

Opko Health, Inc.  
Form 424B2  
February 06, 2019  
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Filed Pursuant to Rule 424(b)(2)

Registration No. 333-229400

# CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount of Securities to be Registered <sup>(1)</sup>	Proposed Maximum Offering Price	Proposed Maximum Aggregate Offering Price <sup>(1)</sup>	Amount of Registration Fee <sup>(2)</sup>
4.50% Convertible Senior Notes due 2025	\$230,000,000	100% of principal amount	\$230,000,000	\$27,876
Common Stock, par value \$0.01 per share	(3)	(3)	(3)	(3)

(1) Includes principal amount of notes which may be purchased by the underwriter to cover over-allotments, if any.

(2) Calculated pursuant to Rule 457(r) of the Securities Act of 1933, as amended (the Securities Act ).

(3) Includes an indeterminate number of shares of common stock, par value \$0.01 per share, issuable upon conversion of the 4.50% Senior Convertible Notes due 2025 for which the registrant will receive no additional consideration and for which no registration fee is payable pursuant to Rule 457(i) under the Securities Act. Pursuant to Rule 416 under the Securities Act, such number of shares of common stock registered hereby shall include an indeterminable number of shares of common stock that may be issued in connection with stock splits, stock dividends, recapitalization and similar events.

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**PROSPECTUS SUPPLEMENT**

**(TO PROSPECTUS DATED JANUARY 28, 2019)**

**OPKO Health, Inc.**

**\$200,000,000**

**4.50% Convertible Senior Notes due 2025**

Interest payable on February 15 and August 15

We are offering \$200,000,000 principal amount of our 4.50% Convertible Senior Notes due 2025 (the "notes"). The notes will bear interest at a rate of 4.50% per year, payable semiannually in arrears on February 15 and August 15 of each year, beginning on August 15, 2019. The notes will mature on February 15, 2025, unless earlier repurchased, redeemed or converted.

Holders may convert their notes 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 (as defined below) per \$1,000 principal amount of 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 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. On or after November 15, 2024, until the close of business on the business day immediately preceding the maturity date, holders of the 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, as described in this prospectus supplement.

The conversion rate for the notes will initially be 236.7424 shares of common stock per \$1,000 principal amount of notes (equivalent to an initial conversion price of approximately \$4.22 per share of common stock). The conversion rate for the notes will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events described in this prospectus supplement that occur prior to the maturity date of the notes or if we deliver a notice of redemption, in certain circumstances we will increase the conversion rate of the 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 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 conversion price for the notes then in effect 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 notes.

If we undergo a fundamental change prior to the maturity date of the 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 notes will be our senior unsecured obligations and will rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the 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.

Concurrently with this offering and by means of a separate prospectus supplement and accompanying prospectus, up to 30,000,000 of shares of our common stock will be offered by selling stockholders, who will borrow such shares through lending arrangements from an affiliate of the underwriter, which, as Share Borrower, is borrowing the shares from us. The borrowed shares are newly-issued shares issued in connection with this transaction and will be cancelled or held as treasury shares by us upon the expiration or the early termination of the share lending arrangements described herein. We expect that the selling stockholders will sell the borrowed shares and use the resulting short position to establish their initial hedge with respect to their investments in the notes. The selling stockholders may effect such transactions by selling the borrowed shares at various prices from time to time through the Share Borrower or its affiliates. The selling stockholders will receive all of the net proceeds from the sale of the borrowed shares, and we will not receive any of those proceeds, but we will receive from the Share Borrower a one-time nominal fee of \$0.01 per share for each newly issued share. The concurrent offering of the borrowed shares is conditioned upon the closing of this offering.

**Investing in the notes and our common stock involves risks. See Risk Factors beginning on page S-18 of this prospectus supplement, as well as the documents we file with the Securities and Exchange Commission that are incorporated by reference herein for more information.**

PRICE: 100%, PLUS ACCRUED INTEREST, IF ANY

The notes are a new issue of securities with no established trading market. We do not currently intend to apply to list the notes on any securities exchange or any automated dealer quotation system. Our common stock is listed on the Nasdaq Global Select Market under the symbol OPK. The last reported sale price of our common stock on the Nasdaq Global Select Market on February 4, 2019 was \$3.52 per share.

	<b>Per Note</b>	<b>Total</b>
Public Offering Price(1)	\$ 1,000.00	\$ 200,000,000.00
Underwriting Discounts	\$ 35.00	\$ 7,000,000.00
Proceeds to Us (before expenses)	\$ 965.00	\$ 193,000,000.00

(1) Plus accrued interest, if any, from February 7, 2019

If the underwriter sells more than the total principal amount of notes set forth above, the underwriter has an option, exercisable within a 30-day period, to purchase up to an additional \$30,000,000 principal amount of notes from us solely to cover overallocments, if any.

**Neither the U.S. Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

We expect that delivery of the notes will be made to investors in book-entry form through The Depository Trust Company on or about February 7, 2019. The issue price will include accrued interest, if any, from February 7, 2019 if settlement occurs after that date.

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**Jefferies**

February 4, 2019

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

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**ABOUT THIS PROSPECTUS SUPPLEMENT**

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

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

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

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

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

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**PROSPECTUS SUPPLEMENT SUMMARY**

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

**Our Company**

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

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

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

**Current Products and Services and Related Markets**

**Diagnostics**

*BioReference Laboratories*

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



diseases, including esoteric testing, molecular diagnostics, anatomical pathology, genetics, women's

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health and correctional healthcare. We market and sell these services to physician offices, clinics, hospitals, employers and governmental units nationally, with the largest concentration of business in the larger metropolitan areas across New York, New Jersey, Florida, Texas, Maryland, California, Pennsylvania, Delaware, Washington DC, Illinois and Massachusetts.

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

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

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

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

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

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

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

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

*Laboratorio Bueno Salud.* National testing laboratory dedicated to serving the Spanish-speaking population in the U.S., where all business is conducted in Spanish including patient and physician interaction. We have one of the largest marketing staffs of any laboratory in the country with sales and marketing groups dedicated to urology, oncology, women's health, genetic testing and correctional health, as well as cross-over groups selling to large institutions. All of our sales and marketing personnel operate in a dual capacity, as both marketing and client support representatives, which we believe provides better customer service and a strong connection with our customers.

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

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

#### *4Kscore Test*

We offer the *4Kscore* test through our BioReference laboratory located in Elmwood Park, New Jersey. We began selling the *4Kscore* test in the U.S. in March 2014 and in Europe and Mexico in September 2014 and January 2015, respectively. The *4Kscore* test is a laboratory developed test that measures the blood plasma levels of four different prostate-derived kallikrein proteins: Total PSA, Free PSA, Intact PSA and Human Kallikrein-2 ( hK2 ). These biomarkers are then combined with a patient's age, Digital Rectal Exam ( DRE ) status (nodule / no nodule), and prior negative biopsy status (yes / no) using a proprietary algorithm to calculate the risk (probability) of finding a Gleason Score 7 or higher prostate cancer. The four kallikrein panel of biomarkers utilized in the *4Kscore* test is based on decades of research conducted by scientists at Memorial Sloan-Kettering Cancer Center and leading European institutions. Investigators at the Lund University, Sweden, University of Turku, Finland and Memorial Sloan Kettering Cancer Center, New York, have also demonstrated that the *4Kscore* test can risk stratify the 20-year risk for development of prostate metastases and mortality in men who present at age 50 or 60 years old with an elevated PSA.

The *4Kscore* test was developed by OPKO and validated in two prospective, blinded studies of 1,012 and 366 men, respectively. The first study was done in collaboration with 26 urology centers across the U.S. and the second study was conducted at eight VA centers in the U.S. with a predominantly African American cohort. African Americans are 1.7 times more likely to be diagnosed with prostate cancer than Caucasian men and 2.2 times more likely to die from the disease. Results showed that the *4Kscore* test was highly accurate for predicting the presence of high-grade cancer (Gleason score 7 or higher) prior to prostate biopsy, regardless of race. The full data from the blinded, prospective U.S. clinical validation studies have been published in peer reviewed medical journals.

The clinical data from both studies demonstrated the ability of the *4Kscore* test to discriminate between men with high-grade, aggressive prostate cancer and those men who had no findings of cancer or had low-grade or indolent form of the disease. The discrimination, measured by Area Under the Curve ( AUC ) analysis, was greater than 0.80 and is significantly higher than previously developed tests. Furthermore, the *4Kscore* test demonstrated excellent risk calibration, indicating the accuracy of the result for an individual patient, both Caucasian and African American. The high value of AUC and the excellent risk calibration make the *4Kscore* test result valuable information for the shared decision-making between the urologist and patient on whether or not to perform a prostate biopsy.

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

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intermediate-risk and high-risk categories, respectively. Notably, the *4Kscore* test results influenced biopsy decisions in 88.7% of the men. In the three risk groups, a biopsy was avoided in 94.0%, 52.9% and 19.0% of men in the low, intermediate and high-risk categories, respectively.

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

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

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

### *Point-of-Care Diagnostics*

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

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

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

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### **Pharmaceutical Business**

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

#### *Renal Products*

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

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

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

In May 2016, we entered into a collaboration with Vifor Fresenius Medical Care Renal Pharma ( VFMC RP ) for the development and commercialization of *Royaldee* 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 *Royaldee* in Canada and will receive up to \$230 million in additional regulatory and sales-based milestones. In addition, VFMC RP will pay OPKO tiered, double digit royalties on sales of the product at percentage rates that range from the mid-teens to the mid-twenties or a minimum royalty, whichever is greater, upon commencement of sales of the product. OPKO and VFMC RP are also collaborating to develop and commercialize a new dosage form of *Royaldee* for the treatment of SHPT in hemodialysis patients. OPKO granted VFMC RP an option to acquire rights to this dosage form for the U.S. market; if exercised, OPKO will receive up to \$555 million in additional milestones and double digit royalties.

On October 12, 2017, we entered into a Development and License Agreement (the JT Agreement ) with Japan Tobacco Inc. ( JT ) granting JT the exclusive rights for the development and commercialization of *Royaldee* in Japan (the JT Territory ). The license grant to JT covers the therapeutic and preventative use of the product for (i) SHPT in non-dialysis and dialysis patients with CKD, (ii) rickets, and (iii) osteomalacia, as well as such additional indications as may be added to the scope of the license subject to the terms of the JT Agreement. Under the terms of the JT Agreement, OPKO received an initial upfront payment of \$6 million and we received another \$6 million milestone payment triggered by the initiation of OPKO's U.S. phase 2 study with *Royaldee* 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 *Royaldee* 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

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

The FDA approval of *Royaldee* 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 *Royaldee* as a new treatment for SHPT in adults with stage 3 or 4 CKD and vitamin D insufficiency.

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

Studies in CKD patients have demonstrated that currently available over-the-counter and prescription vitamin D supplements cannot reliably raise blood vitamin D prohormone levels and effectively treat SHPT, a condition commonly associated with CKD in which the parathyroid glands secrete excessive amounts of PTH. Prolonged elevation of blood PTH causes excessive calcium and phosphorus to be released from bone, leading to elevated serum calcium and phosphorus levels, softening of the bones (osteomalacia) and calcification of vascular and renal tissues. SHPT affects 40-82% of patients with stage 3 or 4 CKD and approximately 95% of patients with stage 5 CKD.

The completed phase 3 trials for *Royaldee* successfully met all primary efficacy and safety endpoints. The primary efficacy endpoint was a responder analysis in which responder was defined as any treated subject who demonstrated an average decrease in PTH of at least 30% from pre-treatment baseline during the last six weeks of the 26-week treatment period. A significantly higher response rate was observed with *Royaldee* compared to placebo treatment in both trials and safety and tolerability data were comparable in both treatment groups. The PTH-lowering response rates with *Royaldee* were similar in both stage 3 and 4 CKD. Patients completing the two pivotal trials were treated, at their election, for an additional six months with *Royaldee* during an open-label extension study. Data from the extension study indicated that the PTH lowering response rate steadily increased with duration of *Royaldee* treatment without deterioration in safety profile.

