Operations. The following table summarizes the losses and gains recorded for the years ended December 31, 2020, 2019 and 2018:

	For the years ended December 31,		
(In thousands)	2020	2019	2018
Derivative gain (loss):			
Common stock options/warrants	$ (46)	$ (601)	$ 2,643
Forward contracts	$ 96	$ 775	$ 400
Total	$ 50	$ 174	$ 3,043

Note 21 Selected Quarterly Financial Data (Unaudited)

	For the 2020 Quarters Ended			
(In thousands, except per share data)	March 31	June 30	September 30	December 31
Total revenues	$ 211,466	$ 301,207	$ 428,064	$ 494,676
Total costs and expenses	252,228	274,028	406,125	445,318
Net income (loss)	(59,132)	33,703	23,717	32,298
Earnings (loss) per share, basic and diluted	$ (0.09)	$ 0.05	$ 0.04	$ 0.05

	For the 2019 Quarters Ended			
(In thousands, except per share data)	March 31	June 30	September 30	December 31
Total revenues	$ 222,451	$ 226,368	$ 228,772	$ 224,344
Total costs and expenses	297,769	273,628	267,783	336,807
Net loss	(80,762)	(59,806)	(62,007)	(112,350)
Loss per share, basic and diluted	$ (0.14)	$ (0.10)	$ (0.11)	$ (0.18)

Note 22 Subsequent Events

We have reviewed all subsequent events and transactions that occurred after the date of our December 31, 2020 Consolidated Balance Sheet date, through the time of filing this Annual Report on Form 10-K.

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 our 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 Exchange Act) as of December 31, 2020. 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, 2020.

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 Exchange Act. 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, 2020, 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"). Based on our evaluation under the 2013 Internal Control-Integrated Framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2020.

The effectiveness of the Company's internal control over financial reporting as of December 31, 2020 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

There have been no changes to the Company's internal control over financial reporting that occurred during quarter ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

On February 12, 2021, the Board of Directors of the Company appointed Adam Logal, the Company's current Senior Vice President, Chief Financial Officer, as the Company's Chief Accounting Officer and Treasurer. Mr. Logal previously served as the Company's Senior Vice President, Chief Financial Officer, Chief Accounting Officer, and Treasurer from March 2014 until July 2020 when he ceased to be the Chief Accounting Officer and Treasurer. Mr. Logal also served as Vice President of Finance, Chief Accounting Officer and Treasurer from July 2012 until March 2014, and Director of Finance, Chief Accounting Officer and Treasurer from March 2007 until July 2012.

There are no family relationships between Mr. Logal and any director or executive officer of the Company. Since the beginning of the Company's last fiscal year, the Company has not engaged in any transaction, or any currently proposed transaction, in which Mr. Logal had or will have a direct or indirect material interest that would require disclosure under Item 404(a) of Regulation S-K promulgated by the SEC.

No new compensatory plan arrangements were entered into with Mr. Logal in connection with his appointment as the Company's Chief Accounting Officer and Treasurer. Mr. Logal is otherwise entitled to receive such benefits of employment as

are generally available to the Company's other executive officers, as described in the Company's definitive proxy statement on Schedule 14A for the Company's 2020 Annual Meeting of Stockholders, as filed with the SEC on April 29, 2020.

On February 12, 2021 the Board of Directors of the Company approved an amendment to the Company's Amended and Restated Bylaws (the "Bylaws") to enhance the advance notice provisions for director nominations and stockholder proposals. Under the amended Bylaws, a stockholder who wishes to nominate a director must include (1) a written questionnaire in the form required by the Company, (2) additional information about the structure, ownership and trading in Company's securities or any related derivative agreements and (3) any associated performance-related fees. The recommending stockholder also has obligations to update any notice provided to the Company in a timely manner.

The Bylaws are effective February 12, 2021. The preceding summary does not purport to be complete and is qualified in its entirety by reference to the complete text of the Bylaws, which are filed as Exhibit 3.2 to this Form 10-K and incorporated herein by reference.

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 2020 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2020.

PART IV.

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

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

Schedule I - Condensed Financial Information of Registrant. 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. Other schedules are omitted because they are not required.

(2) Exhibits: See Index to Exhibits below.

INDEX TO EXHIBITS

Exhibit Number	Description
1.1[12]	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.
1.2[43]	Underwriting Agreement, dated October 24, 2019, by and among OPKO Health, Inc., Jeffries LLC, Piper Jaffray & Co., and Guggenheim Securities, LLC as representatives of 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[3]+	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[9]	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[14]+	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[15]	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[17]+	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[18]	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[19]+	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[21]+	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[22]+	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[23]	Asset Purchase Agreement, dated March 1, 2013, by and between RXi Pharmaceuticals Corporation and OPKO Health, Inc.
2.12[24]	Agreement and Plan of Merger, dated April 23, 2013, by and among OPKO Health, Inc., POM Acquisition Inc., and PROLOR Biotech, Inc.
2.13[27]+	Agreement for the Sale and Purchase of Shares in EirGen Pharma Limited, dated May 5, 2015 by and among OPKO Ireland Limited, OPKO Health, Inc. and the Sellers named therein.
2.14[27]+	Form of Additional Agreement for the Sale and Purchase of Shares in EirGen Pharma Limited, dated May 5, 2015 by and among OPKO Ireland Limited and the Sellers named therein.
2.15[28]+	Agreement and Plan of Merger by and among the Company, Bamboo Acquisition, Inc. and Bio-Reference Laboratories, Inc. dated as of June 3, 2015.
2.16[31]	Arrangement Agreement by and among the Company, OPKO Global Holdings, Inc. and Transition Therapeutics Inc. dated as of June 29, 2016.
3.1[26]	Amended and Restated Certificate of Incorporation, as amended.

3.2**	Amended and Restated Bylaws.
3.3[7]	Certificate of Designation of Series D Preferred Stock.
3.4[42]	Amendment to Amended and Restated Certificate of Incorporation
4.1[1]	Form of Common Stock Warrant.
4.2[7]	Form of Common Stock Warrant.
4.3[25]	Indenture, dated January 30, 2013, between OPKO Health, Inc. and Wells Fargo Bank, National Association.
4.4[39]	Base Indenture related to the 4.50% Convertible Senior Notes due 2025, dated as of February 7, 2019, by and between OPKO Health, Inc. and U.S. Bank National Association, as trustee.
4.5[39]	Supplemental Indenture related to the 4.50% Convertible Senior Notes due 2025, dated as of February 7, 2019, by and between OPKO Health, Inc. and U.S. Bank National Association, as trustee.
4.6**	Description of Securities
10.1[1]	Form of Lockup Agreement.
10.2[2]	Stock Purchase Agreement, dated December 4, 2007, by and between OPKO Health, Inc. and the members of The Frost Group, LLC.
10.3[3]	Form of Director Indemnification Agreement.
10.4[3]	Form of Officer Indemnification Agreement.
10.5[4]	Stock Purchase Agreement, dated August 8, 2008 by and between OPKO Health, Inc. and the Purchasers named therein.
10.6[5]	Stock Purchase Agreement, dated February 23, 2009 by and between OPKO Health, Inc. and Frost Gamma Investments Trust.
10.7[6]	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.
10.8[6]	Stock Purchase Agreement, dated June 10, 2009, by and among OPKO Health, Inc. and Sorrento Therapeutics, Inc.
10.9[7]	Form of Securities Purchase Agreement for Series D Preferred Stock.
10.10[8]*	Form of Restricted Share Award Agreement for Directors.
10.11[8]	Cocrystal Discovery, Inc. Agreements.
10.12[11]	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.
10.13[10]+	Asset Purchase Agreement, dated October 12, 2009, by and between OPKO Health, Inc. and Schering Corporation.
10.14[10]	Letter Agreement, dated June 29, 2010, by and between OPKO Health, Inc. and Schering Corporation.

10.15[16]+	Exclusive License Agreement by and between TESARO, Inc. and OPKO Health, Inc. dated December 10, 2010.
10.16[13]	Third Amended and Restated Subordinated Note and Security Agreement, dated February 22, 2011, between OPKO Health, Inc. and The Frost Group, LLC.
10.17[15]+	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.
10.18[20]	Form of Note Purchase Agreement, dated as of January 25, 2013, by and among OPKO Health, Inc. and each purchaser a party thereto.
10.19[29]+	Development and Commercialization License Agreement by and between OPKO Ireland, Ltd., a subsidiary of OPKO Health, Inc., and Pfizer, Inc. dated December 13, 2014.
10.20[32]	Credit Agreement by and between Bio-Reference Laboratories, Inc. and certain of its subsidiaries and JPMorgan Chase Bank, N.A. dated November 5, 2015.
10.21[33]	OPKO Health, Inc. 2016 Equity Incentive Plan.
10.22[34]	Development and License Agreement between OPKO Health, Inc. and Vifor Fresenius Medical Care Renal Pharma Ltd., dated May 8, 2016.
10.23[35]	Amendment No. 3 to Credit Agreement, dated as of March 17, 2017, among Bio-Reference Laboratories, Inc. and certain of its subsidiaries and JPMorgan Chase Bank, N.A.
10.24[36]	Amendment No. 4 to Credit Agreement, dated as of August 7, 2017, among Bio-Reference Laboratories, Inc. and certain of its subsidiaries and JPMorgan Chase Bank, N.A.
10.25[36]	Commitment Letter by and between OPKO Health, Inc. and Veterans Accountable Care Group, LLC, dated August 15, 2017.
10.26[37]+	Development and License Agreement by and between EirGen Pharma Limited, a subsidiary of OPKO Health, Inc., and Japan Tobacco Inc., dated October 12, 2017.
10.27[37]	Amendment No. 5 to Credit Agreement, dated as of November 8, 2017, among Bio-Reference Laboratories, Inc. and certain of its subsidiaries and JPMorgan Chase Bank, N.A.
10.28[37]	Amendment No. 6 to Credit Agreement, dated as of December 22, 2017, among Bio-Reference Laboratories, Inc. and certain of its subsidiaries and JPMorgan Chase Bank, N.A.
10.29[37]	Form of 5% Convertible Promissory Note dated February 27, 2018.
10.30[38]	Amendment No. 7 to Credit Agreement by and between BioReference Laboratories, Inc. and certain of its subsidiaries, and JPMorgan Chase, N.A. dated February 28, 2018.
10.31[39]	Share Lending Agreement, dated February 4, 2019, by and between the OPKO Health, Inc. and Jefferies Capital Services, LLC.
10.32[40]	Credit Agreement, dated as of November 8, 2018, by and between the OPKO Health, Inc. and Frost Gamma Investments Trust.
10.33[40]	Stock Purchase Agreement, dated as of November 8, 2018, between certain investors and OPKO Health, Inc.