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

In August 2014, we also announced the submission of an Investigational New Drug Application ( IND ) to the FDA to evaluate *Royaldee* as an adjunctive therapy for the prevention of skeletal-related events in patients with bone metastases undergoing anti-resorptive therapy. We commenced a phase 1 dose escalation study in the fourth quarter of 2014 in breast and prostate cancer patients with bone metastases who were receiving anti-resorptive therapy. The study, which has been completed, was designed to evaluate safety, markers of vitamin D and mineral metabolism and tumor progression. We are currently collecting the final data and will shortly complete a final analysis of the study.

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

Our second most advanced renal product, Alpharen (Fermagate Tablets), is a new and potent non-absorbed phosphate binder to treat hyperphosphatemia in stage 5 CKD patients requiring regular hemodialysis. Alpharen (Fermagate Tablets) has been shown to be safe and effective in treating hyperphosphatemia in phase 2 and 3 trials in stage 5 CKD patients undergoing chronic hemodialysis. Hyperphosphatemia, or elevated serum phosphorus, is common in dialysis patients and tightly linked to the progression of SHPT and vascular

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calcification, both of which drive morbidity and mortality. The kidneys provide the primary route of excretion for excess phosphorus absorbed from ingested food. As kidney function worsens, serum phosphorus levels increase and directly stimulate PTH secretion. Stage 5 CKD patients requiring dialysis must reduce their dietary phosphate intake and usually require regular treatment with orally administered phosphate binding agents to lower serum phosphorus to meet the recommendations of the Kidney Disease Improving Global Outcomes ( KDIGO ) Clinical Practice Guidelines that elevated serum phosphorus levels should be lowered. Hyperphosphatemia contributes to soft tissue mineralization and affects approximately 90% of dialysis patients. Dialysis patients require ongoing phosphate binder treatment to maintain controlled serum phosphorus levels. A single additional phase 3 clinical trial is required to support marketing approvals for Alpharen in North America and in Europe.

We believe the CKD patient population is large and growing as a result of obesity, hypertension and diabetes; therefore this patient population represents a significant global market opportunity. According to the National Kidney Foundation, CKD afflicts over 40 million people in the U.S., including more than 21 million patients with stage 3 or 4 CKD. In stage 5 CKD, kidney function is minimal to absent and most patients require regular dialysis or a kidney transplant for survival. An estimated 71-97% of CKD patients have vitamin D insufficiency which can lead to SHPT and its debilitating consequences. CKD continues to be associated with poor outcomes, reflecting the inadequacies of the current standard of care.

Vitamin D insufficiency, hyperphosphatemia and SHPT, when inadequately treated, are major contributors to poor CKD outcomes. We intend to develop and commercialize *Rayaldee* and Alpharen to constitute part of the foundation for a new and markedly improved standard of care for CKD patients having SHPT and/or hyperphosphatemia.

## ***SARM***

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

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

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*Oxyntomodulin*

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

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

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

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

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

*Biologics*

Our biologics business focuses on developing and commercializing longer-acting proprietary versions of already approved therapeutic proteins. One of our innovative platform technologies uses a short, naturally-occurring amino acid sequence, carboxyl terminal peptide ( CTP ), which has the effect of slowing the removal from the body of the therapeutic protein to which it is attached. This CTP can be readily attached to a wide array of existing therapeutic proteins, stabilizing the therapeutic protein in the bloodstream and extending its life span without additional toxicity or loss of desired biological activity. We are using the CTP technology to develop new, proprietary versions of certain existing therapeutic proteins that have longer life spans than therapeutic proteins without CTP. We believe that our products will have greatly improved therapeutic profiles and distinct market advantages.

*hGH-CTP*

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

In December 2014, we entered into an exclusive worldwide agreement with Pfizer for the development and commercialization of hGH-CTP for the treatment of GHD in adults ( Adult GHD ) and in children ( Pediatric

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GHD), as well as for the treatment of growth failure in children born small for gestational age (SGA). In connection with the transaction, we granted Pfizer an exclusive license to commercialize hGH-CTP worldwide, and we received non-refundable and non-creditable upfront payments of \$295 million and are eligible to receive up to an additional \$275 million upon the achievement of certain regulatory milestones. In addition, we are eligible to receive initial tiered royalty payments associated with the commercialization of hGH-CTP for Adult GHD with percentage rates ranging from the high teens to mid-twenties. Upon the launch of hGH-CTP for Pediatric GHD in certain major markets, the royalties will transition to regional, tiered gross profit sharing for both hGH-CTP and Pfizer's Genotropin®.

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

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

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

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

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

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



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

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

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

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

### *Factor VII*

In addition to hGH-CTP, we are developing a product to extend the life span of Factor VIIa (hemophilia) using the CTP technology. In February 2013, the FDA granted orphan drug designation to our longer-acting version of clotting Factor VIIa, Factor VIIa-CTP, for the treatment of bleeding episodes in patients with hemophilia A or B with inhibitors to Factor VIII or Factor IX. Currently, Factor VIIa therapy is available only as an intravenous (IV) formulation which, due to Factor VIIa's short half-life, requires multiple infusions to treat a bleeding episode. In addition, frequent infusions are onerous when used as preventative prophylactic therapy, especially for children.

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

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

### *APIs*

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

### *Oligonucleotide Therapeutics*

OPKO CURNA, LLC ( CURNA ), previously CURNA Inc., is engaged in the discovery of new drugs for the treatment of a wide variety of illnesses, including cancer, heart disease, metabolic disorders and a range of genetic anomalies. CURNA's platform technology utilizes a short, single strand oligonucleotide and is based on the up-regulation of protein production through interference with non-coding RNA's or natural antisense. This strategy contrasts with established approaches which down-regulate protein production. CURNA has designed a novel type of therapeutic modality, termed AntagoNAT, and has initially demonstrated this approach for up-regulation of several therapeutically relevant proteins in *in vitro* and animal models.

CURNA has identified and developed potential active compounds which increase the production of over 80 key proteins involved in a large number of individual diseases. We have ongoing pre-clinical studies for several of these compounds. A lead compound has been identified for the treatment of Dravet Syndrome. Orphan disease designations are granted by FDA and EMA.

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### *NK-1 Program*

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

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

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

### *Commercial Operations*

We also intend to continue to leverage our global commercialization expertise to pursue acquisitions of commercial businesses that will both drive our growth and provide geographically diverse sales and distribution opportunities. During 2015, we acquired EirGen Pharma Ltd. ( EirGen ), a specialty pharmaceutical company based in Ireland. EirGen is focused on the development and commercial supply of high potency, high barrier to entry, pharmaceutical products. Through its facility in Waterford, Ireland, EirGen currently manufactures high potency pharmaceutical products and exports to over 50 countries. High potency drugs such as those used for cancer chemotherapy are typically unsuitable for manufacture in normal multi-product facilities due to cross contamination risks.

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

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

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

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

OPKO Chile (previously Pharma Genexx, S.A.) markets, sells and distributes pharmaceutical products to the private, hospital, pharmacy and public institutional markets in Chile for a wide range of indications, including, cardiovascular products, vaccines, antibiotics, gastro- intestinal products and hormones, among others. ALS Distribuidora Limitada ( ALS ) is engaged in the business of importation, commercialization and distribution of pharmaceutical products for private markets in Chile. ALS started operations in 2009 as the exclusive product distributor of Arama Laboratorios y Compañía Limitada ( Arama ), a company with more than 20 years of experience in the pharmaceutical products market. In connection with the acquisition of ALS, OPKO acquired all of the product registrations and trademarks previously owned by Arama, as well as the Arama name. We distribute food supplements and over the counter products through Arama.

### *Strategic Investments*

We have and may continue to make investments in other early stage companies that we perceive to have valuable proprietary technology and significant potential to create value for OPKO as a shareholder.

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**The Offering**

The summary below describes the principal terms of the notes. Certain of the terms and conditions described below are subject to important limitations and exceptions. A more detailed description of the terms and conditions of the notes is contained under the heading "Description of Notes" in this prospectus supplement. As used in this section, "we," "our" and "us" refer to OPKO Health, Inc. and not to its consolidated subsidiaries.

<b>Issuer</b>	OPKO Health, Inc., a Delaware corporation.
<b>Securities</b>	\$200,000,000 principal amount of 4.50% Convertible Senior Notes due 2025 (the "notes") (or \$230,000,000 if the underwriter exercises its overallotment option to purchase additional notes in full).
<b>Maturity</b>	February 15, 2025, unless earlier repurchased, redeemed or converted.
<b>Interest</b>	4.50% per year. Interest will accrue from February 7, 2019 and will be payable semiannually in arrears on February 15 and August 15 of each year, beginning on August 15, 2019.
<b>Conversion Rights</b>	<p>Holders may convert their notes at their option prior to the close of business on the business day immediately preceding November 15, 2024, in multiples of \$1,000 principal amount, only under the following circumstances:</p> <p>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, and including, 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;</p> <p>during the five business day period after any five consecutive trading day period (the "measurement period") in which the trading price (as defined under "Description of Notes—Conversion Rights—Conversion upon Satisfaction of Trading Price Condition") per \$1,000 principal amount of 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</p>

each such trading day;

if we call the notes for redemption, at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date; or

upon the occurrence of specified corporate events described under  
Description of Notes Conversion Rights Conversion upon Specified  
Corporate Events.

On or after November 15, 2024 until the close of business on the business day immediately preceding February 15, 2025, holders may

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convert all or any portion of their notes, in multiples of \$1,000 principal amount, at the option of the holder regardless of the foregoing circumstances.

The conversion rate for the notes is initially 236.7424 shares of common stock per \$1,000 principal amount of notes (equivalent to an initial conversion price of approximately \$4.22 per share of common stock), subject to adjustment as described in this prospectus supplement.

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. If we satisfy our conversion obligation solely in cash or through payment and delivery, as the case may be, of a combination of cash and shares of our common stock, the amount of cash and shares of common stock, if any, due upon conversion will be based on a daily conversion value (as described herein) calculated on a proportionate basis for each trading day in a 25 trading-day observation period (as described herein). See Description of Notes Conversion Rights Settlement upon Conversion.

In addition, following certain corporate events that occur prior to the maturity date or if we deliver a notice of redemption, we will, in certain circumstances, increase the conversion rate 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, as described under Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption.

You will not receive any additional cash payment or additional shares representing accrued and unpaid interest, if any, upon conversion of a note, except in limited circumstances. Instead, interest will be deemed to be paid by the cash, shares of our common stock, or a combination of cash and shares of our common stock paid or delivered, as the case may be, to you upon conversion of a note.

**Redemption at our Option**

We may not redeem the 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 conversion price for the notes then in effect 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.

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No sinking fund is provided for the notes, which means that we are not required to redeem or retire the notes periodically.

We will give notice of any optional redemption not less than 30 scheduled trading days nor more than 60 calendar days before the redemption date by mail or electronic delivery to the trustee, the paying agent and each holder of notes. See Description of Notes Optional Redemption.

**Fundamental Change**

If we undergo a fundamental change (as defined under the heading Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes in this prospectus supplement) prior to the maturity date of the notes, subject to certain conditions, holders may require us to repurchase for cash all or part of their notes in principal amounts of \$1,000 or a multiple thereof. The fundamental change repurchase price will be 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. See Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes.

**Ranking**

The notes will be our senior unsecured obligations and will rank:

senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the notes;

equal in right of payment to any of our unsecured indebtedness that is 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 existing and future indebtedness and other liabilities of our current or future subsidiaries (including trade payables).

As of September 30, 2018, we had \$205.6 million of outstanding indebtedness for borrowed money (excluding intercompany debt). Our subsidiaries had \$486.8 million of other liabilities including trade

payables but excluding intercompany obligations and liabilities of a type not required to be reflected on a balance sheet of such subsidiaries in accordance with U.S. generally accepted accounting principles ( U.S. GAAP ). After giving effect to the issuance of the notes (assuming no exercise of the underwriter's overallotment option to purchase additional notes, our and our subsidiaries' indebtedness for borrowed money (excluding intercompany debt) would have been \$405.6 million.

The indenture governing the notes does not limit the amount of debt that we or our current or future subsidiaries may incur.

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### **Certain Covenants**

The indenture contains limitations on, among other things, our ability to consolidate, merge or dispose of all or substantially all of our assets. Although these types of transactions are permitted under the indenture, certain of the foregoing transactions could constitute a fundamental change permitting each holder to require us to repurchase the notes of such holder as described herein.