10.34[41]	Amendment No. 8 to Credit Agreement by and between BioReference Laboratories, Inc. and certain of its subsidiaries, and JPMorgan Chase, N.A. dated February 26, 2019.
10.35[44]	Amendment No. 9 to Credit Agreement by and between BioReference Laboratories, Inc. and certain of its subsidiaries, and JPMorgan Chase, N.A. dated August 6, 2019.
10.36[45]	Amendment No. 10 to Credit Agreement by and between BioReference Laboratories, Inc. and certain of its subsidiaries, and JPMorgan Chase, N.A. dated November 4, 2019.
10.37[45]	Amendment No. 11 to Credit Agreement by and between BioReference Laboratories, Inc. and certain of its subsidiaries, and JPMorgan Chase, N.A. dated February 25, 2020.
10.38[45]	Credit Agreement, dated as of February 25, 2020, by and between OPKO Health, Inc. and Frost Gamma Investment Trust.
10.39[46]	Amendment to Development and License Agreement between EirGen Pharma Ltd. and Vifor Fresenius Medical Care Renal Pharma Ltd., dated May 5, 2020.
10.40[46]	Amended and Restated Development and Commercialization License Agreement by and between Pfizer Inc. and OPKO Ireland Ltd., dated May 12, 2020.
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 year ended December 31, 2020.
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 year ended December 31, 2020.
32.1	Certification by Phillip 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 year ended December 31, 2020., 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 year ended December 31, 2020.
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 year ended December 31, 2020.

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.
** Filed herewith.
+ 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 31, 2008 and incorporated herein by reference.
(3) 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.
(4) 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.
(5) 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.
(6) 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.
(7) 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.
(8) 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.
(9) 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.
(10) Filed with the Company's Amendment to Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 3, 2011.
(11) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 17, 2010.
(12) 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.
(13) 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.
(14) 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.
(15) 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.
(16) Filed with the Company's Annual Report on Form 10-K/A filed with the Securities and Exchange Commission on July 28, 2011.
(17) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 15, 2012.
(18) 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.
(19) 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.
(20) 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.

(21) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 18, 2013.
(22) 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.
(23) Filed with the Company's Schedule 13D filed with the Securities and Exchange Commission on March 22, 2013, and incorporated herein by reference.
(24) 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.
(25) 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.
(26) 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.
(27) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 5, 2015 for the Company's three month period ended June 30, 2015, and incorporated herein by reference.
(28) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 4, 2015, and incorporated herein by reference.
(29) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 27, 2015, and incorporated herein by reference.
(30) Filed under Part II, Item 8, of the Bio-Reference Laboratories, Inc. Form 10-K filed with the Securities and Exchange Commission on January 13, 2015 (File No. 0-15266), and incorporated herein by reference.
(31) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 30, 2016 and incorporated herein by reference.
(32) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 29, 2016, and incorporated herein by reference.
(33) Filed with the Company's Definitive Proxy Statement on Schedule 14A filed with the Securities and Exchange Commission on March 25, 2016, and incorporated herein by reference.
(34) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 8, 2016 for the Company's three month period ended June 30, 2016, and incorporated herein by reference.
(35) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 23, 2017 and incorporated herein by reference.
(36) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 8, 2017 and incorporated herein by reference.
(37) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 1, 2018 and incorporated herein by reference.
(38) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 7, 2018 for the Company's three month period ended June 30, 2018, and incorporated herein by reference
(39) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on February 7, 2019 and incorporated herein by reference.
(40) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 1, 2019 and incorporated herein by reference.
(41) Filed with the Company's Annual Report on Form 10-Q filed with the Securities and Exchange Commission on May 8, 2019 and incorporated herein by reference.
(42) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 21, 2019.
(43) Filed with the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on October 29, 2019.
(44) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 5, 2019.
(45) Filed with the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 2, 2020 and incorporated herein by reference.
(46) Filed with the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on July 31, 2020.

Schedule I - Condensed Financial Information of Registrant

OPKO Health, Inc.
PARENT COMPANY CONDENSED BALANCE SHEETS
(In thousands, except share and per share data)

	December 31,	
	2020	2019
ASSETS		
Current assets:		
Cash and cash equivalents	$ 3,740	$ 58,627
Other current assets and prepaid expenses	2,433	12,463
Total current assets	6,173	71,090
Investments	1,901,104	1,778,885
Operating lease right-of-use assets	3,958	4,672
Other assets	25	66
Total assets	$ 1,911,260	$ 1,854,713
LIABILITIES AND EQUITY		
Current liabilities:		
Accounts payable	$ 1,194	$ 1,791
Accrued expenses	8,324	18,280
Current maturities of operating leases	1,113	1,075
Current portion of notes payable	3,765	3,524
Total current liabilities	14,396	24,670
Operating lease liabilities	2,845	3,597
Convertible notes	221,989	211,208
Deferred tax liabilities, net	479	479
Total long-term liabilities	225,313	215,284
Total liabilities	239,709	239,954
Equity:		
Common Stock - $0.01 par value, 1,000,000,000 shares authorized; 670,585,576 and 670,378,701 shares issued at December 31, 2020 and 2019, respectively	6,706	6,704
Treasury Stock, at cost - 549,907 shares at December 31, 2020 and 2019, respectively	(1,791)	(1,791)
Additional paid-in capital	3,152,694	3,142,993
Accumulated other comprehensive income (loss)	(4,225)	(22,070)
Accumulated deficit	(1,481,833)	(1,511,077)
Total shareholders' equity	1,671,551	1,614,759
Total liabilities and equity	$ 1,911,260	$ 1,854,713

The accompanying Notes to Parent Company Condensed Financial Statements are an integral part of these statements.

OPKO Health, Inc.
PARENT COMPANY CONDENSED STATEMENTS OF INCOME
(In thousands)

	For the years ended December 31,		
	2020	2019	2018
Revenues:			
Revenue from products	$ —	$ 796	$ —
Revenue from transfer of intellectual property and other	1,069	1,150	1,069
Total revenues	1,069	1,946	1,069
Costs and expenses:			
Costs of revenue	260	1,382	2,358
Selling, general and administrative	41,736	47,949	52,397
Research and development	1,951	2,027	4,184
Total costs and expenses	43,947	51,358	58,939
Operating loss	(42,878)	(49,412)	(57,870)
Other income and (expense), net:			
Interest income	967	2,186	631
Interest expense	(23,585)	(21,172)	(8,608)
Fair value changes of derivative instruments, net	(46)	(601)	1,991
Other income (expense), net	10,354	(8,887)	3,906
Other income and (expense), net	(12,310)	(28,474)	(2,080)
Loss before income taxes and investment losses	(55,188)	(77,886)	(59,950)
Income tax provision	(175)	(5)	(11)
Net loss before investment losses	(55,363)	(77,891)	(59,961)
Loss from investments in investees	(480)	(2,900)	(10,822)
Net income (loss) from subsidiaries, net of taxes	86,429	(234,134)	(82,257)
Net income (loss)	$ 30,586	$ (314,925)	$ (153,040)

The accompanying Notes to Parent Company Condensed Financial Statements are an integral part of these statements.

OPKO Health, Inc.
PARENT COMPANY CONDENSED STATEMENTS OF COMPREHENSIVE INCOME
(In thousands)

	For the years ended December 31,		
	2020	2019	2018
Net income (loss)	$ 30,586	$ (314,925)	$ (153,040)
Other comprehensive income (loss), net of tax:			
Change in foreign currency translation and other comprehensive income (loss)	17,845	(1,939)	(14,727)
Investments:			
Change in unrealized gain (loss), net of tax	—	—	—
Reclassification adjustments due to adoption of ASU 2016-01	—	—	(4,876)
Reclassification adjustments for losses included in net loss, net of tax	—	—	—
Comprehensive income (loss)	$ 48,431	$ (316,864)	$ (172,643)

The accompanying Notes to Parent Company Condensed Financial Statements are an integral part of these statements.

OPKO Health, Inc.
PARENT COMPANY CONDENSED STATEMENTS OF CASH FLOWS
(In thousands)

	For the years ended December 31,		
	2020	2019	2018
Cash flows from operating activities:			
Net income (loss)	$ 30,586	$ (314,925)	$ (153,040)
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Depreciation and amortization	—	59	91
Non-cash interest	9,994	8,545	4,564
Amortization of deferred financing costs	787	922	551
Losses from investments in investees	480	2,900	10,822
(Income) loss from subsidiaries	(86,429)	234,134	82,257
Equity-based compensation – employees and non-employees	8,947	13,421	21,761
Realized loss (gain) on equity securities and disposal of fixed assets	(10,324)	(796)	208
Change in fair value of derivative instruments	(6)	9,523	(6,124)
Adoption of ASC 326 and other	(1,311)	—	—
Changes in other assets and liabilities	(243)	3,907	6,846
Net cash used in operating activities	(47,519)	(42,310)	(32,064)
Cash flows from investing activities:			
Investments in investees	—	(1,200)	(1,000)
Subsidiary financing	(23,234)	(152,376)	(123,787)
Proceeds from sale of equity securities	15,110	—	1,516
Net cash used in investing activities	(8,124)	(153,576)	(123,271)
Cash flows from financing activities:			
Issuance convertible notes, net	—	200,293	55,000
Issuance of common stock	—	76,061	92,500
Debt issuance costs	—	(7,762)	—
Proceeds from the exercise of Common Stock options and warrants	756	(3)	1,174
Borrowings on lines of credit	—	28,800	—
Repayments of lines of credit	—	(28,800)	—
Redemption of 2033 Senior Notes	—	(28,800)	—
Net cash provided (used in) by financing activities	756	239,789	148,674
Net increase (decrease) in cash and cash equivalents	(54,887)	43,903	(6,661)
Cash and cash equivalents at beginning of period	58,627	14,724	21,385
Cash and cash equivalents at end of period	$ 3,740	$ 58,627	$ 14,724
SUPPLEMENTAL INFORMATION:			
Interest paid	$ 10,908	$ 5,224	$ 956
Income taxes paid, net of refunds	$ (903)	$ (1,300)	$ (578)
Operating lease right-of-use assets due to adoption of ASU No. 2016-02	$ —	$ 4,855	$ —
Operating lease liabilities due to adoption of ASU No. 2016-02	$ —	$ 4,855	$ —
Non-cash financing:			
Shares issued upon the conversion of:			
Common Stock options and warrants, surrendered in net exercise	$ —	$ 20	$ 806

The accompanying Notes to Parent Company Condensed Financial Statements are an integral part of these statements.

OPKO Health, Inc.
Notes to Parent Company Condensed Financial Statements

Note 1. Organization and Basis of Presentation

We are a diversified healthcare company that seeks to establish industry-leading positions in large and rapidly growing medical markets. The parent company condensed financial statements included in this Schedule I represent the financial statements of OPKO Health, Inc., the parent company (or "OPKO"), on a stand-alone basis and do not include results of operations from our consolidated subsidiaries. The Parent Company Condensed Financial Statements should be read in conjunction with our audited consolidated financial statements included in Item 8 of Part II of this Form 10-K. As of December 31, 2020 and 2019, approximately $1.9 billion and $1.8 billion, respectively, of our Investments, net have not been eliminated in the parent company condensed financial statements.