### **Use of Proceeds**

We estimate that the net proceeds from this offering will be approximately \$192.3 million (or approximately \$221.3 million if the underwriter exercises its overallotment option to purchase additional notes in full), after deducting the underwriter's discount and estimated offering expenses payable by us.

We intend to use the net proceeds we receive from sales of securities offered hereby to fund research and development to further develop and commercialize our portfolio of proprietary pharmaceutical and diagnostic products and for working capital, capital expenditures, acquisitions and other general corporate purposes, which will include the repayment or repurchase of indebtedness or debt securities outstanding from time to time including \$28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit with an affiliate of our Chairman and Chief Executive Officer, Phillip Frost, M.D. See Use of Proceeds.

### **Book-Entry Form**

The notes will be issued in book-entry form and will be represented by permanent global certificates deposited with, or on behalf of, The Depository Trust Company ( DTC ) and registered in the name of a nominee of DTC. Beneficial interests in any of the notes will be shown on, and transfers will be effected only through, records maintained by DTC or its nominee and any such interest may not be exchanged for certificated securities, except in limited circumstances.

### **Absence of a Public Market for the Notes**

The notes are new securities and there is currently no established market for the notes. Accordingly, we cannot assure you as to the development or liquidity of any market for the notes. The underwriter has advised us that it currently intends to make a market in the notes. However, it is not obligated to do so, and it may discontinue any market making with respect to the notes without notice. We do not intend to apply for a listing of the notes on any securities exchange or any automated dealer quotation system.

### **U.S. Federal Income Tax Considerations**

For certain U.S. federal income tax considerations applicable to the holding, disposition and conversion of the notes, and the holding and

disposition of shares of our common stock, see U.S. Federal Income Tax Considerations.

**Nasdaq Global Select Market Symbol for Our Common Stock** Our common stock is listed on the Nasdaq Global Select Market under the symbol OPK.

**Trustee, Paying Agent and Conversion Agent** U.S. Bank National Association

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**Governing Law**

The notes and the indenture governing the notes will be governed by the laws of the State of New York.

**Concurrent Offering of Borrowed Shares** Concurrently with this offering and by means of a separate prospectus supplement and accompanying prospectus, up to 30,000,000 of shares of our common stock will be offered by selling stockholders, who will borrow such shares through lending arrangements from an affiliate of the underwriter, which, as Share Borrower, is borrowing the shares from us. The borrowed shares are newly-issued shares issued in connection with this transaction and will be cancelled or held as treasury shares by us upon the expiration or the early termination of the share lending arrangements described herein. We expect that the selling stockholders will sell the borrowed shares and use the resulting short position to establish their initial hedge with respect to their investments in the notes. The selling stockholders may effect such transactions by selling the borrowed shares at various prices from time to time through the Share Borrower or its affiliates. The selling stockholders will receive all of the net proceeds from the sale of the borrowed shares, and we will not receive any of those proceeds, but we will receive from the Share Borrower a one-time nominal fee of \$0.01 per share for each newly issued share. The concurrent offering of the borrowed shares is conditioned upon the closing of this offering. See Description of Share Lending Agreement and Underwriting.

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**RISK FACTORS**

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

***Risks Related to Our Business***

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

We are not profitable and have incurred losses since our inception. We may not generate substantial revenue from the sale of proprietary pharmaceutical products or certain of our diagnostic products for some time and we have generated only limited revenue from our pharmaceutical operations in the U.S., Chile, Mexico, Israel, Spain and Ireland, and from sale of the *4Kscore* test. We may not successfully leverage the national marketing, sales and distribution resources of BioReference to enhance sales of, and reimbursement for, our *4Kscore* test and our other diagnostic products under development, which would adversely impact our ability to generate substantial revenue from the sale of these products for some time. *Royaldee* is our only pharmaceutical product that has been approved for marketing, other than those products sold by our Chilean, Mexican, Israeli, Spanish and Irish subsidiaries. We continue to incur substantial research and development and general and administrative expenses related to our operations and, to date, we have devoted most of our financial resources to research and development, including our pre-clinical development activities and clinical trials. We may incur losses from our operations for the foreseeable future and these losses could increase as we continue our research activities and conduct development of, and seek regulatory approvals and clearances for, our product candidates, and prepare for and begin to commercialize any approved or cleared products, particularly if we are unable to generate profits and cash flow from BioReference and our other commercial businesses. If we are unable to generate profits and cash flow from BioReference and our other commercial businesses, our product candidates fail in clinical trials or do not gain regulatory approval or clearance, or if our approved products and product candidates do not achieve market acceptance, we may never become profitable. In particular, if we are unable to successfully commercialize *Royaldee*, we may never generate substantial revenues from *Royaldee* or achieve profitability. In addition, if we are required by the FDA to perform studies in addition to those we currently anticipate, our expenses will increase beyond current expectations and the timing of any potential product approval may be delayed. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

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

As of September 30, 2018, we had cash and cash equivalents of approximately \$43.7 million. We have not generated sustained positive cash flows sufficient to offset our operating and research and development expenses and our primary source of cash has been from the public and private placement of stock, the issuance of the 2033 Senior Notes and 2023 Convertible Notes (each as defined below) and credit facilities available to us.

On November 8, 2018, we entered into stock purchase agreements with certain investors pursuant to which we agreed to sell to such investors in private placements (the "Private Placements") an aggregate of approximately 26.5 million shares of our common stock (the "Shares") at a purchase price of \$3.49 per share, which was the closing bid price of our common stock on the Nasdaq Global Select Market on such date, for an aggregate purchase price of \$92.5 million. In addition, 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 the line of credit will bear interest at a rate of 10% per annum and may be repaid and reborrowed at any time. The line of credit matures on November 8, 2023. On February 1, 2019, we borrowed \$28.8 million under the line of credit; no amounts were previously outstanding under the line of credit. We intend

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to use the proceeds of the \$28.8 million borrowing to repurchase the 2033 Senior Notes (as defined below) tendered by holders thereof pursuant to such holders' option to require us to repurchase such 2033 Senior Notes pursuant to the terms of the indenture governing the 2033 Senior Notes. We intend to use a portion of the proceeds of this offering to repay the \$28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit and to terminate the line of credit thereafter.

We believe that the cash and cash equivalents on hand or available to us from operations or through our lines of credit, together with the proceeds of this offering, are sufficient to meet our anticipated cash requirements for operations and debt service beyond the next 12 months. We have based this estimate on assumptions that may prove to be wrong or subject to change, and we may be required to use our available capital resources sooner than we currently expect or curtail aspects of our operations in order to preserve our capital.

Because of the numerous risks and uncertainties associated with the development and commercialization of our products and product candidates, the success of our relationships with Pfizer, VFMCRP and JT and the success of our integration of BioReference and other acquisitions, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials and our expanded commercial operations. Our future capital requirements will depend on a number of factors, including the successful commercialization of *Royaldee*, our relationships with Pfizer, VFMCRP and JT, cash flow generated by BioReference and costs associated with the integration of the BioReference and other acquisitions, the continued progress of our research and development of product candidates, the timing and outcome of clinical trials and regulatory approvals, the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights, the status of competitive products, the availability of financing and our success in developing markets for our products and product candidates. Until we can generate a sufficient amount of product and service revenue to finance our cash requirements for research, 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. Disruptions in the U.S. and global financial markets may adversely impact the availability and cost of credit, as well as our ability to raise money in the capital markets. Economic conditions have been, and continue to be, volatile. Continued instability in these market conditions may limit our ability to replace, in a timely manner, maturing liabilities and access the capital necessary to fund and grow our business. Additionally, our continuing operating losses and the recent lawsuits involving us and our Chief Executive Officer ( CEO ) and Chairman of our Board of Directors ( Chairman ) by the SEC and other parties increase the difficulty in obtaining additional capital.

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;

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be difficult or impossible to manufacture on a commercial scale;

be uneconomical to market or otherwise not be effectively marketed;

fail to be successfully commercialized if adequate reimbursement from government health administration authorities, private health insurers and other organizations for the costs of these products is unavailable;

be impossible to commercialize because they infringe on the proprietary rights of others or compete with products marketed by others that are superior; or

fail to be commercialized prior to the successful marketing of similar products by competitors.

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

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

Further, our drug candidates may not be approved or cleared even if they achieve their primary endpoints in phase 3 clinical trials or registration trials. In addition, our diagnostic test candidates may not be approved or cleared, as the case may be, even though clinical or other data are, in our view, adequate to support an approval or clearance. The FDA or other non-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.

Safety concerns with drug products over the years have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products, and establishment of risk management programs that may, for

instance, restrict distribution of drug products. Attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

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***The failure to successfully commercialize Rayaldee would have a material adverse effect on our business.***

In June 2016, the FDA approved our NDA for *Rayaldee* (calcifediol) extended release capsules for the treatment of SHPT in adults with stage 3 or 4 CKD and serum total 25-hydroxyvitamin D levels less than 30 ng/mL. The commercial launch for *Rayaldee* began in November 2016. *Rayaldee* is our only pharmaceutical product approved for marketing in the U.S. and our ability to generate revenue from product sales and achieve profitability is substantially dependent on our ability to effectively commercialize *Rayaldee*. Our failure to successfully commercialize *Rayaldee* would have a material adverse effect on our business, financial condition, cash flows and results of operations.

Additionally, the market perception and reputation of *Rayaldee* and its safety and efficacy are important to our business and the continued acceptance of our product candidates and products. Any negative publicity about *Rayaldee*, such as the discovery of safety issues, adverse events or even public rumors about such events, could have a material adverse effect on our business. Levels of market acceptance for *Rayaldee* could be impacted by several factors, some of which are not within our control, including but not limited to the:

safety, efficacy, convenience and cost-effectiveness of our products compared to products of our competitors;

scope of approved uses and marketing approval;

availability of patent or regulatory exclusivity;

timing of market approvals and market entry;

ongoing regulatory obligations following approval;

any restrictions or "black box" warnings required on the labeling of such products;

availability of alternative products from our competitors;

acceptance of the price of our products;

effectiveness of our sales forces and promotional efforts;

the level of reimbursement of our products;

acceptance of our products on government and private formularies;

ability to market our products effectively at the retail level or in the appropriate setting of care; and

the reputation of our products.

If *Royaldee* fails to gain, or loses, market acceptance, our revenues would be adversely impacted and we may be required to take material impairment charges, all of which could have a material adverse effect on our business, financial condition, cash flows and results of operations.

***We rely on licensing agreements with VFMCRP and JT for the international development and marketing of Royaldee. Failure to maintain these license agreements could prevent us from successfully developing and commercializing Royaldee worldwide.***

In May 2016, EirGen, our wholly-owned subsidiary, partnered with VFMCRP through a Development and License Agreement (the "VFMCRP Agreement") for the development and marketing of *Royaldee* 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. We received a non-refundable and non-creditable upfront payment of \$50 million and a \$2.0 million payment triggered by the approval of *Royaldee* in Canada for the treatment of SHPT in adults with stage 3 or 4 CKD and vitamin D

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insufficiency. EirGen is also eligible to receive up to an additional \$35 million in regulatory milestones and \$195 million in launch and sales-based milestones. In addition, we are eligible to receive tiered, double digit royalty payments or a minimum royalty, whichever is greater, upon commencement of sales of the product. The success of the VFMCRRP Agreement is dependent in part on, among other things, the skills, experience and efforts of VFMCRRP's employees responsible for the project, VFMCRRP's commitment to the arrangement and the financial condition of VFMCRRP, all of which are beyond our control. In the event that VFMCRRP, for any reason, including but not limited to early termination of the agreement, fails to devote sufficient resources to successfully develop and market *Royaldee* 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 the JT Agreement under which JT was granted the exclusive rights for the development and commercialization of *Royaldee* 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 received an initial upfront payment of \$6 million and received another \$6 million upon the initiation of our phase 2 study for *Royaldee* in dialysis patients in the U.S. We are 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 *Royaldee* 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 *Royaldee* in Japan and for all commercial activities pertaining to *Royaldee* in Japan, except for certain preclinical expenses for 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 *Royaldee* 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 is important to our business. If we do not successfully develop hGH-CTP and/or Pfizer does not successfully commercialize hGH-CTP, our business could be adversely affected.***

In December 2014, we entered into a development and commercialization agreement with Pfizer relating to our long-acting hGH-CTP for the treatment of Adult GHD and Pediatric GHD (the Pfizer Agreement). Under the terms of the Pfizer Agreement, we received non-refundable and non-creditable upfront payments of \$295 million and are eligible to receive up to an additional \$275 million upon the achievement of certain regulatory milestones. In addition, we are eligible to receive initial royalty payments associated with the commercialization of hGH-CTP for Adult GHD. Upon the launch of hGH-CTP for Pediatric GHD, the royalties will transition to a regional, tiered gross profit sharing for both hGH-CTP and Pfizer's Genotropin®. We are responsible for the development program and are obligated to pay for the development up to an agreed cap, which may be exceeded under certain circumstances. We will exceed the development cap and if we are unable to reach an agreement with Pfizer regarding cost sharing for the overruns as well as other obligations, including development obligations, it could have a material adverse impact on the expected benefits to us from the Pfizer transaction and our overall financial condition. 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, Pfizer's commitment to the arrangement, and the financial condition of Pfizer, all of which are beyond our control. In the event that Pfizer, for any reason, including but not limited to early termination of the Pfizer Agreement, fails to devote sufficient resources to successfully develop and commercialize any product resulting from the collaboration arrangement, our ability to earn milestone payments or receive royalty or profit



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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 the success of clinical trials for hGH-CTP and our ability to achieve regulatory approval for the marketing of this product.***

There is no assurance that clinical trials for hGH-CTP will be successful or support marketing approval, or that we will be able to obtain marketing approval for the product, or any other product candidate we are developing. Before they can be marketed, our products in development must be approved by the FDA or similar foreign governmental agencies. The process for obtaining FDA approval is both time-consuming and costly, with no certainty of a successful outcome. Before obtaining regulatory approval for the sale of any drug candidate, we must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Although the safety profile for hGH-CTP has been consistent with that observed with those treated with daily growth hormone, further testing or patient use may undermine those determinations or unexpected side effects may arise. A failure of any preclinical study or clinical trial can occur at any stage of testing. The results of preclinical and initial clinical testing of these products may not necessarily indicate the results that will be obtained from later or more extensive testing. It also is possible to suffer significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials. In December 2016, we announced preliminary topline data from our 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 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 a BLA will be submitted or that the FDA will consider the sensitivity analysis or consider the product for approval for adults with GHD. If phase 3 clinical trials for hGH-CTP are not successful or we are unable to achieve regulatory approval for this product, our business will be significantly adversely impacted, which could have a materially adverse effect on our business, financial condition and results of operations.

***Our business is substantially 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, including the *Claros I*. 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 diagnostic tests. If we fail to leverage the national marketing, sales and distribution resources of BioReference to enhance sale of, and reimbursement for, the *4Kscore* test and other diagnostic products including the *Claros I*, our ability to generate substantial revenue from the sale of these products will be adversely impacted. 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, obtain reimbursement for, or successfully integrate BioReference, we will not generate any meaningful revenue from the sale of such tests. Even if we are able to develop effective diagnostic tests for sale in the marketplace, a number of factors could impact our ability to sell such tests or generate any significant revenue from the sale of such tests, including without limitation:

our ability to establish and maintain adequate infrastructure to support the commercial launch and sale of our diagnostic tests, including establishing adequate laboratory space, information technology infrastructure, sample collection and tracking systems, electronic ordering and reporting systems and other infrastructure and hiring adequate laboratory and other personnel;

the success of the validation studies for our diagnostic tests under development and our ability to publish study results in peer-reviewed journals;

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the availability of alternative and competing tests or products and technological innovations or other advances in medicine that cause our technologies to be less competitive;

the accuracy rates of such tests, including rates of false-negatives and/or false-positives;

concerns regarding the safety or effectiveness or clinical utility of our diagnostic tests;

changes in the regulatory environment affecting health care and health care providers, including changes in laws regulating laboratory testing and/or device manufacturers;

the extent and success of our sales and marketing efforts and ability to drive adoption of our diagnostic tests;

coverage and reimbursement levels by government payors and private insurers;

pricing pressures and changes in third-party payor reimbursement policies; and

intellectual property rights held by others or others infringing our intellectual property rights.

***Our 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. A reduction in tests ordered, specimens submitted by existing clients or payment rates, without offsetting growth in our client base, could impact our ability to successfully grow our business and could have a material adverse impact on our ability to generate profits and cash flow from the laboratory operations.

***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 Clinical Laboratory Improvement Amendments ( 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

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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.***

The pharmaceutical, diagnostic and laboratory 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 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. 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.

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. We are much smaller than these national laboratories.

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

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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;

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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.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including in December 2018 and January 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

***We currently have a seventy-nine person specialized sales and marketing team for Rayaldee in the U.S. If we are unable to develop or maintain a strong sales, marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing Rayaldee or our other pharmaceutical products or product candidates in the U.S.***

Other than our 79-person specialized sales and marketing team dedicated to *Rayaldee*, we currently have no pharmaceutical marketing, sales or distribution capabilities in the U.S. Any failure or inability to maintain adequate sales, marketing and distribution capabilities would adversely impact the commercialization of *Rayaldee* or our other pharmaceutical products or candidates. If we are not successful in commercializing our existing and future pharmaceutical products and product candidates, either on our own or through collaborations with one or more third parties, our product revenue will suffer and we may incur significant additional losses.

***Our approved products or product candidates may have undesirable side effects and cause our products to be taken off the market.***

If we or others identify undesirable side effects caused by our products:

regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;

regulatory authorities may withdraw their approval of the product and require us to take our approved product off the market;

we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product;

we may have limitations on how we promote our products;

sales of products may decrease significantly;

we may be subject to litigation or product liability claims; and

our reputation may suffer.

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

***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.



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***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

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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 coverage and adequate 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, use other techniques that may restrict access to our products or set a lower reimbursement rate than anticipated.

On May 18, 2018, Novitas, the MAC for a jurisdiction that includes the State of New Jersey, where our 4KScore test samples are processed, issued a draft non-coverage determination ( LCD ) that proposed no coverage for our 4KScore test. We submitted comments to the draft LCD during the public comment period, which ended on July 5, 2018. In January 2019, Novitas issued a notice of future non-coverage determination for the 4KScore test to be effective March 20, 2019. We are currently evaluating options to appeal the decision and undertake other steps with CMS in an effort to have this determination rescinded or reversed, however, there can be no assurance that we will be successful in doing so. If we are not able to successfully appeal Novitas' decision, we may not be able to obtain Medicare reimbursement for the 4KScore test, which could result in a loss of revenues and could have a material adverse effect on our cash flows, results of operations, net income, financial conditions and the trading prices of our securities.

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 a governmental payor program, a substantial portion of our 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

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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.

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

***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 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, particularly Dr. Phillip Frost, our Chairman and CEO, 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 ( 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

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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.

In 2017, Congress reauthorized the Generic Drug User Fee Act (the "GDUFA"). The generic drug user fee program, established in 2012, is designed to speed the approval of new generic drugs. In addition, over the past few months, the FDA has used its regulatory authority to enact other programs to streamline the path to market for generic drugs. In addition, a regulatory pathway for biosimilars was established in 2012 including a new user fee program to promote the development of these products that show no clinically meaningful differences from innovator biologics. Though they have their own statutory market pathway, like generic drugs, biosimilars can receive FDA approval by providing less clinical data than the innovator product. Biosimilars are expected to be less expensive competitors to innovator biologics reducing prices overall. We anticipate several new biosimilars reaching the market over the next year.

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

We intend to continue to rely on acquisitions and in-licensing as a source of our products and product candidates for development and commercialization. The success of this strategy depends upon our ability to identify, select and acquire pharmaceutical and diagnostic products, drug delivery technologies and medical device product candidates. Proposing, negotiating and implementing an economically viable product acquisition or license is a lengthy and complex process. We compete for partnering arrangements and license agreements with pharmaceutical, biotechnology and medical device companies and academic research institutions. Our competitors may have stronger relationships with third parties with whom we are interested in collaborating and/or may have more established histories of developing and commercializing products.

Most of our competitors also have substantially greater financial and other resources than us. As a result, our competitors may have a competitive advantage in entering into partnering arrangements with such third parties, as such partnering arrangements are often decided in an auction process in which the highest bidder wins. In addition, even if we find promising products and product candidates, and generate interest in a partnering or strategic arrangement to acquire such products or product candidates, we may not be able to acquire rights to additional product candidates or approved products on terms that we find acceptable, or at all.

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

***We 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.

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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 current Good Manufacturing Practices ( 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 will not be our employees, and we will not be able to control, other than by contract, the amount of resources, including time, that they devote to products that we develop. If independent investigators fail to devote sufficient resources to the development of product candidates or clinical trials, or if their performance is substandard, it will delay the marketing approval or clearance and commercialization of any products that we develop. Further, the FDA requires that we comply with standards, commonly referred to as good clinical practice, for conducting, recording and reporting clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial subjects are protected. If our independent clinical investigators and contract research organizations fail to comply with good clinical practice, the results of our clinical trials could be called into question and the clinical development of our product candidates could be delayed.

Failure of clinical investigators or contract research organizations to meet their obligations to us or comply with federal regulations and good clinical practice procedures could adversely affect the clinical development of our product candidates and harm our business, results of operations and financial condition.

***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

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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 ( CPT ) codes and the World Health Organization establishes diagnostic codes using a data set called International Statistical Classification of Diseases ( 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 implemented a new billing system for our laboratory business in the third quarter of 2016. The adoption of the new billing system, which replaced the old billing system, poses several challenges relating to, among other things, training of personnel, communication of new rules and procedures, changes in corporate culture, migration of data and the potential instability of the new system. As an integral part of our billing compliance program, we assess our billing and coding practices in the ordinary course of business, 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 us. 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.

***Failure in our information technology systems, including by cybersecurity attacks or other data security incidents, could significantly increase testing turn-around time or billing processes and otherwise disrupt our operations.***



Our operations depend, in part, on the continued performance of our information technology systems. Our information technology systems are potentially vulnerable to physical or electronic break-ins, computer viruses

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and similar disruptions. In addition, we are in the process of integrating the information technology systems of our subsidiaries, and we may experience system failures or interruptions as a result of this process. Sustained system failures or interruption of our systems in one or more of our laboratory operations could disrupt our ability to process laboratory requisitions, perform testing, provide test results in a timely manner and/or bill the appropriate party. Failure of our information technology systems could adversely affect our business, profitability and financial condition.

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. It is possible that a cybersecurity attack might not be noticed for some period of time. The occurrence of a cybersecurity attack or incident could result in business interruptions from the disruption of our information technology systems, or negative publicity resulting in reputational damage with our customers, shareholders and other stakeholders and/or increased costs to prevent, respond to or mitigate cybersecurity events. In addition, the unauthorized dissemination of sensitive personal information or proprietary or confidential information could expose us or other third parties to regulatory fines or penalties, litigation and potential liability, or otherwise harm our business.

***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, impose more stringent cost controls and 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.

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

We have entered into and expect in the future to enter into collaborative arrangements with established multi-national pharmaceutical, diagnostic and medical device companies, which will finance or otherwise assist in the development, manufacture and marketing of products incorporating our technology. We anticipate deriving some revenues from research and development fees, license fees, milestone payments and royalties from collaborative partners. Our prospects, therefore, may depend to some extent upon our ability to attract and retain collaborative partners and to develop technologies and products that meet the requirements of prospective collaborative partners. In addition, our

collaborative partners may have the right to abandon research projects, guide strategy regarding prosecution of relevant patent applications and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed-upon research terms. There can be no

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assurance that we will be successful in establishing collaborative arrangements on acceptable terms or at all, that collaborative partners will not terminate funding before completion of projects, that our collaborative arrangements will result in successful product commercialization or that we will derive any revenues from such arrangements. To the extent that we are unable to develop and maintain collaborative arrangements, we would need substantial additional capital to undertake research, development and commercialization activities on our own.