The Parent Company Condensed Financial Statements included herein have been prepared in accordance with Rule 12-04, Schedule I of Regulation S-X, as substantially all the assets of BioReference, a wholly-owned subsidiary, and its subsidiaries are restricted from sale, transfer, lease, disposal or distributions to OPKO under the credit agreement with JPMorgan Chase Bank, N.A. (the "Credit Agreement"), subject to certain exceptions. BioReference and its subsidiaries' net assets as of December 31, 2020 were approximately $1.0 billion, which includes goodwill of $434.8 million and intangible assets of $329.5 million. BioReference's restricted net assets exceeds 25% of OPKO's consolidated net assets of $2.5 billion as of December 31, 2020.

Note 2 Debt

On February 25, 2020, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to provide us with an unsecured line of credit in the amount of $100 million. Borrowings under this line of credit will bear interest at a rate of 11% per annum and may be repaid and reborrowed at any time. The credit agreement includes various customary remedies for the lender following an event of default, including the acceleration of repayment of outstanding amounts under this line of credit. This line of credit matures on February 25, 2025. This line of credit also calls for a commitment fee equal to 0.25% per annum of the unused portion of the line. As of December 31, 2020, no funds were borrowed under this line of credit.

In February 2019, we issued $200.0 million aggregate principal amount of Senior Convertible Notes due 2025 (the "2025 Notes") in an underwritten public offering. The 2025 Notes bear interest at a rate of 4.50% per year, payable semiannually in arrears on February 15 and August 15 of each year. The 2025 Notes mature on February 15, 2025, unless earlier repurchased, redeemed or converted.

Holders may convert their 2025 Notes into shares of Common Stock at their option at any time prior to the close of business on the business day immediately preceding November 15, 2024 only under the following circumstances: (1) during any calendar quarter commencing after the calendar quarter ended March 31, 2019 (and only during such calendar quarter), if the last reported sale price of our Common Stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; (2) during the five business day period after any five consecutive trading day period (the "measurement period") in which the trading price per $1,000 principal amount of 2025 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our Common Stock and the conversion rate on each such trading day; (3) if we call any or all of the 2025 Notes for redemption, at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date; or (4) upon the occurrence of specified corporate events set forth in the indenture governing the 2025 Notes. On or after November 15, 2024, until the close of business on the business day immediately preceding the maturity date, holders of the 2025 Notes may convert their notes at any time, regardless of the foregoing conditions. Upon conversion, we will pay or deliver, as the case may be, cash, shares of our Common Stock, or a combination of cash and shares of our Common Stock, at our election.

The initial and current conversion rate for the 2025 Notes is 236.7424 shares of Common Stock per $1,000 principal amount of 2025 Notes (equivalent to a conversion price of approximately $4.22 per share of Common Stock). The conversion rate for the 2025 Notes is subject to adjustment in certain events, but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date of the 2025 Notes or if we deliver a notice of redemption, in certain circumstances the indenture governing the 2025 Notes requires an increase in the conversion rate of the 2025 Notes for a holder who elects to convert its notes in connection with such a corporate event or notice of redemption, as the case may be.

We may not redeem the 2025 Notes prior to February 15, 2022. We may redeem for cash any or all of the notes, at our option, on or after February 15, 2022, if the last reported sale price of our Common Stock has been at least 130% of the then current conversion price for the notes for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period (including the last trading day of such period) ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. No sinking fund is provided for the 2025 Notes.

If we undergo a fundamental change, as defined in the indenture governing the 2025 Notes, prior to the maturity date of the 2025 Notes, holders may require us to repurchase for cash all or any portion of their notes at a repurchase price equal to 100% of the principal amount of the notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. The 2025 Notes are our senior unsecured obligations and rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the 2025 Notes; equal in right of payment to any of our existing and future liabilities that are not so subordinated; effectively junior in right of payment to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of our current or future subsidiaries.

In conjunction with the issuance of the 2025 Notes, we agreed to loan up to 30,000,000 shares of our Common Stock to affiliates of the underwriter in order to assist investors in the 2025 Notes to hedge their position. As of December 31, 2020, a total of 29,250,000 shares were issued under the share lending arrangement. We will not receive any of the proceeds from the sale of the borrowed shares, but we received a one-time nominal fee of $0.3 million for the newly issued shares. Shares of our Common Stock outstanding under the share lending arrangement are excluded from the calculation of basic and diluted earnings per share. See Note 4.

As required by ASC 470-20, “Debt with Conversion and Other Options,” we calculated the equity component of the 2025 Notes, taking into account both the fair value of the conversion option and the fair value of the share lending arrangement. The equity component was valued at $52.6 million at issue date and this amount was recorded as Additional paid-in capital, which resulted in a discount on the 2025 Notes. The discount is being amortized to Interest expense over the term of the 2025 Notes, which results in an effective interest rate on the 2025 Notes of 11.2%.

The following table sets forth information related to the 2025 Notes which is included in our Consolidated Balance Sheet as of December 31, 2020:

(In thousands)	2025 Senior Notes	Discount	Debt Issuance Costs	Total
Balance at December 31, 2019	$ 200,000	$ (46,774)	$ (5,086)	$ 148,140
Amortization of debt discount and debt issuance costs	—	7,237	786	8,023
Balance at December 31, 2020	$ 200,000	$ (39,537)	$ (4,300)	$ 156,163

On November 8, 2018, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to provide us with an unsecured line of credit in the aggregate principal amount of $60 million. The credit agreement was terminated on or around February 20, 2019 and we repaid the $28.8 million outstanding thereunder from the proceeds of the 2025 Notes offering.

In February 2018, we issued a series of 5% Convertible Promissory Notes (the “2023 Convertible Notes”) in the aggregate principal amount of $55.0 million. The 2023 Convertible Notes mature 5 years from the date of issuance. Each holder of a 2023 Convertible Note has the option, from time to time, to convert all or any portion of the outstanding principal balance of such 2023 Convertible Note, together with accrued and unpaid interest thereon, into shares of our Common Stock at a conversion price of $5.00 per share of Common Stock. We may redeem all or any part of the then issued and outstanding 2023 Convertible Notes, together with accrued and unpaid interest thereon, pro rata among the holders, upon no fewer than 30 days, and no more than 60 days, notice to the holders. The 2023 Convertible Notes contain customary events of default and representations and warranties of OPKO.

Purchasers of the 2023 Convertible Notes included an affiliate of Dr. Phillip Frost, M.D., our Chairman and Chief Executive Officer, and Dr. Jane H. Hsiao, Ph.D., MBA, our Vice-Chairman and Chief Technical Officer.

In January 2013, we entered into note purchase agreements with respect to the issuance and sale of our 3.0% Senior Notes due 2033 (the “2033 Senior Notes”) in a private placement exempt from registration under the Securities Act. We issued the 2033 Senior Notes on January 30, 2013. The 2033 Senior Notes, which totaled $175.0 million in original principal amount, bear interest at the rate of 3.0% per year, payable semiannually on February 1 and August 1 of each year. The 2033 Senior

Notes mature on February 1, 2033, unless earlier repurchased, redeemed or converted. Upon a fundamental change as defined in the indenture, 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 related fundamental change repurchase date.

From 2013 to 2016, holders of the 2033 Senior Notes converted $143.2 million in aggregate principal amount into an aggregate of 21,539,873 shares of Common Stock. On February 1, 2019, approximately $28.8 million aggregate principal amount of 2033 Senior Notes were tendered by holders pursuant to such holders' option to require us to repurchase the 2033 Senior Notes as set forth in the indenture, governing the 2033 Senior Notes, following which repurchase only $3.0 million aggregate principal amount of the 2033 Senior Notes remained outstanding. Holders of the remaining $3.0 million principal amount of the 2033 Senior Notes may require us to repurchase such notes for 100% of their principal amount, plus accrued and unpaid interest, on February 1, 2023, on February 1, 2028, or following the occurrence of a fundamental change as described above.

The terms of the 2033 Senior Notes, include, among others: (i) rights to convert the notes 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 determined that these specific terms were embedded derivatives. 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 concluded that the embedded derivatives within the 2033 Senior Notes met these criteria and, as such, were valued separate and apart from the 2033 Senior Notes and recorded at fair value each reporting period.

For accounting and financial reporting purposes, we combined these embedded derivatives and valued them together as one unit of accounting. In 2017, certain terms of the embedded derivatives expired pursuant to the original agreement and the embedded derivatives no longer met the criteria to be separated from the host contract and, as a result, the embedded derivatives were no longer required to be valued separate and apart from the 2033 Senior Notes and were reclassified to additional paid in capital.

In November 2015, BioReference and certain of its subsidiaries entered into the Credit Agreement, as amended from time to time, with JPMorgan Chase Bank, which provides for a $75.0 million secured revolving credit facility and includes a $20.0 million sub-facility for swingline loans and a $20.0 million sub-facility for the issuance of letters of credit. The Credit Agreement matures on November 5, 2021 and is secured by substantially all assets of BioReference and its domestic subsidiaries, as well as a non-recourse pledge by us of our equity interest in BioReference.

Note 3 Commitments and Contingencies

See Note 14 of our Consolidated Financial Statements in Item 8 of Part II of this Form 10-K for a discussion of our commitments and contingencies.

Note 4 Dividends

We received a $12 million dividend payment from BioReference during the year ended December 31, 2020. We did not receive any dividend payments from our consolidated subsidiaries for the years ended December 31, 2019 and 2018.

Note 5 Income Taxes

The Parent Company Condensed Financial Statements recognize the current and deferred income tax consequences that result from our activities during the current and preceding periods pursuant to the provisions of Accounting Standards Codification Topic 740, Income Taxes (ASC 740), as if we were a separate taxpayer rather than a member of the consolidated income tax return group. The tax expense and benefit recorded in OPKO's consolidated financial statements was the result of activity at the subsidiaries and therefore all tax benefit and expense was reported in the Net income (loss) from subsidiaries, net of taxes line in the Condensed Statement of Income.

Note 6 Subsequent Events

We have reviewed all subsequent events and transactions that occurred after the date of our December 31, 2020 Consolidated Balance Sheet date, through the time of filing this Annual Report on Form 10-K.