***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. Moreover, the U.S. Patent and Trademark Office (the USPTO) may commence interference proceedings involving our patents or patent applications. In addition, court decisions may introduce uncertainty in the enforceability or scope of patents owned by biotechnology, pharmaceutical and medical device companies. Any challenge to, finding of unenforceability or invalidation or circumvention of, our patents or patent applications would be costly, would require significant time and attention of our management, and could have a material adverse effect on our business, results of operations and financial condition.

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

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,

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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.

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

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

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

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

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

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

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

We have obtained licenses from, among others, INEOS Healthcare, the President and Fellows of Harvard College, The Scripps Research Institute, Arctic Partners, TESARO and Academia Sinica, that are necessary or useful for our business. In addition, we intend to enter into additional licenses of third-party intellectual property in the future. 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

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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 generally have agreed to indemnify the licensor for costs incurred in connection with litigation relating to intellectual property rights. The cost to us of any litigation or other proceeding relating to intellectual property rights, even if resolved in our favor, could be substantial, and the litigation would divert our management's efforts. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of any litigation could limit our ability to continue our operations. Our involvement in patent litigation and other proceedings could have a material adverse effect on our business, results of operations and financial condition.

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



products, which could limit our ability to generate revenues or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations.

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***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 a third party or patent office might take the position that one or more patents or patent applications constitute prior art in the field of genomic-based diagnostics. 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 a future product candidate harms people, or is alleged to be harmful, we may be subject to costly and damaging product liability claims brought against us by clinical trial participants, consumers, health care providers, corporate partners or others. We have product liability insurance covering commercial sales of current products and our ongoing clinical trials. Any defects or errors could lead to the filing of product liability claims, which could be costly and time-consuming to defend and result in substantial damages. If we experience a sustained material defect or error, this could result in loss or delay of revenues, delayed market acceptance, damaged reputation, diversion of development resources, legal claims, increased insurance costs or increased service and warranty costs, any of which could 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.

***We are the subject of pending civil litigation which could require us to pay substantial damages or could otherwise have a material adverse effect on us.***

On September 7, 2018, the SEC filed a lawsuit in the Southern District of New York (the "Complaint"), against a number of individuals and entities (each a "Defendant" and, collectively, the "Defendants") including us and our CEO and

Chairman, Dr. Phillip Frost. The SEC alleged that we (i) aided and abetted a purported pump and dump scheme in connection with one company perpetrated by a number of the Defendants, and (ii) failed to file required Schedules 13D or 13G with the SEC. The Complaint also alleged that Dr. Frost

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(i) participated in the alleged market manipulation in connection with two companies, (ii) failed to file required Schedule 13Ds with the SEC, and (iii) sold unregistered securities without an applicable exemption. Following the SEC's announcement of the Complaint, a number of class action and derivative suits were filed against us and our directors and officers concerning the allegations in the Complaint and related matters.

In December 2018, we and Dr. Frost entered into settlements with the SEC, which, upon approval by the court in January 2019, resolved the claims against us and Dr. Frost raised in the Complaint. Pursuant to the settlement between us and the SEC, and without admitting or denying any of the allegations of the Complaint, we agreed to an injunction from violations of Section 13(d) of the Securities Exchange Act of 1934 (the "Exchange Act"), a strict liability claim, and to pay a \$100,000 penalty, which has been paid. We also agreed to, within certain stipulated time periods:

(i) establish a Management Investment Committee ( "MIC" ) that will make recommendations to an Independent Investment Committee ( "IIC" ) of our Board of Directors in connection with existing and future strategic minority investments; and (ii) retain an Independent Compliance Consultant ( "ICC" ) to (a) advise us on whether filings pursuant to Section 13(d) of the Exchange Act for previous strategic investments made at the suggestion of or in tandem with Dr. Frost should be amended or made to reflect group membership with Dr. Frost and his related entities; (b) review our existing policies and procedures relating to compliance with Section 13(d) of the Exchange Act; and (c) review the independence of the MIC and IIC of our Board of Directors solely for purposes of the handling of strategic minority investments. The ICC is required to report its findings (including recommendations as to filings, amendments, improvements to policies and procedures, and improvement to the composition of the MIC and the IIC to our Board of Directors) to the SEC within 15 days of completion of its work, and we are required to implement the ICC's recommendations, and to certify our compliance with these undertakings in writing.

Under the terms of the settlement between the SEC and Dr. Frost, and without admitting or denying any of the allegations in the Complaint, Dr. Frost agreed to injunctions from violations of Sections 5(a) and (c) and 17(a)(2) of the Securities Act of 1933, as amended, (the "Securities Act"), claims which may be satisfied by strict liability and negligence, respectively, and Section 13(d) of the Exchange Act, also a strict liability claim; to pay approximately \$5.5 million in penalty, disgorgement and pre-judgment interest, which has been paid; and to be prohibited, with certain exceptions, from trading in penny stocks.

The settlements include no restriction on Dr. Frost's ability to continue to serve as our CEO and Chairman.

We are separately evaluating our strategic minority investments and reporting under Section 13(d) of the Exchange Act. In connection with this evaluation, we may make additional or amended filings pursuant to Section 13(d) of the Exchange Act reflecting group membership.

Although the SEC matter against us and Dr. Frost is resolved, there can be no assurance that additional charges from other governmental authorities will not be brought against one or more parties named in the Complaint.

We also continue to face a number of class actions and derivative suits concerning the allegations in the SEC Complaint. We cannot predict with certainty the outcome or effect of the class actions or derivative suits, which could require us to pay substantial damages or could otherwise have a material adverse effect on us.

Our primary and side A directors and officers liability insurance carrier has denied coverage for the class action and derivative suits filed against us and our directors and officers concerning the allegations in the Complaint. We believe that this denial is in error and are in the process of appealing this coverage determination. If we are unsuccessful in this appeal, or if other third-party insurers deny, cancel, or refuse coverage, which we are not able to successfully appeal, or are otherwise unable to provide us with adequate insurance coverage for all or any of the aforementioned lawsuits, then our overall risk exposure and operational expenses could increase and the management of our business

operations could be disrupted, which could cause a material adverse impact on our business, operations and financial condition. Further, an unusually large liability claim or a string of

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claims, like these lawsuits, could potentially exceed our available insurance coverage. In addition, the availability of, and our ability to collect on, insurance coverage can be subject to factors beyond our control.

As our current insurance policies expire, increased premiums for renewed or new coverage, if such coverage can be secured at all, may increase our insurance expense and/or require us to increase our self-insured retention or deductibles. If the number of claims or the dollar amounts of any such claims rise in any policy year, we could suffer additional costs associated with accessing excess coverage policies. Also, an increase in the loss amounts attributable to such claims could expose us to uninsured damages if we are unable or elect not to insure against certain claims because of increased premiums or other reasons. These lawsuits or the resolution of such lawsuits may affect the availability or cost of some of our insurance coverage, which could materially adversely impact our business, results of operations and cash flows and potentially expose us to increased risks that would be uninsured.

### ***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, we are subject to pending legal proceedings with respect to alleged violations of securities laws. See *Adverse results in material litigation matters or governmental inquiries could have a material adverse effect upon our business and financial condition* above.

Legal actions 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 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 laboratory developed tests ( 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

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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, the U.S. Department of Health and Human Services (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 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. We have received FDA approval of the PMA for our Sangia Total PSA Test using the Claros Analyzer and a CE Mark for our 4KScore test, 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;

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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.

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

responsible for the development, validation and commercialization of the assay.

Such LDT testing is currently under the purview of CMS and state agencies that provide oversight of the safe and effective use of LDTs. However, the FDA has consistently asserted that it has the regulatory authority to regulate LDTs despite historically exercising enforcement discretion. In furtherance of that position, the FDA issued two draft guidance documents in October 2014: (1) Framework for Regulatory Oversight of Laboratory Developed Tests (the Framework Guidance ); and (2) FDA Notification and Medical Device Reporting for Laboratory Developed Tests (the Notification Guidance ). The Framework Guidance outlines the FDA's plan to adopt over time a risk-based approach to regulating LDTs whereby different classifications of LDTs would be subject to different levels of FDA oversight and enforcement, including, for example, prohibitions on adulteration and misbranding, establishment registration and device listing, premarket notification, banned devices, records and reports, good manufacturing practices, adverse event reporting, premarket review of safety,

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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. 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. The outcome and ultimate impact of such proposals on the business is difficult to predict at this time. However, the FDA's authority to regulate LDTs continues to be challenged and the regulatory situation is fluid. The timeline and process for finalizing the draft guidance documents is unknown. We will continue to monitor changes to all domestic and international LDT regulatory policy so as to ensure compliance with the current regulatory scheme.

***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 cGMPs, 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.

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

We are subject to numerous federal and state regulations, including, but not limited to:

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 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 federal False Claims Act ( 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.

***Tax reform may significantly affect us and our stockholders.***

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act (the Tax Act ) that significantly reforms the Internal Revenue Code of 1986, as amended. The Tax Act, among other things, includes changes to U.S. federal tax rates, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitations of the tax deduction for interest expense to 30% of adjusted earnings (except for

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certain small businesses), limitations of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, modifying or repealing many business deductions and credits and putting into effect the migration from a worldwide system of taxation to a territorial system.

***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, 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, it could be subject to monetary fines, civil penalties or criminal sanctions. Under the HITECH amendments to HIPAA, HIPAA was expanded to require certain data breach notification, to extend certain HIPAA privacy and security standards directly to business associates, to heighten penalties for noncompliance and enhance enforcement efforts.

We may also be required to comply with the data privacy and security laws of other countries in which it operates or from which it receives data transfers. The European Union ( EU ) enacted the General Data Protection Regulation ( GDPR ) to replace the current data protection directive, Directive 95/46/EC, which took effect May 25, 2018, and which has a broader application and enhanced penalties for noncompliance. The GDPR, which is wide-ranging in scope, governs the collection and use of personal data in the EU and imposes operational requirements for companies that receive or process personal data of residents of the EU that are different than those currently in place in the EU. The GDPR will apply to our European operations and possibly to our laboratory and clinical development operations. We have implemented policies and procedures required to comply with the new EU regulations and will continue to evaluate compliance.

In March 2014, CareEvolve, BioReference's wholly-owned connectivity subsidiary, became aware that there had been a HIPAA breach with regard to one of its servers managed at an internet service provider site called XAND, where the server was inadvertently configured so that it was accessible to the Internet for a brief period. Upon becoming aware of the matter, CareEvolve immediately took the server offline and removed all indexed files that could be located on the internet. In the meantime, an Internet data collection robot operated by Google, Inc. had briefly acquired data from a server and made it available to Internet searches. To the best of our knowledge, there were no known disclosures of this Patient Health Information ( PHI ) to unauthorized parties. BioReference self-reported this incident to the appropriate government agency, the Office of Civil Rights ( OCR ). OCR notified BioReference that it has initiated an investigation of the breach report, and we are awaiting further discussion, investigation and action by OCR. Since March 2014, BioReference has taken meaningful steps to further improve its HIPAA and cybersecurity platform, including engaging independent and specialized IT consultants to conduct HIPAA and cybersecurity assessments, reviewing data security and internal safeguards and continuously implementing enhanced security measures to minimize the risk of similar occurrences in the future. We have had other 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 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

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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, among other things, require work practice controls, protective clothing and equipment, training, medical follow-up, vaccinations and other measures 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. Federal regulations require licensure of interstate transporters of medical waste. In New Jersey, we are subject to the Comprehensive Medical Waste Management Act 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. The hauler provides a manifest of the disposition of the waste products as well as a certificate of incineration, which is retained by us. These records are audited by the State of New Jersey on a yearly basis. We are also subject to the Federal Hazardous Materials Transportation Act, 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. These regulations preempt state regulation, which must be substantively the same, meaning that the non-federal requirement must conform in every significant respect to the federal requirement. Editorial and other similar de minimis changes are permitted, 49 CFR 107.202(d).

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 on 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.***

Compliance with the ICD-10-CM Code Set was required to be in place by October 1, 2015. We will continue our assessment of information systems, applications and processes for compliance with these 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, days sales and cash collections.

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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 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

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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. In April 2015, changes to the physician fee schedule were enacted under the Medicare Access and CHIP Reauthorization Act of 2015 ( MACRA ).

Our reimbursement for our pathology services is paid primarily under the physician fee schedule of Medicare and Medicaid. Historically, the physician fee schedule was governed by a complex formula, referred to as the Sustainable Growth Rate ( SGR ). However, in April 2015, MACRA was passed, which permanently replaces the SGR formula with a value-based payment system. The passage of MACRA also repealed the 21.1% reduction of the physician fee schedule that was scheduled for April 1, 2015. Under MACRA, the physician fee schedule conversion factor increases of 0.5% from July 1, 2015 to December 31, 2015, and 0.5% in each of years 2016-2019, followed by 0.0% updates for 2020-2025. Subsequent years will vary based on participation in alternative payment models. Beginning in 2019, rates were adjusted under the new Merit-based Incentive Payment System.

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. Recently, 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.

CMS has changed or discussed making changes to certain types of reimbursement which could affect our rate of reimbursement. Certain cases are comprised of both a technical component and a professional component. In certain specified areas of testing, primarily in the area of anatomic pathology, CMS has determined that some providers have over-utilized these testing procedures and CMS has introduced changes in reimbursement policies to discourage over-utilization. We are always subject to review by CMS and cannot be certain that CMS won't interpret our practices differently than we do.

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 will be 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.

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

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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 (the ACA) and the reconciliation law known as Health Care and Education Affordability Reconciliation Act (the Reconciliation Act and, collectively with the ACA, the 2010 Health Care Reform Legislation). The constitutionality of the 2010 Health Care Reform Legislation was confirmed on June 28, 2012 by the Supreme Court of the United States. However, as discussed in further detail below, the current Presidential administration has attempted to repeal and replace the 2010 Health Care Reform Legislation.

Beyond coverage and reimbursement changes, the 2010 Health Care Reform Legislation subjects manufacturers of medical devices to an excise tax of 2.3% on certain U.S. sales of medical devices beginning in January 2013. However, a two-year moratorium on the tax was issued on December 18, 2015. The moratorium was extended for an additional two-year period on January 22, 2018. As such, the excise tax does not apply to sales in 2016 through 2019. The return of the tax in January 2020 will likely increase our expense in the future.

Additionally, the 2010 Health Care Reform Legislation included significant fraud and abuse measures, including (i) required disclosures under the Open Payments Program (which implements the requirements of the Physician Payments Sunshine Act), which in conjunction with its implementing regulations, requires certain manufacturers of certain drugs, biologics and devices that are reimbursed by Medicare and Medicaid to report annually certain payments or transfers of value provided to physicians and teaching hospitals and to report annually ownership and investment interests held by physicians and their immediate family members during the preceding calendar year, (ii) lower thresholds for violations and (iii) increasing potential penalties for such violations. Federal funding available for combating health care fraud and abuse generally has increased. Many of the laws and regulations applicable to our business, particularly those relating to billing and reimbursement of tests and those relating to relationships with physicians, hospitals and patients, contain language that has not been interpreted by courts. We must rely on our interpretation of these laws and regulations based on the advice of our counsel and regulatory or law enforcement authorities may not agree with our interpretation of these laws and regulations and may seek to enforce legal remedies or penalties against us for violations. From time to time we may need to change our operations, particularly pricing or billing practices, in response to changing interpretations of these laws and regulations or regulatory or judicial determinations with respect to these laws and regulations. These occurrences, regardless of their outcome, could damage our reputation and harm important business relationships that we have with healthcare providers, payors and others. Furthermore, if a regulatory or judicial authority finds that we have not complied with applicable laws and regulations, we could be required to refund amounts that were billed and collected in violation of such laws and regulations. In addition, we may voluntarily refund amounts that were alleged to have been billed and collected in violation of applicable laws and regulations. In either case, we could suffer civil and criminal damages, fines and penalties, exclusion from participation in governmental healthcare programs and the loss of licenses, certificates and authorizations necessary to operate our business, as well as incur liabilities from third-party claims, all of which could harm our operating results and financial condition. Moreover, regardless of the outcome, if we or physicians or other third parties with whom we do business are investigated by a regulatory or law enforcement authority we could incur substantial costs, including legal fees, and our management may be required to divert a substantial amount of time to an investigation.

Prior to the 2016 U.S. elections (including the current Presidential administration), regulations under the 2010 Health Care Reform Legislation were expected to continue being drafted, released and finalized throughout the next several



years. In 2017, the President and members of Congress sought to repeal and replace the 2010 Health Care Reform Legislation. It is uncertain whether such repeal and replacement legislation will be enacted into law, and if enacted, what the impact might be on our business. It is also uncertain whether regulatory

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changes to the implementation of the 2010 Health Care Reform Legislation will restrict patient access to affordable insurance and impact their access to novel, biosimilar and complex generic products. The full effects of any repeal and replacement of the 2010 Health Care Reform Legislation, or regulatory changes to its implementation, cannot be known until a new law is enacted or existing law is implemented through regulations or guidance issued by the CMS and other federal and state health care agencies. Because of the continued uncertainty about the implementation of the 2010 Health Care Reform Legislation, including the potential for further legal challenges or repeal of that legislation, we cannot quantify or predict with any certainty the likely impact of the 2010 Health Care Reform Legislation or its repeal on our business model, prospects, financial condition or results of operations. We also anticipate that Congress, state legislatures and third-party payors may continue to review and assess alternative healthcare delivery and payment systems and may in the future propose and adopt legislation or policy changes or implementations effecting additional fundamental changes in the healthcare delivery system. 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 United States 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 described in Section 8B2.1 of the United States Sentencing Commission Guidelines Manual, and for many years the OIG has made available a model compliance program targeted to the clinical laboratory industry (the "Model Compliance Program"). In addition, certain states, such as New York, require that health care providers, such as clinical laboratories, that engage in substantial business under the state Medicaid program have a compliance program that generally adheres to the standards set forth in the Model Compliance Program. Also, under the 2010 Health Care Reform Legislation, 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 EU 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

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and regulations in those jurisdictions relating to our product. In some countries, particularly countries of the EU, 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 (the FCPA ), and any determination that we violated the FCPA could have a material adverse effect on our business.***

We are subject to the 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

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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 EU, 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.

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***Risks Related to Acquisitions and Investments***

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

difficulty integrating acquired technologies, products, services, operations and personnel with the existing businesses;

diversion of management's attention in connection with both negotiating the acquisitions and integrating the businesses;

strain on managerial and operational resources as management tries to oversee larger operations and investments;

difficulty implementing and maintaining effective internal control over financial reporting at businesses that we acquire or invest in, particularly if they are not located near our existing operations;

exposure to unforeseen liabilities of acquired companies or companies in which we invest;

potential costly and time-consuming litigation, including stockholder lawsuits;

potential issuance of securities to equity holders of the company being acquired with rights that are superior to the rights of holders of our common stock, or which may have a dilutive effect on our stockholders;

the need to incur additional debt or use cash; and

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

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



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

***We may fail to realize the anticipated benefits of the mergers with BioReference, Transition and other acquisitions.***

The success of the mergers will depend on, among other things, our ability to combine our business with that of BioReference and Transition in a manner that facilitates growth opportunities and realizes synergies and cost savings. We believe that the mergers will provide an opportunity for revenue growth. However, we must successfully combine our business with that of BioReference and Transition in a manner that permits these benefits to be realized. In addition, we must achieve the anticipated growth and cost savings without adversely affecting current revenues and investments in future growth. If we are not able to successfully achieve these objectives, the anticipated benefits of the mergers may not be realized fully, or at all, or may take longer to realize than expected.

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***The failure to integrate successfully the business and operations of BioReference in the expected time frame may adversely affect our future results.***

Historically, we and BioReference have operated as independent companies. There can be no assurances that our and BioReference's businesses can be integrated successfully. It is possible that the integration process could result in the loss of our or BioReference's key employees, the loss of customers, the disruption of either company's or both companies' ongoing businesses or in unexpected integration issues, higher than expected integration costs and an overall post-completion integration process that takes longer than originally anticipated. Specifically, the following issues, among others, must be addressed in integrating our operations with BioReference's operations in order to realize the anticipated benefits of the merger so we perform as expected:

combining the companies' operations and corporate functions, as well as obtaining anticipated synergies;

combining our business with BioReference's business and meeting the capital requirements of the combined company, in a manner that permits us to achieve the cost savings or revenue synergies anticipated to result from the merger, the failure of which would result in the anticipated benefits of the merger not being realized in the time frame currently anticipated or at all;

integrating the companies' technologies;

integrating and unifying the offerings and services available to customers;

identifying and eliminating redundant and underperforming functions and assets;

harmonizing and/or addressing differences in the companies' operating practices, employee development and compensation programs, internal controls and other policies, procedures and processes;

maintaining existing agreements with customers, distributors, providers and vendors and avoiding delays in entering into new agreements with prospective customers, distributors, providers and vendors;

addressing possible differences in business backgrounds, corporate cultures and management philosophies;

consolidating the companies' administrative and information technology infrastructure;

coordinating distribution and marketing efforts;

managing the movement of certain positions to different locations;

coordinating geographically dispersed organizations; and

effecting actions that may be required in connection with obtaining regulatory approvals.

In addition, at times the attention of our management and resources may be focused on the integration of the businesses of the two companies and diverted from day-to-day business operations, which may disrupt our ongoing business.

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

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

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***We have a large amount of goodwill and other intangible assets as a result of acquisitions and have not yet tested goodwill for impairment as of October 1, 2018 or December 31, 2018. A significant write-down of goodwill and/or other intangible assets could have a material adverse effect on our reported results of operations and net worth and the trading prices of our securities.***

We have a large amount of goodwill and other intangible assets. At September 30, 2018, we have goodwill and other intangible assets of \$2.0 billion, or approximately 80% of our total assets, which exceeded our market cap on such date. 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. The estimated fair value of a reporting unit is highly sensitive to changes in projections and assumptions; therefore, in some instances, changes in these assumptions could potentially lead to impairment. We perform sensitivity analyses around our assumptions in order to assess the reasonableness of the assumptions and the results of our testing. Ultimately, future potential changes in these assumptions may impact the estimated fair value of a reporting unit and cause the fair value of the reporting unit to be below its carrying value. We believe that our estimates are consistent with assumptions that marketplace participants would use in their estimates of fair value. However, if actual results are not consistent with our estimates and assumptions, we may be exposed to a non-cash impairment charge that could be material. We have not yet tested goodwill for impairment as of October 1, 2018 or December 31, 2018 and any goodwill impairment recorded as a result of such testing or any impairment charges in the future will adversely affect our results of operations. A significant write down of goodwill and/or other intangible assets could have a material adverse effect on our reported results of operations and net worth and the trading prices 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 securities 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.

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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 securities, 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 28, 2019, our directors, executive officers, principal stockholders and affiliated entities beneficially owned, in the aggregate, approximately 44.2% of our outstanding voting securities. Phillip Frost, M.D., our Chairman and CEO, is deemed to beneficially own, in the aggregate, approximately 36.9% of our common stock as of January 28, 2019. 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 December 31, 2018, investors held a short position of approximately 56,212,686 shares of our common stock which represented approximately 9.6% 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 holders of our securities could lose confidence in our financial reporting, which could have a material adverse effect on the trading prices of our securities.***

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

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a material adverse effect on our business and operating results. Our acquisition of BioReference and Transition and possible future acquisitions may increase this risk by expanding the scope and nature of operations over which we must develop and maintain internal control over financial reporting. 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 the trading prices of our securities 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 SEC 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, CEO, 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.

***Additional Risks Related to this Offering and the Notes***

***Although the notes are referred to as convertible senior notes, they will be effectively subordinated to any of our secured debt and any liabilities of our subsidiaries.***

The notes will rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the notes; equal in right of payment to any of our 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 subsidiaries. In the event of our bankruptcy, liquidation, reorganization or other winding up, our assets that secure debt ranking senior in right of payment to the notes will be available to pay obligations on the notes only after the secured debt has been repaid in full from these assets, and the assets of our subsidiaries will be available to pay obligations on the notes only after all claims senior to the notes have been repaid in full. There may not be sufficient assets remaining to pay amounts due on any or all of the notes then outstanding. The indenture governing the notes does not prohibit us from incurring additional senior debt or secured debt, nor does it prohibit any of our current or future subsidiaries from incurring additional liabilities.