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 18, 2021

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 18, 2021
/s/ Jane H. Hsiao, Ph.D., MBA Jane H. Hsiao, Ph.D., MBA	Vice Chairman and Chief Technical Officer	February 18, 2021
/s/ Steven D. Rubin Steven D. Rubin	Director and Executive Vice President – Administration	February 18, 2021
/s/ Adam Logal Adam Logal	Senior Vice President, Chief Financial Officer, Chief Accounting Officer and Treasurer (Principal Financial Officer)	February 18, 2021
/s/ Jon R. Cohen Jon R. Cohen, M.D.	Director and Senior Vice President	February 18, 2021
/s/ Robert S. Fishel, M.D. Robert S. Fishel, M.D.	Director	February 18, 2021
/s/ Richard Krasno, Ph.D. Richard Krasno, Ph.D.	Director	February 18, 2021
/s/ Richard A. Lerner, M.D. Richard A. Lerner, M.D.	Director	February 18, 2021
/s/ Roger J. Medel, M.D. Roger J. Medel, M.D.	Director	February 18, 2021
/s/ John A. Paganelli John A. Paganelli	Director	February 18, 2021
/s/ Richard C. Pfenniger, Jr. Richard C. Pfenniger, Jr.	Director	February 18, 2021
/s/ Alice Lin-Tsing Yu, M.D., Ph.D. Alice Lin-Tsing Yu, M.D., Ph.D.	Director	February 18, 2021

Exhibit Number	Description
3.2	Amended and Restated Bylaws
4.6	Description of Securities
21	Subsidiaries of the Company.
23.1	Consent of Independent Registered Public Accounting Firm.
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 year ended December 31, 2020.
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 year ended December 31, 2020.
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 year ended December 31, 2020.
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 year ended December 31, 2020.
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

AMENDED AND RESTATED BYLAWS
OF
OPKO HEALTH, INC.
(A DELAWARE CORPORATION)
Effective: February 12, 2021

Article I.
OFFICES

Section 1.1 Registered Office. The registered office of OPKO Health, Inc. (the "Corporation") shall be in the City of Wilmington, County of New Castle, State of Delaware. Notwithstanding the foregoing, the registered office may be changed at any time upon a resolution adopted by the Corporation's Board of Directors (the "Board'').

Section 1.2 Other Offices. The Corporation may also have offices at such other places within or without the State of Delaware as the Board may from time to time determine or the business of the Corporation may require.

Article II.
MEETINGS OF STOCKHOLDERS

Section 2.1 Place. All meetings of the stockholders shall be held at such place within or without the State of Delaware as shall be designated from time to time by the Board and stated in the notice of the meeting or in a duly executed waiver thereof.

Section 2.2 Annual Meetings. An annual meeting of the stockholders shall be held on such day at such time and place (within or without the State of Delaware) as the Board shall fix, at which time the stockholders shall elect a Board and transact such other business as may properly be brought before the meeting. Any business may be transacted at the meeting, irrespective of whether the notice of such meeting contains a reference thereto, except as otherwise provided in these bylaws of the Corporation (as amended from time to time in accordance with the provisions hereof, these "Bylaws"), or by statute.

Section 2.3 Special Meetings. Special meetings of stockholders may be called at any time, but only by the chairman of the Board (the "Chairman of the Board"), the Chief Executive Officer of the Corporation (the "CEO"), or upon a resolution adopted upon the affirmative vote of a majority of the whole Board, and not by the stockholders.

Section 2.4 Notice Of Meetings. Notice of all stockholders' meetings stating the time, place and the objects for which such meetings are called shall be given by the Chairman of the Board, the CEO, or any vice-president (a "Vice-President") or the Secretary (the "Secretary") or any assistant secretary (an "Assistant Secretary") of the Corporation to each stockholder of record entitled to vote at such meeting not less than ten (10) days or more than sixty (60) days prior to the date of the meeting by written notice delivered personally, by electronic transmission (as defined in Section 10.2 hereof), mailed or delivered via overnight courier to each stockholder. If delivered personally, such notice shall be deemed to be delivered when received. If mailed or delivered via overnight courier service, such notice shall be deemed to be delivered when deposited in the United States mail in a sealed envelope with postage thereon prepaid, or deposited with the overnight courier service, as the case may be, addressed to the

stockholder at his address as it appears on the stock record books of the Corporation, unless he shall have filed with the Secretary a written request that notice intended for him be mailed to some other address, in which case it shall be mailed to the address designated in such request. If delivered by electronic transmission, such notice shall be sent consistent with Article X hereof.

Any meeting at which all stockholders entitled to vote have waived or at any time shall waive notice shall be a legal meeting for the transaction of business, notwithstanding that notice has not been given as herein before provided. The waiver must be in writing, signed by the stockholder entitled to the notice, and be delivered to the Corporation for inclusion in the minutes or filing with the corporate records.

Section 2.5 Notice for Nominations and Proposals.

2.5.1 Annual Meetings.

(a) Nominations for the election of directors and proposals for any new business to be taken up at any annual meeting of stockholders may be made by the Board or, as provided in this Section 2.5, by any stockholder of the Corporation entitled to vote generally in the election of directors, subject to the rights of the holders of preferred stock, if applicable. For nominations or other business to be properly brought before an annual meeting by a stockholder, the stockholder must have given timely notice thereof in writing to the Secretary of the Corporation and such other business must otherwise be a proper matter for stockholder action. To be timely, a stockholder's notice with respect to any annual meeting must be received by the Secretary at the principal executive offices of the Corporation not later than the 60th day nor earlier than the 90th day prior to the first anniversary of the preceding year's annual meeting; provided, however, that in the event that the date of the annual meeting is more than sixty (60) days before or more than sixty (60) days after such anniversary date, notice by the stockholder must be so received not earlier than the 90th day prior to the annual meeting and not later than the later of the 60th day prior to the annual meeting or the 15th day following the day on which public announcement of the date of the meeting is first made by the Corporation. In no event shall the public announcement of an adjournment or postponement of an annual meeting commence a new time period for the giving of a stockholder's notice as described above. A stockholder's notice shall set forth:

(i) as to each person whom the stockholder proposes to nominate for election or reelection as a director, (A) all information relating to such person that is required to be disclosed in solicitations of proxies for election of directors in an election contest, (B) a description of all relationships between the proposed nominee and the recommending stockholder and any agreements or understandings between the recommending stockholder and the nominee regarding the nomination, (C) a description of all relationships between the proposed nominee and any of the Corporation's competitors, customers, suppliers, labor unions (if any) and any other persons with special interests regarding the Corporation, and (D) a written questionnaire with respect to the background and qualification of such proposed nominee in the form required by the Corporation (which form such recommending stockholder shall request in writing from the Secretary prior to submitting notice and which the Secretary shall provide to such recommending stockholder within ten (10) days after receiving such request);

(ii) as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business desired to be brought before the meeting, the reasons for conducting such business at the meeting and any material interest in such business of such stockholder and the beneficial owner, if any, on whose behalf the proposal is made;

(iii) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the nomination or proposal is made, (A) the name and address of such stockholder, as they appear on the Corporation's books, the telephone number of such stockholder, and the name, address and telephone number of such beneficial owner, (B) the class and number of shares of the Corporation which are owned of record by such stockholder and beneficially by such beneficial owner and the time period such shares have been held, (C) a representation that such stockholder and beneficial owner intend to appear in person or by proxy at the meeting, and (D) a representation that such stockholder and such beneficial owner intend to continue to hold the reported shares through the date of the Corporation's next annual meeting of stockholders. For purposes of satisfying the requirements of clause (B) of this paragraph with respect to a beneficial owner, the beneficial owner shall supply to the Corporation either (1) a statement from the record holder of the shares verifying the holdings of the beneficial owner and indicating the length of time the shares have been held by such beneficial owner, or (2) a current Schedule 13D, Schedule 13G, Form 3, Form 4 or Form 5 filed with the Securities and Exchange Commission reflecting the holdings of the beneficial owner, together with a statement of the length of time that the shares have been held; and

(iv) as to the recommending stockholder, each person whom the stockholder proposes to nominate for election or reelection as a director and each stockholder associated person (as defined below), (A) a complete and accurate description of all agreements, arrangements or understandings that have been entered into by, or on behalf of, such recommending stockholder or any stockholder associated person, the effect or intent of which is to mitigate loss, manage risk or benefit from changes in the price of any securities of the Corporation, or maintain, increase or decrease the voting power of such recommending stockholder or any stockholder associated person with respect to securities of the Corporation (any of the foregoing, a "Derivative Instrument"), (B) any information about the ownership or trading of the securities of the Corporation that would be required to be disclosed in a proxy statement for election of directors in an election contest, and of Derivative Instruments, if such Derivative Instruments were treated the same as securities of the Corporation under such requirements, and (C) a complete and accurate description of any performance-related fees (other than an asset-based fee) to which such recommending stockholder or any stockholder associated person may be entitled as a result of any increase or decrease in the value of the Corporation's securities or any Derivative Instruments.

For purposes of these Bylaws, "stockholder associated person" shall mean, with respect to any recommending stockholder, (A) any person directly or indirectly controlling, controlled by, under common control with such recommending stockholder, (B) any member of the immediate family of such recommending stockholder sharing the same household, (C) any person who is a member of a "group" (as such term is used in Rule 13d5 under the Securities Exchange Act of 1934 as amended (the "Exchange Act") (or any successor provision at law)) with or otherwise acting in concert with such recommending stockholder or stockholder associated person with respect to the stock of the Corporation, (D) any beneficial owner of shares of stock of the Corporation owned of record by such recommending stockholder or stockholder associated person (other than a stockholder that is a depositary), (E) any affiliate or associate of such recommending stockholder or any stockholder associated person, (F) any participant (as defined in paragraphs (a)(ii)(vi) of Instruction 3 to Item 4 of Schedule 14A) with such recommending stockholder or stockholder associated person with respect to any proposed business or nominations, as applicable, and (G) any proposed nominee.

(v) If a recommendation is submitted by a group of two or more stockholders, the information regarding the recommending stockholders and beneficial owners, if any, must be submitted with respect to each stockholder in the group and any beneficial owners.

(b) A recommending stockholder shall update such notice, if necessary, such that the information provided or required to be provided in such notice shall be true and correct (i) as of the record date for determining the stockholders entitled to receive notice of the meeting and (ii) as of the date that is ten (10) business days prior to the meeting (or any postponement, rescheduling or adjournment thereof) and such update shall be received by the Secretary at the principal executive offices of the Corporation (A) not later than the close of business five (5) business days after the record date for determining the stockholders entitled to receive notice of such meeting (in the case of an update required to be made under clause (i)) and (B) not later than the close of business seven (7) business days prior to the date for the meeting (in the case of an update required to be made pursuant to clause (ii)).

(c) Notwithstanding anything in paragraph (a) of this Section 2.5.1 to the contrary, in the event that the number of directors to be elected to the Board at the annual meeting is increased pursuant to an act of the Board and there is no public announcement by the Corporation naming all of the nominees for director or specifying the size of the increased Board on or before the date which is 15 days before the latest date by which a stockholder may timely notify the Corporation of nominations or other business to be brought by a stockholder in accordance with paragraph (a) of this Section 2.5.1, a stockholder's notice required by this Section 2.5.1 shall also be considered timely, but only with respect to nominees for any new positions created by such increase, if it shall be received by the Secretary at the principal executive offices of the Corporation not later than the 15th day following the day on which such public announcement is first made by the Corporation.