As of September 30, 2018, we had \$205.6 million of outstanding indebtedness for borrowed money (excluding intercompany debt). Our subsidiaries had \$486.8 million of other liabilities (including trade payables but excluding intercompany obligations and liabilities of a type not required to be reflected on a balance sheet of such subsidiaries in accordance with U.S. GAAP). After giving effect to the issuance of the notes (assuming no exercise of the



underwriter's overallotment option to purchase additional notes), our and our subsidiaries' indebtedness for borrowed money (excluding intercompany debt) would have been \$405.6 million.

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***The notes are our obligations exclusively and a substantial portion of our operations are conducted through, and a substantial portion of our consolidated assets are held by, our subsidiaries.***

The notes are our obligations exclusively and are not guaranteed by any of our subsidiaries. A substantial portion of our consolidated assets are held by our subsidiaries. Accordingly, our ability to service our debt, including the notes, depends on the results of operations and cash flows of the consolidated company, including our subsidiaries and upon the ability of such subsidiaries to provide us with cash, whether in the form of dividends, loans or otherwise, to pay amounts due on our obligations, including the notes. Our subsidiaries are separate and distinct legal entities and have no obligation, contingent or otherwise, to make payments on the notes or to make any funds available for that purpose. In addition, dividends, loans or other distributions to us from such subsidiaries may be subject to contractual and other restrictions and are subject to other business considerations.

***Recent and future regulatory actions and other events may adversely affect the trading price and liquidity of the notes.***

We expect that many investors in, and potential purchasers of, the notes will employ, or seek to employ, a convertible arbitrage strategy with respect to the notes. Investors would typically implement such a strategy by selling short the common stock underlying the notes and dynamically adjusting their short position while continuing to hold the notes. Investors may also implement this type of strategy by entering into swaps on our common stock in lieu of or in addition to short selling the common stock.

The SEC and other regulatory and self-regulatory authorities have implemented various rules and taken certain actions, and may in the future adopt additional rules and take other actions, that may impact those engaging in short selling activity involving equity securities (including our common stock). Such rules and actions include Rule 201 of SEC Regulation SHO, the adoption by the Financial Industry Regulatory Authority, Inc. and the national securities exchanges of a Limit Up-Limit Down program, the imposition of market-wide circuit breakers that halt trading of securities for certain periods following specific market declines, and the implementation of certain regulatory reforms required by the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010. Any governmental or regulatory action that restricts the ability of investors in, or potential purchasers of, the notes to effect short sales of our common stock, borrow our common stock or enter into swaps on our common stock could adversely affect the trading price and the liquidity of the notes.

***Volatility in the market price and trading volume of our common stock could adversely impact the trading price of the notes.***

The stock market in recent years has experienced significant price and volume fluctuations that have often been unrelated to the operating performance of companies. The market price of our common stock could fluctuate significantly for many reasons, including in response to the risks described in this section, elsewhere in this prospectus supplement or the documents incorporated by reference in this prospectus supplement or for reasons unrelated to our operations, such as reports by industry analysts, investor perceptions or negative announcements by our customers, competitors or suppliers regarding their own performance, as well as industry conditions and general financial, economic and political instability. A decrease in the market price of our common stock would likely adversely impact the trading price of the notes. The price of our common stock could also be affected by possible sales of our common stock by investors who view the notes as a more attractive means of equity participation in us and by hedging or arbitrage trading activity that we expect to develop involving our common stock. This trading activity could, in turn, affect the trading prices of the notes.

***We may not have sufficient cash flow from our business to service our indebtedness or pay our indebtedness.***

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, depends on our future performance, which is subject to economic, financial, competitive and other

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factors beyond our control. Our business may not continue to generate cash flow from operations in the future sufficient to service our indebtedness and make necessary capital expenditures. If we are unable to generate adequate cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring indebtedness or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default under our debt obligations, which could, in turn, adversely affect our business, financial condition and operating results.

***We and our subsidiaries have a significant amount of debt and substantial debt service requirements, and we may still incur substantially more debt or take other actions, which would intensify the risks discussed above.***

We and our subsidiaries have a significant amount of debt and substantial debt service requirements. This level of debt could have significant consequences on our future operations, including:

making it more difficult for us and our subsidiaries to meet our payment and other obligations;

our and our subsidiaries' failure to comply with the financial and other restrictive covenants contained in our and their debt agreements, which could trigger events of default that could result in all of our or our subsidiaries' debt becoming immediately due and payable;

reducing the availability of our and our subsidiaries' cash flows to fund working capital, capital expenditures, acquisitions or strategic investments and other general corporate requirements, and limiting our and our subsidiaries' ability to obtain additional financing for these purposes;

subjecting us and our subsidiaries to increased interest expense related to our and their indebtedness with variable interest rates, including borrowings under our credit facility;

limiting our and our subsidiaries' flexibility in planning for, or reacting to, and increasing our vulnerability to changes in our business, the industry in which we operate and the general economy; and

placing us at a competitive disadvantage compared to our competitors that have less debt or are less leveraged.

In addition, we and our subsidiaries may incur substantial additional debt in the future, some of which may be secured debt. We will not be restricted under the terms of the indenture governing the notes from incurring additional debt, securing existing or future debt, recapitalizing our debt or taking a number of other actions that are not limited by the terms of the indenture governing the notes that could have the effect of diminishing our ability to make payments on the notes when due.

***We may not have the ability to raise the funds necessary to settle conversions of the notes or to repurchase the notes upon a fundamental change, and our future debt may contain limitations on our ability to repurchase the notes.***

Holders of the notes will have the right to require us to repurchase their notes upon the occurrence of a fundamental change at a repurchase price equal to 100% of their principal amount, plus accrued and unpaid interest, if any, as described under Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes. In addition, upon conversion of the notes, unless we elect to deliver solely shares of our common stock to settle such conversion (other than paying cash in lieu of delivering any fractional share), we will be required to make cash payments in respect of the notes being converted as described in under Description of Notes Conversion Rights Settlement upon Conversion. However, we may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of notes surrendered therefor or notes being converted.

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In addition, our ability to repurchase the notes or to pay cash upon conversion of the notes may be limited by law, by regulatory authority or by agreements governing our future indebtedness. Our failure to repurchase or pay cash amounts due upon conversion of the notes as required would constitute a default under the indenture. A default under the indenture or the fundamental change itself could also lead to a default under agreements governing our future indebtedness. Moreover, the occurrence of a fundamental change under the indenture may constitute an event of default under agreements governing our future indebtedness. If the payment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the notes or to pay cash upon conversion of the notes.

***Redemption may adversely affect your return on the notes.***

We may not redeem the 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 price of our common stock has been at least 130% of the conversion price for the notes then in effect 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. As a result, we may choose to redeem the notes at times when prevailing interest rates are relatively low. As a result, you may not be able to reinvest the proceeds you receive from the redemption in a comparable security at an effective interest rate as high as the interest rate on your notes being redeemed. See Description of Notes Optional Redemption.

***The conditional conversion feature of the notes, if triggered, may adversely affect our financial condition and operating results.***

In the event the conditional conversion feature of the notes is triggered, holders of notes will be entitled to convert the notes at any time during specified periods at their option. See Description of Notes Conversion Rights. If one or more holders elect to convert their notes, unless we elect to satisfy our conversion obligation by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our conversion obligation through the payment of cash, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

***The accounting method for convertible debt securities that may be settled in cash, such as the notes, could have a material effect on our reported financial results.***

Under Accounting Standards Codification 470-20, Debt with Conversion and Other Options, which we refer to as ASC 470-20, an entity must separately account for the liability and equity components of certain convertible debt instruments (such as the notes) that may be settled entirely or partially in cash upon conversion in a manner that reflects the issuer's economic interest cost. The effect of ASC 470-20 on the accounting for the notes is that the equity component is required to be included in the additional paid-in capital section of stockholders' equity on our consolidated balance sheet, and the value of the equity component is treated as original issue discount for purposes of accounting for the debt component of the notes. As a result, we expect that we will be required to record a greater amount of non-cash interest expense in current periods presented as a result of the amortization of the discounted carrying value of the notes to their respective face amounts over their respective terms. We expect that we will report lower net income in our financial results because ASC 470-20 will require interest to include both the current period's amortization of the debt discount and the instrument's coupon interest, which could adversely affect our financial

results, the trading price of our common stock and the trading price of the notes.

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In addition, under certain circumstances, convertible debt instruments (such as the notes) that may be settled entirely or partly in cash are currently accounted for utilizing the treasury stock method, the effect of which is that any shares issuable upon conversion of the notes are not included in the calculation of diluted earnings per share except to the extent that the conversion value of the notes exceeds their respective principal amounts. Under the treasury stock method, for diluted earnings per share purposes, the transaction is accounted for as if the number of shares of common stock that would be necessary to settle such excess, if we elected to settle such excess in shares, are issued. We cannot be sure that the accounting standards in the future will continue to permit the use of the treasury stock method. If we are unable to use the treasury stock method in accounting for the shares issuable upon conversion of the notes, then our diluted earnings per share would be adversely affected.

***Future sales of our common stock, as well as sales of the borrowed shares in the concurrent offering, or the issuance of other equity-related securities could lower the market price for our common stock and adversely impact the trading price of the notes.***

In the future, we may sell additional shares of our common stock or other equity-related securities. In addition, a substantial number of shares of our common stock are reserved for issuance upon the exercise of stock options pursuant to our equity benefit plans, warrants to purchase shares of our common stock, upon conversion of the 2033 Senior Notes, the 2023 Convertible Notes, in each case as defined below, and upon conversion of the notes offered hereby. We cannot predict the size of future issuances or the effect, if any, that they may have on the market price for our common stock. The issuance and sale of substantial amounts of common stock, or the perception that such issuances and sales may occur, could adversely affect the trading price of the notes and the market price of our common stock and impair our ability to raise capital through the sale of additional equity or equity-related securities.

Concurrently with this offering and by means of a separate prospectus supplement and accompanying prospectus, up to 30,000,000 of shares of our common stock will be offered by selling stockholders, who will borrow such shares through lending arrangements from an affiliate of the underwriter, which is borrowing the shares, as Share Borrower, from us. We expect that the selling stockholders will sell the borrowed shares and use the resulting short position to establish their initial hedge with respect to their investments in the notes. The selling stockholders may effect such transactions by selling the borrowed shares at various prices from time to time through the Share Borrower or its affiliates. The selling stockholders will receive all of the net proceeds from the sale of the borrowed shares, and we will not receive any of those proceeds, but we will receive from the Share Borrower a one-time nominal fee of \$0.01 per share for each newly issued share. Pursuant to a share lending agreement between us and the Share Borrower, the Share Borrower has agreed to pay us an amount of cash equal to the aggregate dividend paid for any cash dividend or distribution we make in respect of the borrowed shares.

All borrowed shares (or identical shares or, in certain circumstances, the cash value thereof) must be returned to us on or about the maturity date of the notes or, if earlier, on or about the date as of which all of the notes cease to be outstanding as a result of redemption, repurchase, conversion or other acquisition for value (or earlier in certain other circumstances). See Description of Share Lending Agreement. The existence of these arrangements, the short sales of shares of our common stock effected in connection with the sale of the notes or any unwind of such short sales could cause the market price of our common stock to be lower over the term of these arrangements than it otherwise would have been, due to the effect of the increase in the number of outstanding shares of our common stock being traded in the market or otherwise.

***The adjustments by holders of the notes of their hedging positions in shares of our common stock and the expectation thereof may have a negative effect on the market price of our common stock.***



The short positions in shares of our common stock resulting from the share lending arrangements and the sale of borrowed shares in the concurrent offering are expected to be used by the Share Borrower to facilitate hedging, including through short sales of shares of our common stock, by holders of the notes. The borrowed shares sold in the concurrent offering may be more or less than the number of shares that will be needed from

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time to time by the holders of the notes to hedge their exposure under the notes. Any buying or selling of shares of our common stock by the holders of the notes to adjust their hedging positions may affect the market price of our common stock.