2.5.2 Special Meetings. Only such business shall be conducted at a special meeting of stockholders as shall have been brought before the meeting pursuant to the Corporation's notice of meeting. Nominations of persons for election to the Board at a special meeting of stockholders at which directors are to be elected pursuant to the Corporation's notice of meeting may be made (i) by or at the direction of the Board or (ii) provided that the Board has determined that directors shall be elected at such meeting, by any stockholder of the Corporation who is a stockholder of record at the time of giving of notice provided for in this Section 2.5, who shall be entitled to vote at the meeting and who complies with the notice procedures set forth in this Section 2.5. In the event the Corporation calls a special meeting of stockholders for the purpose of electing one or more directors to the Board, any such stockholder may nominate a person or persons (as the case may be), for election to such position(s) as specified in the Corporation's notice of meeting for inclusion in the stockholder's notice required by Section 2.5.1 of these Bylaws if such nomination shall be delivered to the Secretary at the principal executive offices of the Corporation not earlier than the close of business on the 90th day prior to such special meeting and not later than the close of business on the later of the 60th day prior to such special meeting or the 15th day following the day on which public announcement is first made of the date of the special meeting and of the nominees proposed by the Board to be elected at such meeting. In no event shall the public announcement of an adjournment of a special meeting commence a new time period for the giving of a stockholder's notice as described above.

2.5.3 General. Only such persons who are nominated in accordance with the procedures set forth in this Section 2.5 shall be eligible to stand for election to the Board at a meeting of stockholders, and only such business shall be conducted at a meeting of stockholders as shall have been brought before the meeting in accordance with the procedures set forth in this Section 2.5. Except as otherwise provided by law, the Certificate of Incorporation of the Corporation as amended and restated (the "Certificate of Incorporation") or these Bylaws, the Chairman of the Board shall have the power and duty to determine whether a nomination or any business proposed to be brought before the meeting was made or proposed, as the case may be, in accordance with the procedures set forth in this

bylaw and, if any proposed nomination or business is not in compliance with this Section 2.5, to declare that such defective proposal or nomination shall be disregarded.

2.5.4 Public Announcement. For purposes of this Section 2.5, "public announcement" shall mean disclosure in a press release reported by the Dow Jones News Service, Associated Press or comparable national news service or in a document publicly filed by the Corporation with the Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the Exchange Act.

2.5.5 Non-Exclusivity. If the Corporation is required under Rule 14a-8 under the Exchange Act to include a stockholder's proposal in its proxy statement, such stockholder shall be deemed to have given timely notice for purposes of this Section 2.5 with respect to such proposal. Nothing in this Section 2.5 shall be deemed to affect any rights of the holders of any series of preferred stock of the Corporation to elect directors.

Section 2.6 Quorum. Except as may be otherwise provided by law, a majority of the voting power of all the outstanding shares of tile Corporation entitled to vote, represented in person or by proxy, shall constitute a quorum at a meeting of stockholders. In the event that the voting power of a majority of the outstanding shares are represented at any meeting, action on a matter is approved if the votes cast favoring the action exceed the votes cast opposing the action, unless the question is one upon which by express provision of law or of the Certificate of Incorporation or of these Bylaws a larger or different vote is required, in which case such express provision shall govern and control the decision of each question. If a quorum of the shares entitled to vote shall fail to be obtained at any meeting, or in the event of any other proper business purpose, the chair of the meeting or the holders of a majority of the shares present, in person or by proxy, may adjourn the meeting to another place, date or time by announcement to stockholders present in person at the meeting and no other notice of such place, date or time need be given.

Section 2.7 Organization. At every meeting of the stockholders the Chairman of the Board, or, in his absence, the CEO, or in the absence of the Chairman of the Board and the CEO, a director or an officer of the Corporation designated by the Board shall act as chairman. The Secretary, or, in his absence, an Assistant Secretary, shall act as secretary at all meetings of the stockholders. In the absence from any such meeting of the Secretary and any Assistant Secretary, the chairman may appoint any person to act as secretary of the meeting.

Section 2.8 Closing of Transfer Books or Fixing of Record Date. For the purpose of determining the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, the Board may fix in advance a date as the record date for any such determination of stockholders, such date in any case to be not more than sixty (60) days and not less than ten (10) days prior to the date on which the particular action requiring such determination of stockholders is to be taken. If the stock transfer books are not closed and no record date is fixed for the determination of stockholders entitled to notice of or to vote at a meeting of stockholders, or stockholders entitled to receive payment of a dividend, the date on which notice of the meeting is mailed or the date on which the resolution of the Board declaring such dividend is adopted, as the case may be, shall be the record date for such determination of stockholders. When a determination of stockholders entitled to vote at any meeting of stockholders has been made as provided in this Section 2.8, such determination shall apply to any adjournment thereof.

Section 2.9 Voting Lists. The officer or agent having charge of the stock transfer books for common shares of the Corporation shall make available, within two (2) business days after notice of a meeting is given, a complete list of the stockholders entitled to vote at such meeting or any adjournment thereof, arranged in alphabetical order, with the address of and the number of shares held by each stockholder, which list, for a period beginning within two (2) business days after notice of such meeting is given, shall be subject to inspection by any stockholder at any time either (a) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (b) during ordinary business hours, at the principal place of business of the Corporation. If the meeting is to be held at a place, then the list shall be produced and kept at the time and place of the meeting during the whole time thereof and may be inspected by any stockholder who is present. If the meeting is to be held solely by means of remote communication, then the list shall also be open to the examination of any stockholder during the whole time of the meeting on a reasonably accessible electronic network, and the information required to access such list shall be provided with the notice of the meeting. In the event of any challenge to the right of any person to vote at the meeting, the presiding officer at such meeting may rely on said list as proper evidence of the right of parties to vote at such meeting.

Section 2.10 Proxies. Stockholders of record who are entitled to vote may vote at any meeting either in person or by written proxy, which shall be filed with the secretary of the meeting before being voted. Such proxy shall entitle the holders thereof to vote at any adjournment of such meeting, but shall not be valid after the final adjournment thereof. No proxy shall be valid after the expiration of eleven (11) months from the date of its execution unless the stockholder executing it shall have specified therein the length of time it is to continue in force, which shall be for some limited period. A proxy is revocable by the stockholder unless it conspicuously states that it is irrevocable and the appointment of the proxy is coupled with an interest.

Section 2.11 Voting of Shares. Except as otherwise provided in the Certificate of Incorporation or these Bylaws, each share of Common Stock shall have all voting rights accorded to holders of Common Stock pursuant to the Delaware General Corporation Law (“DGCL’’), at the rate of one vote per share.

Section 2.12 Business and Order of Business. At each meeting of the stockholders such business may be transacted as may properly be brought before such meeting, except as otherwise provided by law or in these Bylaws. The order of business at all meetings of the stockholders shall be as determined by the Chairman of the Board, unless otherwise determined by a majority in interest of the stockholders present in person or by proxy at such meeting and entitled to vote thereat.

Article III.
BOARD OF DIRECTORS

Section 3.1 Number. The number of directors of the Corporation shall be such number, neither fewer than three (3) nor more than fifteen (15) (exclusive of directors, if any, to be elected by holders of any class or series of preferred stock of the Corporation, voting separately as a class), as determined from time to time by the Board. The Board has the power to fix or change the number of directors, including an increase or decrease in the number of directors, from time to time as established by the Board. A director need not be a stockholder or a resident of the State of Delaware.

Section 3.2 Powers of Directors. The Board shall have the entire management of the business of the Corporation. In the management and control of the property, business and affairs of the Corporation, the Board is hereby vested with all the powers possessed by the Corporation itself, so far as this delegation of authority is not inconsistent with the laws of the State of Delaware, the Certificate of Incorporation, or these Bylaws. The Board shall have the power to determine what constitutes net earnings, profits, and surplus, respectively, what amount shall be reserved for working capital and to establish reserves for any other proper purpose, and what amount shall be declared as dividends, and such determination by the Board shall be final and conclusive. The Board shall have the power to declare dividends for and on behalf of the Corporation, which dividends may include or consist of stock dividends.

Section 3.3 Regular Meetings of the Board. Immediately after the annual election of directors, the newly elected directors may meet at the same place for the purpose of organization, the election of corporate officers and the transaction of other business; if a quorum of the directors is then present, no prior notice of such meeting shall be required. Other regular meetings of the Board shall be held at such times and places as the Board by resolution may determine and specify, and if so determined no notice thereof need be given, provided that, unless all the directors are present at the meeting at which said resolution is passed, the first meeting held pursuant to said resolution shall not be held for at least five (5) days following the date on which the resolution is passed.

Section 3.4 Special Meetings. Special meetings of the Board may be held at any time or place whenever called by the Chairman of the Board, the CEO, the Chief Financial Officer or the Secretary, or by written request of at least two directors, notice thereof being given to each director by the Secretary or other officer calling the meeting, or they may be held at any time without formal notice provided all of the directors are present or those not present shall at any time waive or have waived notice thereof.

Section 3.5 Notice. Notice of any special meetings shall be given at least two (2) days previously thereto by written notice delivered personally, by telegram, by overnight courier service, by facsimile communication or by electronic transmission, or at least five (5) days previously thereto by written notice sent by mail. The time when such notice is received, if delivered personally, or when such notice is dispatched, if delivered through the mail, by overnight courier service, by facsimile telecommunication or by electronic transmission, shall be the time of the giving of the notice.

Section 3.6 Quorum. A majority of the members of the Board, as constituted for the time being, shall constitute a quorum for the transaction of business, but a lesser number may adjourn any meeting and the meeting may be held as adjourned without further notice. If a quorum is present when a vote is taken, the affirmative vote of a majority of the directors present is the act of the Board, except as otherwise provided by law or by these Bylaws. The fact that a director has an interest in a matter to be voted on by the meeting shall not prevent his being counted for purposes of a quorum.

Section 3.7 Informal Action by Directors. Any action required to be taken at a meeting of the Board, or any other action which may be taken at a meeting of the Board, may be taken without a meeting if all directors consent to taking such action without a meeting. The action must be evidenced by one or more written consents describing the action taken, signed by each director, and shall be included in the minutes or filed with the corporate records reflecting the action taken.

Section 3.8 Meetings by any Form of Communication. The Board shall have the power to permit any and all directors to participate in a regular or special meeting by, or conduct the meeting through the use of any means of communication by which all directors participating may simultaneously hear each other during the meeting. A director participating in a meeting by this means is deemed to be present in person at the meeting.

Section 3.9 Organization. At each meeting of the Board, the Chairman of the Board, or in the absence of the Chairman of the Board, a director designated by the Board shall act as chairman. The Secretary, or, in the Secretary's absence, any person appointed by the chairman, shall act as secretary of the meeting.

Section 3.10 Resignations. A director may resign at any time by delivering written notice to the Board, the Chairman of the Board or the CEO. Resignation is effective when the notice is delivered, unless the notice specifies a later effective date.

Section 3.11 Removal of Directors. Subject to the rights of the holders of one or more series of Preferred Stock, any director or the entire board of directors may be removed from the office by the affirmative vote of the holders of least a majority of the voting power of the then outstanding capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class.

Section 3.12 Vacancies. Any vacancy occurring in the Board, including vacancies resulting from an increase in the number of directors, may be filled solely by the affirmative vote of a majority of the remaining directors, though less than a quorum, and unless the Board of Directors determines otherwise (and subject to the rights of the holders or any series of preferred stock), vacancies shall not be filled by stockholders. A director elected to fill any vacancy shall hold office for a term expiring at the annual meeting of stockholders at which the term of the class to which he or she has been elected expires, and until such director's successor shall have been duly elected and qualifies or until his or her earlier death, resignation or removal.

Section 3.13 Compensation. By resolution of the Board, the directors may be paid their expenses, if any, of attendance at each meeting of the Board. No such payment shall preclude any director from serving the Corporation in any other capacity and receiving compensation therefor.

Article IV.
COMMITTEES

Section 4.1 Appointment and Powers. The Board may create one or more committees, each committee to consist of two or more directors of the Corporation, which, to the extent provided in said resolution or in these Bylaws and not inconsistent with the DGCL, shall have and may exercise the powers of the Board in the management of the business and affairs of the Corporation, and may authorize the seal of the Corporation to be affixed to all papers which may require it. Such committee or committees shall have such name or names as may be determined from time to time by resolution adopted by the Board. The Board may abolish any such committee at any time.

Section 4.2 Term of Office and Vacancies. Each member of a committee shall continue in office until a director to succeed him shall have been elected and shall have qualified, or until he ceases to be a director or until he shall

have resigned or shall have been removed in the manner hereinafter provided. Any vacancy in a committee shall be filled by the Board.

Section 4.3 Organization. Unless otherwise provided by the Board, each committee shall appoint a chairman. Each committee shall keep a record of its acts and proceedings and report the same from time to time to the Board as the Board may require.

Section 4.4 Resignations. Any member of a committee may resign from the committee at any time by giving written notice to the Chairman of the Board, the CEO, or the Secretary. Such resignation shall take effect at the time of the receipt of such notice or at any later time specified therein, and, unless otherwise specified therein, the acceptance of such resignation shall not be necessary to make it effective.

Section 4.5 Removal. Any member of a committee may be removed from the committee with or without cause at any time by resolution of the Board.

Section 4.6 Meetings. Regular meetings of each committee, of which no notice shall be required, shall be held on such days and at such places as the chairman of the committee shall determine or as shall be fixed by a resolution passed by a majority of all the members of such committee. Special meetings of each committee will be called by the Secretary at the request of any two (2) members of such committee, or in such other manner as may be determined by the committee. Notice of any special meetings shall be given at least two (2) days previously thereto by written notice delivered personally, by telegram, by overnight courier service, by facsimile communication or by electronic transmission, or at least five (5) days previously thereto by written notice sent by mail. Every such notice shall state the date, time and place of the meeting, but need not state the purposes of the meeting. No notice of any meeting of a committee shall be required to be given to any alternate. The time when such notice is received, if delivered personally, or when such notice is dispatched, if delivered through the mail, by overnight courier service, by facsimile telecommunication or by electronic transmission, shall be the time of the giving of the notice.

Section 4.7 Quorum and Manner of Acting. Unless otherwise provided by resolution of the Board, a majority of a committee shall constitute a quorum for the transaction of business and the act of a majority of those present at a meeting at which a quorum is present shall be the act of such committee, except as otherwise provided by law or by these Bylaws. The members of each committee shall act only as a committee and the individual members shall have no power as such. Actions taken at a meeting of any committee shall be reported to the Board at its next meeting following such committee meeting; provided that, when the meeting of the Board is held within two (2) days after the committee meeting, such report may be made to the Board at its second meeting following such committee meeting.

Section 4.8 Compensation. Each member of a committee shall be paid such compensation, if any, as shall be fixed by the Board.

Article V.
WAIVER OF NOTICE

Whenever any notice is required to be given by these Bylaws, the Certificate of Incorporation, or any laws of the State of Delaware, a waiver thereof in writing signed by the person or persons entitled to such notice and filed

with the minutes or corporate records, whether before or after the time stated therein, shall be deemed equivalent thereto. Where the person or persons entitled to such notice sign the minutes of any stockholders' or directors' meeting, which minutes contain the statement that said person or persons have waived notice of the meeting, then such person or persons are deemed to have waived notice in writing. A stockholder's attendance at a meeting waives objection to lack of notice or defective notice of the meeting, unless the stockholder at the beginning of the meeting (or promptly upon the stockholder's arrival) objects to holding the meeting or transacting business at the meeting, and also waives objection to consideration of a particular matter at the meeting that is not within the purpose or purposes described in the meeting notice, unless the stockholder objects to considering the matter when it is presented. A director's attendance at or participation in a meeting waives any required notice to the director of the meeting unless the director at the beginning of the meeting (or promptly upon the director's arrival) objects to holding the meeting or transacting business at the meeting and does not thereafter vote for or assent to action taken at the meeting.

Article VI.
OFFICERS

Section 6.1 Number. The officers of the Corporation shall be a Chairman of the Board, CEO, Chief Financial Officer, one or more Vice-Presidents (the number thereof to be determined by the Board), a Secretary, and a Treasurer, each of whom shall be elected by the Board. Such other officers and assistant officers as may be deemed necessary may be elected or appointed by the Board. Any two or more offices may be held by the same person, except the offices of CEO and Secretary.

Section 6.2 Election and Term of Office. The officers of the Corporation to be elected by the Board shall be elected annually by the Board at the first meeting of the Board held after each annual meeting of the stockholders. If the election of officers shall not be held in such meeting, such election shall be held as soon thereafter as conveniently may be. Each officer shall hold office until his successor is duly elected and is qualified or until his death or until he resigns or is removed in the manner hereinafter provided.

Section 6.3 Removal. Any officer or agent elected or appointed by the Board may be removed by the Board whenever in its judgment the best interests of the Corporation would be served thereby, but such removal shall be without prejudice to the contract rights, if any, of the person so removed.

Section 6.4 Vacancies. A vacancy in any office because of death, resignation, removal, disqualification or otherwise, may be filled by the Board for the unexpired portion of the term.

Section 6.5 Chairman of the Board. The Chairman of the Board shall preside at all meetings of the stockholders and the directors. The Chairman of the Board shall represent the Corporation in all matters involving the stockholders of the Corporation. He shall also perform such other duties the Board may assign to him from time to time.

Section 6.6 Chief Executive Officer. The CEO shall in general supervise and control all of the business and affairs of the Corporation. He shall, in the absence of the Chairman of the Board, preside at all meetings of the stockholders and shall enforce the observance of the Bylaws and the roles of order for the meetings of the Board and the stockholders. He shall keep the Board appropriately informed on the business and affairs of the Corporation. He

may sign, either alone or with the Secretary, an Assistant Secretary or any other proper officer of the Corporation thereunto authorized by the Board, certificates for shares of the Corporation, any deed, mortgages, bonds, contracts, or other instruments which the Board has authorized to be executed, except in cases where the signing and execution thereof shall be expressly delegated by the Board or by these Bylaws to some other officer or agent of the Corporation, or shall be required by law to be otherwise signed or executed, and in general shall perform all duties incident to the office of CEO and such other duties as may be prescribed by the Board from time to time.

Section 6.7 President. The President, if any, shall see that all orders and resolutions of the Board are carried into effect and shall have general and active management of the business of the Corporation. He or she shall have the authority to execute bonds, mortgages and other contracts requiring a seal, under the seal of the Corporation, except where required or permitted by law to be otherwise signed and executed arid except where the signing and execution thereof shall be expressly delegated by the Board to some other officer or agent of the Corporation. If, for any reason, the Corporation does not have a Chairman or CEO, or such officers are unable to act, the President, if any, shall assume the duties of those officers as well.

Section 6.8 Chief Financial Officer or Chief Accounting Officer and Treasurer. The Chief Financial Officer or Chief Accounting Officer, as the case may be, shall also serve as the Treasurer of the Corporation and shall arrange for the keeping of adequate records of all assets, liabilities and transactions of the Corporation. He shall provide for the establishment of internal controls and see that adequate audits are currently and regularly made. He shall submit to the CEO, the President, if any, the Chief Operating Officer, the Chairman of the Board and the Board timely statements of the accounts of the Corporation and the financial results of the operations thereof.

Section 6.9 Assistant Treasurers. The Assistant Treasurer or if there shall be more than one, the Assistant Treasurers in the order determined by the Board (or if there be no such determination, then in the order of their election), shall, in the absence of the Treasurer or in the event of his inability or refusal to act, perform the duties and exercise the powers of the Treasurer and shall perform such other duties and have such other powers as the Board may from time to time prescribe.

Section 6.10 Chief Operating Officer. If a Chief Operating Officer is elected, the Chief Operating Officer shall supervise the operation of the Corporation, subject to the policies and directions of the Board. He shall provide for the proper operation of the Corporation and oversee the internal interrelationship amongst any and all departments of the Corporation. He shall submit to the CEO, the President, if any, and the Board timely reports on the operations of the Corporation.

Section 6.11 The Vice-Presidents. In the absence of the CEO and the President, if any, or in the event of their death, inability or refusal to act, the Vice-President (or in the event there be more than one Vice-President, the Vice-Presidents in the order designated at the time of their election, or in the absence of any designation, then in the order of their election) shall perform the duties of the CEO and the President, if any, and when so acting, shall have all the powers of and be subject to all the restrictions upon the CEO and the President, if any. Any Vice-President may sign, either alone or with the Secretary or an Assistant Secretary, certificates for shares of the Corporation any deed, mortgages, bonds, contracts or other instruments which the Board has authorized to be executed, except in cases where the signing and execution thereof shall be expressly delegated, by the Board or by these bylaws to some other officer or agent of the Corporation, or shall be required by law to be otherwise signed or executed, and shall perform such other duties as from time to time may be assigned to him by the CEO, the President, if any, or by the Board.

Section 6.12 The Secretary. The Secretary shall: (a) prepare and keep the minutes of the stockholders' and of the Boards' meetings in one or more books provided for that purpose; (b) see that all notices are duly given in accordance with the provisions of these bylaws or as required by law; (c) be custodian of the corporate records and of the seal (if any) of the Corporation and see that said seal is affixed to all documents, the execution of which on behalf of the Corporation under its seal is duly authorized; (d) keep a register of the post office address of each stockholder which shall be furnished to the Secretary by such stockholder; (e) sign with the CEO, the President, if any, or a Vice-President certificates for shares of the Corporation, the issuance of which shall have been authorized by resolution of the Board; (f) have general charge of the stock transfer books of the Corporation; and (g) in general perform all duties as from time to time may be assigned to him by the CEO, the President, if any, or by the Board.

Section 6.13 Assistant Secretaries. The Assistant Secretaries, when authorized by the Board, may sign with the CEO, the President, if any, or a Vice-President certificates for shares of the Corporation the issuance of which shall have been authorized by a resolution of the Board. The Assistant Secretaries, in general, shall perform such duties as shall be assigned to them by the Secretary, or by the CEO, the President, if any, or the Board.

Section 6.14 Registered Agent. The Board shall appoint a registered agent for the Corporation in accordance with the DGCL and may pay the agent such compensation from time to time as it may deem appropriate.

Article VII.
INDEMNIFICATION AND INSURANCE

Section 7.1 Indemnification by Corporation. The Corporation shall indemnify to the fullest extent permitted by applicable law as the same exists or may hereafter be in effect, any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Corporation) by reason of the fact that he or she is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee or agent of another Corporation, partnership, joint venture, trust or other enterprise, against expenses including attorneys' fees, judgments, fines and amounts paid in settlement actually and reasonably incurred by him or her in connection with such action, suit or proceeding if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of *nolo contendere* or its equivalent, shall not, of itself; create a presumption that the person did not act in good faith and in a manner which he or she reasonably believed to be in or not opposed to the best interests of the Corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

Section 7.2 Suit by or in the Right of the Corporation. The Corporation shall indemnify any person who was or is a party, or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that he or she is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee or agent of another Corporation, partnership, joint venture, trust or other enterprise against expenses (including attorneys' fees) actually and reasonably incurred by him or her in connection with the defense or

settlement of such action or suit if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the Corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Section 7.3 Success on the Merits. To the extent that a director, officer, employee or agent of the Corporation has been successful on the merits or otherwise in defense of any action, suit or proceeding referred to in Section 7.1 or Section 7.2 of this Article, or in defense of any claim, issue or matter therein, he or she shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by him or her in connection therewith.

Section 7.4 Determination that Indemnification is Proper. Any indemnification under Section 7.1 or Section 7.2 of this Article (unless ordered by a court) shall be made by the Corporation only as authorized in the specific case upon a determination that indemnification of the director, officer, employee or agent is proper in the circumstances because he or she has met the applicable standard of conduct set forth in such section. Such determination shall be made:

(a) by the Board by a majority vote of a quorum consisting of directors who were not parties to such action, suit or proceeding; or

(b) if such a quorum is not obtainable, or, even if obtainable a quorum, of disinterested directors so directs, by independent legal counsel in a written opinion; or

(c) by the stockholders.

Section 7.5 Expenses. Expenses (including attorneys' fees) incurred by an officer or director in defending a civil, criminal, administrative or investigative action, suit or proceeding may be paid by the Corporation in advance of the final disposition of such action, suit or proceeding upon receipt of an undertaking by or on behalf of such director or officer to repay such amount if it shall ultimately be determined that he or she is not entitled to be indemnified by the Corporation as authorized in this Article VII. Such expenses (including attorneys' fees) incurred by other employees and agents may be so paid upon such terms and conditions, if any, as the Board deems appropriate.

Section 7.6 Non-Exclusivity of Indemnification Rights. The indemnification and advancement of expenses provided by or granted pursuant to the other sections of this Article VII shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his or her official capacity and as to action in another capacity while holding such office.

Section 7.7 Insurance. The Corporation shall have power to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee or agent of another Corporation, partnership, joint venture, trust or other enterprise against any liability asserted against him or her and incurred by him or her in any such capacity, or

arising out of his or her status as such, whether or not the Corporation would have the power to indemnity him or her against such liability under the provisions of this Article VII.

Section 7.8 Continuance of Indemnification. The indemnification and advancement of expenses provided by or granted pursuant to this Article VII shall, unless otherwise provided when authorized or ratified, continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person. The rights to indemnification and advancement of expenses provided by or granted pursuant to this Article VII shall constitute a contract between the Corporation and each director, officer, employee or agent of the Corporation in each circumstance, and each such person shall have all rights available in law or equity to enforce such contract rights against the Corporation. Any repeal or modification of any provision of this Article VII shall not adversely affect or deprive any director, officer, employee or agent of any right or protection offered by such provision prior to such repeal or modification.

Section 7.9 Definition of "the Corporation". For purposes of this Article VII, references to "the Corporation" shall include, in addition to the resulting Corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, and employees or agents, so that any person who is or was a director, officer employee or agent of such constituent Corporation, or is or was serving at the request of such constituent Corporation as a director, officer, employee or agent of another Corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under this Article VII with respect to the resulting or surviving Corporation as he or she would have with respect to such constituent Corporation of its separate existence bad continued.

Section 7.10 Definition of "Other Enterprises". For purposes of this Article VII, references to "other enterprises" shall include employee benefit plans; references to "fines" shall include any excise taxes assessed on a person with respect to any employee benefit plan; and references to "serving at the request of the Corporation" shall include any service as a director, officer, employee or agent of the Corporation which imposes duties on, or involves services by, such director, officer, employee, or agent with respect to an employee benefit plan, its participants or beneficiaries; and a person who acted in good faith and in a manner he or she reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner "not opposed to the best interests of the Corporation" as referred to in this Article VII.

Article VIII.
CONTRACTS, LOANS, CHECKS AND DEPOSITS

Section 8.1 Contracts. The Board may authorize any officer or officers, agent or agents, to enter into any contract or execute and deliver any instrument in the name of and on behalf of the Corporation, and such authority may be general or confined to specific instances.

Section 8.2 Loans. The Corporation shall not make any loan other than a sale on credit in the ordinary course of business or a life insurance policy loan, either directly or indirectly, to any director or officer of the Corporation except with the consent of the holders of a majority of all the outstanding shares owned or controlled by stockholders other than a stockholder for whose benefit such action is being taken, or if the Board determines that the loan benefits the Corporation and approves the transaction.

Section 8.3 Checks, Drafts, etc. All checks, drafts, or other orders for the payment of money, notes or other evidences of indebtedness issued in the name of the Corporation, shall be signed by such officer or officers, agent or agents of the Corporation and in such manner as shall from time to time be determined by resolution of the Board.

Section 8.4 Deposits. All funds of the Corporation not otherwise employed shall be deposited from time to time to the credit of the Corporation in such banks, trust companies or other depositories as the Board may select.

Article IX.
CERTIFICATES OF STOCK

Section 9.1 Right to Certificate. Every holder of stock in the Corporation shall be entitled to have a certificate, signed by or in the name of the Corporation by the Chairman or Vice-Chairman of the Board, or the CEO, or the President, if any, or a Vice-President and the Treasurer or an Assistant Treasurer or the Secretary or an Assistant Secretary of the Corporation, certifying the number of shares owned by him in the Corporation.

Section 9.2 Statements Setting Forth Rights. If the Corporation shall be authorized to issue more than one class of stock or more than one series of any class, the designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and rights shall be set forth in full or summarized on the face or back of the certificate which the Corporation shall issue to represent such class or series of stock, provided that, except as otherwise provided in Section 202 of the DGCL, in lieu of the foregoing requirements, there may be set forth on the face or back of the certificate which the Corporation shall issue to represent such class or series of stock; a statement that the Corporation will furnish without charge to each stockholder who so requests the designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and rights.

Section 9.3 Facsimile Signature. Where a certificate is countersigned (a) by a transfer agent other than the Corporation or its employee or (b) by a registrar other than the Corporation or its employee, the signatures of the officers of the Corporation may be facsimiles. In case any officer who has signed or whose facsimile signature has been placed upon a certificate shall have ceased to be such officer before such certificate is issued, it may be issued by the Corporation with the same effect as if he were such officer at the date of issue.

Section 9.4 Lost Certificates. The Board may delegate to its transfer agent the authority to issue without further action or approval of the Board, a new certificate or certificates in place of any certificate or certificates theretofore issued by the Corporation alleged to have been lost, stolen or destroyed, upon the receipt by the transfer agent of an affidavit of that fact by the person claiming the certificate of stock to be lost, stolen or destroyed, and upon the receipt from the owner of such lost, stolen or destroyed certificate, or certificates, or his legal representative of a bond as indemnity against any claim that may be made with respect to the certificate alleged to have been lost, stolen or destroyed.

Section 9.5 Transfers of Stock. Upon surrender to the Corporation or the transfer agent of the Corporation of a certificate for shares duly endorsed or accompanied by proper evidence of succession, assignment or authority to

transfer, and if such shares are not restricted as to transfer, it shall be the duty of the Corporation to issue a new certificate to the person entitled thereto, cancel the old certificate and record the transaction upon its books.

Section 9.6 Transfer Agents and Registrars. The Board may appoint one or more corporate transfer agents and registrars.

Section 9.7 Registered Ownership of Shares. The Corporation shall be entitled to treat the person in whose name any share of its stock is registered as the owner thereof for all purposes and shall not be bound to recognize any equitable or other claim to, or interest in, such share on the part of any other person, whether or not the Corporation shall have notice thereof: except as expressly provided by applicable law.

Article X.
NOTICE BY ELECTRONIC TRANSMISSION

Section 10.1 Notice by Electronic Transmission. Without limiting the manner by which notice otherwise may be given effectively to stockholders pursuant to the DGCL, the Certificate of Incorporation or these Bylaws, any notice to stockholders given by the Corporation under any provision of the DGCL, the Certificate of Incorporation or these Bylaws shall be effective if given by a form of electronic transmission consented to by the stockholder to whom the notice is given. Any such consent shall be revocable by the stockholder by written notice to the Corporation. Any such consent shall be deemed revoked if: (a) the Corporation is unable to deliver by electronic transmission two (2) consecutive notices given by the Corporation in accordance with such consent; and (b) such inability becomes known to the secretary or an assistant secretary of the Corporation or to the transfer agent, or other person responsible for the giving of notice. However, the inadvertent failure to treat such inability as a revocation shall not invalidate any meeting or other action. Any notice given pursuant to Section 10.1 shall be deemed given: (i) if by facsimile telecommunication, when directed to a number at which the stockholder has consented to receive notice; (ii) if by electronic mail, when directed to an electronic mail address at which the stockholder has consented to receive notice; (iii) if by a posting on an electronic network together with separate notice to the stockholder of such specific posting, upon the later of (A) such posting and (B) the giving of such separate notice; and (iv) if by any other form of electronic transmission, when directed to the stockholder. An affidavit of the Secretary or an Assistant Secretary or of the transfer agent or other agent of the Corporation that the notice has been given by a form of electronic transmission shall in the absence of fraud, be prima facie evidence of the facts stated therein.

Section 10.2 Definition of Electronic Transmission. An “electronic transmission” means any form of communication, not directly involving the physical transmission of paper, that creates a record that may be retained, retrieved, and reviewed by a recipient thereof, and that may be directly reproduced in paper form by such a recipient through an automated process. Any requirement in these Bylaws for a written or signed document from any person shall be deemed to be satisfied by an electronic transmission from such person.

Article XI.
GENERAL PROVISIONS

Section 11.1 Dividends. Dividends upon the capital stock of the Corporation, subject to the provisions of the Certificate of Incorporation, if any, may be declared by the Board, subject to applicable legal requirements.

Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of the Certificate of Incorporation.

Section 11.2 Reserves. Before payment of any dividend, there may be set aside out of any funds of the Corporation available for dividends such sum or sums as the directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or for repairing or maintaining any property of the Corporation, or for such other purpose as the directors shall think conclusive to the interest of the Corporation, and the directors may modify or abolish any such reserve in the manner in which it was created.

Section 11.3 Fiscal Year. The fiscal year of the Corporation shall be fixed by resolution of the Board.

Section 11.4 Seal. This Corporation may or may not have a seal and in any event the failure to affix a corporate seal to any instrument executed by the Corporation shall not affect the validity thereof. If a seal is adopted, the seal of this Corporation shall include the following letters cut or engraved thereon: OPKO HEALTH, INC.

Article XII.
AMENDMENTS

Section 12.1 Amendments. The Board is expressly authorized to repeal, alter, amend or rescind these Bylaws. Notwithstanding any other provision of these Bylaws (and notwithstanding some lesser percentage that may be specified by law), the Bylaws may be repealed, altered, amended or rescinded by the stockholders of the Corporation as described in the Certificate of Incorporation or in accordance with the DGCL only upon the affirmative vote of at least sixty-six and two thirds percent (66.66%) of the voting power of the then outstanding capital stock of the Corporation entitled to vote thereon, voting together as a single class.

Exhibit 4.6

DESCRIPTION OF COMMON STOCK

As of the end of the period covered by the most recent Annual Report on Form 10-K of OPKO Health, Inc.(the "registrant"), the common stock, par value $0.01 per share, of the registrant (the "common stock") was registered under Section 12 of the Securities Exchange Act of 1934, as amended. Unless the context otherwise requires, all references herein to "we", "our", "ours", and "us" refer to OPKO Health, Inc.

The following description of the common stock is a summary and does not purport to be complete. A copy of our amended and restated certificate of incorporation, as amended, which we refer to as our Amended and Restated Certificate of Incorporation, and our amended and restated bylaws, which we refer to as our Amended and Restated Bylaws, have been filed as Exhibits 3.1 and 3.2, respectively, to our Annual Report on Form 10-K for the year ended December 31, 2020. Our common stock and the rights of the holders of our common stock are subject to the applicable provisions of the General Corporation Law of the State of Delaware, which we refer to as the DGCL, our Amended and Restated Certificate of Incorporation, our Amended and Restated Bylaws, as well as some of the terms of our outstanding indebtedness. The description below of our common stock and provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws are summaries and are qualified by reference to the Amended and Restated Certificate of Incorporation and our Amended and Restated Bylaws, and by the applicable provisions of the DGCL. We encourage you to read that law and those documents carefully.

General

Our authorized capital stock consists of 1,010,000,000 shares of capital stock, of which: (i) 1,000,000,000 shares are designated as common stock, par value $0.01 per share; and (ii) 10,000,000 shares are designated as preferred stock, par value $0.01 per share. As of February 8, 2021, we had 670,035,399 shares of common stock outstanding and no shares of preferred stock issued and outstanding.

Voting Rights

The holders of shares of the common stock are entitled to one vote per share in connection with the election of directors and all other matters submitted to a vote of stockholders. The holders of shares of the common stock do not have cumulative voting rights.

Dividend Rights

Subject to any preferential dividend rights of holders of any then outstanding shares of the our preferred stock and the Amended and Restated Certificate of Incorporation, the holders of shares of the common stock shall be entitled to receive, on a pro rata basis, such dividends and other distributions in cash, stock or property when, as and if declared thereon by our board of directors from time to time out of our assets or funds legally available therefor. No dividends have been paid to holders of shares of the common stock since our incorporation, and no dividends are anticipated to be declared or paid in the reasonably foreseeable future.

Liquidation Rights

After payments to creditors and subject to any preferential liquidation, dissolution or winding up rights of holders of any then outstanding shares of our preferred stock, the holders of shares of the common stock are entitled to share ratably in all of our remaining assets and funds available for distribution to holders of shares of the common stock upon the liquidation, dissolution or winding-up of our affairs.

Other Matters

Holders of shares of the common stock do not have any preemptive, subscription, redemption or conversion rights. All of the shares of the common stock currently issued and outstanding are fully-paid and nonassessable.

Special Meetings

The Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws provide that, except as otherwise required by law, special meetings of the stockholders may only be called by the chairman of the board of directors, the Chief Executive Officer, or by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the whole board. Only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders.

Requirements for Notice of Stockholder Director Nominations and Stockholder Business

If a stockholder wishes to bring any business before an annual or special meeting or nominate a person for election to our Board of Directors, our Amended and Restated Bylaws contain certain procedures that must be followed for the advance timing required for delivery of stockholder notice of such nomination or other business and the information that such notice must contain.

No Cumulative Voting

Section 214 of the DGCL provides that the certificate of incorporation of any corporation may provide stockholders with the right to cumulate votes in the election of directors. The Amended and Restated Certificate of Incorporation does not provide for cumulative voting of shares of the common stock.

Delaware Anti-Takeover Law

We are a Delaware corporation subject to Section 203 of the DGCL. Under Section 203, certain "business combinations" between a Delaware corporation whose stock is listed on a national securities exchange or held of record by more than 2,000 stockholders and an "interested stockholder" are prohibited for a three-year period following the date that such stockholder became an interested stockholder, unless:

- the corporation has elected in its certificate of incorporation not to be governed by Section 203;
- the business combination or the transaction which resulted in the stockholder becoming an interested stockholder was approved by the board of directors of the corporation before the date of the business combination or the date such stockholder became an interested stockholder, as applicable;
- upon consummation of the transaction that made such stockholder an interested stockholder, the interested stockholder owned at least 85% of the "voting stock" (as defined in Section 203) of the corporation outstanding at the commencement of the transaction excluding voting stock owned by directors who are also officers or held in employee benefit plans in which the employees do not have a confidential right to tender stock held by the plan in a tender or exchange offer; or
- the business combination is approved by the board of directors and by the stockholders (acting at a meeting and not by written consent) by the affirmative vote of at least 66-2/3% of the outstanding voting stock which is not "owned" (as defined in Section 203) by the interested stockholder.

The three-year prohibition also does not apply to some business combinations proposed by an interested stockholder following the announcement or notification of an extraordinary transaction involving the corporation and a person who had not been an interested stockholder during the previous three years or who became an interested stockholder with the approval of a majority of the corporation's directors. The term "business combination" is defined generally to include mergers or consolidations between a Delaware corporation and an interested stockholder, transactions

with an interested stockholder involving the assets or stock of the corporation or its majority-owned subsidiaries and transactions which increase an interested stockholder's percentage ownership of stock, or other transaction resulting in a financial benefit to the interested stockholder. The term "interested stockholder" is defined generally as those stockholders who become beneficial owners of 15% or more of a Delaware corporation's voting stock, together with the affiliates or associates of that stockholder.

Listing

The common stock is listed on the NASDAQ Global Select Market under the trading symbol "OPK."

Transfer Agent and Registrar

The Transfer Agent and Registrar for the common stock is American Stock Transfer & Trust Company.

Exhibit 21

SUBSIDIARIES OF OPKO HEALTH, INC.

NAME	JURISDICTION OF INCORPORATION
OPKO Instrumentation, LLC	Delaware
OPKO Pharmaceuticals, LLC	Delaware
OPKO Diagnostics, LLC	Delaware
OPKO Chile, S.A.	Chile
Arama Natural Products Distribuidora, Ltda	Chile
Pharmacos Exakta S.A. de C.V.	Mexico
FineTech Pharmaceutical Ltd	Israel
OPKO Health Europe, S.L.	Spain
OPKO Biologics, Ltd	Israel
OPKO Ireland Global Holdings, Ltd	Ireland
OPKO Ireland, Ltd	Ireland
OPKO Canada Corp, ULC	Canada
OPKO Renal, LLC	Canada
Curna, Inc.	Delaware
BioReference Laboratories, Inc.	New Jersey
GeneDX, Inc.	New Jersey
Genome Diagnostics, Ltd	Canada
EirGen Pharma Limited	Ireland
Transition Therapeutics, Inc.	Canada

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-3 No. 333-229400) of OPKO Health, Inc.,
2. Registration Statement (Form S-8 No. 333-211209) pertaining to the 2016 Equity Incentive Plan of OPKO Health, Inc.,
3. Registration Statement (Form S-8 No. 333-144040) pertaining to the 2007 Equity Incentive Plan of OPKO Health, Inc.,
4. Registration Statement (Form S-8 No. 333-190899) pertaining to the 2005 Stock Incentive Plan and 2007 Equity Incentive Plan of PROLOR Biotech, Inc. (formerly Modigene Inc.),
5. Registration Statement (Form S-8 No. 333-190900) pertaining to the Amended and Restated 2007 Equity Incentive Plan of OPKO Health, Inc., and
6. Registration Statement (Form S-8 No. 333-206489) pertaining to the 2003 Employee Incentive Stock Option Plan of BioReference Laboratories, Inc.

of our reports dated February 18, 2021, with respect to the consolidated financial statements and schedule of OPKO Health, Inc. and subsidiaries and the effectiveness of internal control over financial reporting of OPKO Health, Inc. and subsidiaries included in this Annual Report (Form 10-K) of OPKO Health, Inc. and subsidiaries for the year ended December 31, 2020.

/s/ Ernst & Young LLP

Miami, Florida
February 18, 2021

Exhibit 31.1

CERTIFICATIONS

I, Phillip Frost, certify that:

(1) I have reviewed this Annual Report on Form 10-K of OPKO Health, Inc.;

(2) Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

(3) Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

(4) The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

(5) The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/Phillip Frost, M.D.
Phillip Frost, M.D.
Chief Executive Officer

Date: February 18, 2021

Exhibit 31.2

CERTIFICATIONS

I, Adam Logal, certify that:

(1) I have reviewed this Annual Report on Form 10-K of OPKO Health, Inc.;

(2) Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

(3) Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

(4) The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

(5) The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 18, 2021

/s/ Adam Logal

Adam Logal

Senior Vice President, Chief Financial Officer, Chief Accounting Officer and Treasurer

Exhibit 32.1

Certification Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

(Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code)

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant section 906 of the Sarbanes-Oxley Act of 2002, I, Phillip Frost, Chief Executive Officer of OPKO Health, Inc. (the "Company"), hereby certify that:

The Annual Report on Form 10-K for the year ended December 31, 2020 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 18, 2021

/s/ Phillip Frost, M.D.
Phillip Frost, M.D.
Chief Executive Officer

Exhibit 32.2

Certification Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

(Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code)

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant section 906 of the Sarbanes-Oxley Act of 2002, I, Adam Logal, Chief Financial Officer of OPKO Health, Inc. (the "Company"), hereby certify that:

The Annual Report on Form 10-K for the year ended December 31, 2020 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 18, 2021

/s/ Adam Logal

Adam Logal

Senior Vice President, Chief Financial Officer
Chief Accounting Officer and Treasurer