***Changes in the accounting guidelines relating to the borrowed shares sold in the concurrent offering could decrease our reported net loss or earnings per share and potentially affect the price of our common stock.***

Because the amount of borrowed shares sold in the concurrent offering (or in certain circumstances, the cash value thereof) must be returned to us upon the expiration or early termination of the share lending arrangements pursuant to their terms, we believe that under U.S. GAAP, as presently in effect, the borrowed shares will not be considered outstanding for the purpose of computing and reporting our earnings or loss per share. If accounting guidelines were to change in the future, we may become required to treat the borrowed shares as outstanding for purposes of computing earnings or loss per share, and our reported earnings or net loss per share would be reduced, which could affect the market price of our common stock.

***Holders of notes will not be entitled to any rights with respect to our common stock, but they will be subject to all changes made with respect to them to the extent our conversion obligation includes shares of our common stock.***

Holders of notes will not be entitled to any rights with respect to our common stock (including, without limitation, voting rights and rights to receive any dividends or other distributions on our common stock) prior to the conversion date relating to such notes (if we have elected to settle the relevant conversion by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share)) or the last trading day of the relevant observation period (if we elect to pay and deliver, as the case may be, a combination of cash and shares of our common stock in respect of the relevant conversion), but holders of notes will be subject to all changes affecting our common stock. For example, if an amendment is proposed to our certificate of incorporation or bylaws requiring stockholder approval and the record date for determining the stockholders of record entitled to vote on the amendment occurs prior to the conversion date related to a holder's conversion of its notes (if we have elected to settle the relevant conversion by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share)) or the last trading day of the relevant observation period (if we elect to pay and deliver, as the case may be, a combination of cash and shares of our common stock in respect of the relevant conversion), such holder will not be entitled to vote on the amendment, although such holder will nevertheless be subject to any changes affecting our common stock.

***The conditional conversion feature of the notes could result in your receiving less than the value of our common stock into which the notes would otherwise be convertible.***

Prior to the close of business on the business day immediately preceding November 15, 2024, you may convert your notes only if specified conditions are met. If the specific conditions for conversion are not met, you will not be able to convert your notes, and you may not be able to receive the value of the cash, common stock or a combination of cash and common stock, as applicable, into which the notes would otherwise be convertible.

***Upon conversion of the notes, you may receive less valuable consideration than expected because the value of our common stock may decline after you exercise your conversion right but before we settle our conversion obligation.***

Under the notes, a converting holder will be exposed to fluctuations in the value of our common stock during the period from the date such holder surrenders notes for conversion until the date we settle our conversion obligation.

Upon conversion of the notes, we have the option to 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. If we elect to satisfy our conversion

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obligation in cash or a combination of cash and shares of our common stock, the amount of consideration that you will receive upon conversion of your notes will be determined by reference to the volume-weighted average prices of our common stock for each trading day in a 25 trading-day observation period. As described under **Description of Notes Settlement upon Conversion**, this period would be (i) subject to clause (ii), if the relevant conversion date occurs prior to November 15, 2024, the 25 consecutive trading day period beginning on, and including, the second trading day after such conversion date; (ii) if the relevant conversion date occurs on or after the date of our issuance of a notice of redemption as described under **Description of Notes Optional Redemption** and prior to the relevant redemption date, the 25 consecutive trading days beginning on, and including, the 26th scheduled trading day immediately preceding such redemption date; and (iii) subject to clause (ii), if the relevant conversion date occurs on or after November 15, 2024, the 25 consecutive trading days beginning on, and including, the 26th scheduled trading day immediately preceding February 15, 2025. Accordingly, if the price of our common stock decreases during this period, the amount and/or value of consideration you receive will be adversely affected. In addition, if the market price of our common stock at the end of such period is below the average of the volume-weighted average price of our common stock during such period, the value of any shares of our common stock that you will receive in satisfaction of our conversion obligation will be less than the value used to determine the number of shares that you will receive.

If we elect to satisfy our conversion obligation solely in shares of our common stock upon conversion of the notes, we will be required to deliver the shares of our common stock, together with cash for any fractional share, on the second business day following the relevant conversion date (provided that, with respect to any conversion date occurring after November 15, 2024, settlement will occur on the maturity date of the notes). Accordingly, if the price of our common stock decreases during this period, the value of the shares that you receive will be adversely affected and would be less than the conversion value of the notes on the conversion date.

### ***The notes are not protected by restrictive covenants.***

The indenture governing the notes does not contain any financial or operating covenants or restrictions on the payments of dividends, the incurrence of indebtedness or the issuance or repurchase of securities by us or any of our subsidiaries. The indenture contains no covenants or other provisions to afford protection to holders of the notes in the event of a fundamental change or other corporate transaction involving us except to the extent described under

**Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes**, **Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption** and **Description of Notes Consolidation, Merger or Sale of Assets**.

### ***The increase in the conversion rate for notes converted in connection with a make-whole fundamental change or redemption may not adequately compensate you for any lost value of your notes as a result of such transaction.***

If a make-whole fundamental change or redemption occurs prior to the maturity date, under certain circumstances, we will increase the conversion rate by a number of additional shares of our common stock for notes converted in connection with such make-whole fundamental change or redemption, as applicable. The increase in the conversion rate will be determined based on the date on which the specified corporate transaction becomes effective or the date of the redemption notice, as the case may be, and the price paid (or deemed to be paid) per share of our common stock in such transaction, as described below under **Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption**. The increase in the conversion rate for notes converted in connection with a make-whole fundamental change or redemption, as applicable, may not adequately compensate you for any lost value of your notes as a result of such transaction or in connection with the redemption, as applicable. In addition, if the price of our common stock in the transaction or in connection with the redemption is greater than \$25.00 per share or less than \$3.52 per share (subject to adjustment), no additional shares will be added to the conversion rate. Moreover, in no event will the conversion rate per \$1,000

principal amount of notes as a result

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of this adjustment exceed 284.0909 shares of common stock, subject to adjustment in the same manner as the conversion rate as set forth under Description of Notes Conversion Rights Conversion Rate Adjustments.

Our obligation to increase the conversion rate for notes converted in connection with a make-whole fundamental change or redemption could be considered a penalty, in which case the enforceability thereof would be subject to general principles of reasonableness and equitable remedies.

***Upon any optional redemption of the notes or any conversion of the notes in connection with a related redemption notice, the cash comprising the redemption price, in the case of an optional redemption, or the applicable conversion rate, in the case of a conversion in connection with a redemption notice, as applicable, may not fully compensate you for future interest payments or lost time value of your notes.***

On or after February 15, 2022, we may redeem for cash any or all of the notes, at our option, if the last reported sale price of our common stock has been at least 130% of the conversion price then in effect 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. If we call the notes for optional redemption, you may convert all or any portion of your notes at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date. Upon such redemption or conversion, the cash comprising the redemption price, in the case of an optional redemption, or the applicable conversion rate, in the case of a conversion in connection with a related redemption notice, in either case, may not fully compensate you for any future interest payments that you would have otherwise received or any other lost time value of your notes. See Description of Notes Optional Redemption.

***The conversion rate of the notes may not be adjusted for all dilutive events.***

The conversion rate of the notes is subject to adjustment for certain events, including, but not limited to, the issuance of certain stock dividends on our common stock, the issuance of certain rights or warrants, subdivisions, combinations, distributions of capital stock, indebtedness, or assets, cash dividends and certain issuer tender or exchange offers as described under Description of Notes Conversion Rights Conversion Rate Adjustments. However, the conversion rate will not be adjusted for other events, such as a third-party tender or exchange offer or an issuance of common stock for cash, that may adversely affect the trading price of the notes or our common stock. An event that adversely affects the value of the notes may occur, and that event may not result in an adjustment to the conversion rate.

***Provisions in the indenture for the notes may deter or prevent a business combination that may be favorable to you.***

If a fundamental change occurs prior to the maturity date of the notes, holders of the notes will have the right, at their option, to require us to repurchase all or a portion of their notes. In addition, if a make-whole fundamental change occurs prior to the maturity date of the notes, we will in some cases be required to increase the conversion rate for a holder that elects to convert its notes in connection with such fundamental change. Furthermore, the indenture for the notes prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the notes. These and other provisions in the indenture could deter or prevent a third party from acquiring us even when the acquisition may be favorable to you.

***Some significant restructuring transactions may not constitute a fundamental change, in which case we would not be obligated to offer to repurchase the notes.***

Upon the occurrence of a fundamental change, you have the right to require us to repurchase your notes. However, the fundamental change provisions will not afford protection to holders of notes in the event of other

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transactions that could adversely affect the notes. For example, transactions such as leveraged recapitalizations, refinancings, restructurings, or acquisitions initiated by us may not constitute a fundamental change requiring us to repurchase the notes. In the event of any such transaction, the holders would not have the right to require us to repurchase the notes, even though each of these transactions could increase the amount of our indebtedness, or otherwise adversely affect our capital structure or any credit ratings, thereby adversely affecting the holders of notes.

***We cannot assure you that an active trading market will develop for the notes.***

Prior to this offering, there has been no trading market for the notes, and we do not intend to apply to list the notes on any securities exchange or to arrange for quotation on any automated dealer quotation system. We have been informed by the underwriter that it intends to make a market in the notes after the offering is completed. However, the underwriter may cease its market-making at any time without notice. In addition, the liquidity of the trading market in the notes, and the market price quoted for the notes, may be adversely affected by changes in the overall market for this type of security and by changes in our financial performance or prospects or in the prospects for companies in our industry generally. As a result, we cannot assure you that an active trading market will develop for the notes. If an active trading market does not develop or is not maintained, the market price and liquidity of the notes may be adversely affected. In that case you may not be able to sell your notes at a particular time or you may not be able to sell your notes at a favorable price.

***Any adverse rating of the notes may cause their trading price to fall.***

We do not intend to seek a rating on the notes. However, if a rating service were to rate the notes and if such rating service were to lower its rating on the notes below the rating initially assigned to the notes or otherwise announces its intention to put the notes on credit watch, the trading price of the notes could decline.

***You may be subject to tax if we make or fail to make certain adjustments to the conversion rate of the notes even though you do not receive a corresponding cash distribution.***

The conversion rate of the notes is subject to adjustment in certain circumstances, including the payment of cash dividends. If the conversion rate is adjusted as a result of a distribution that is taxable to our common stockholders, such as a cash dividend, you may be deemed to have received a dividend subject to U.S. federal income tax without the receipt of any cash. In addition, a failure to adjust (or to adjust adequately) the conversion rate after an event that increases your proportionate interest in us could be treated as a deemed taxable dividend to you. If a make-whole fundamental change or redemption, as the case may be, occurs on or prior to the maturity date of the notes, under some circumstances, we will increase the conversion rate for notes converted in connection with the make-whole fundamental change or during the related redemption period. Such increase may also be treated as a distribution subject to U.S. federal income tax as a dividend. See U.S. Federal Income Tax Considerations. If you are a non-U.S. holder (as defined under U.S. Federal Income Tax Considerations), any deemed dividend would generally be subject to U.S. federal withholding tax at a 30% rate, or such lower rate as may be specified by an applicable treaty, which may be set off against subsequent payments on the notes (including upon conversion, repayment or maturity), or in some circumstances from any payments on our common stock or from sales proceeds subsequently paid or credited to you, or from your other funds or assets. See U.S. Federal Income Tax Considerations.



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**CAUTIONARY STATEMENT ABOUT FORWARD-LOOKING INFORMATION**

This prospectus supplement, the accompanying prospectus and the documents and information incorporated by reference herein and therein may contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Forward-looking statements may include, but are not limited to, statements relating to our objectives, plans and strategies as well as statements, other than historical facts, that address activities, events or developments that we intend, expect, project, believe or anticipate will or may occur in the future. These statements are often characterized by terminology such as may, will, should, expects, plans, anticipates, intends, target, projects, contemplates, believes, estimates, predicts, potential, or continue or the neg terms or other similar expressions.

Forward-looking statements are based on assumptions and assessments made in light of our experience and perception of historical trends, current conditions, expected future developments and other factors believed to be appropriate. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties, many of which are outside of our control. You should not place undue reliance on these forward-looking statements, which reflect our view only as of the date of this prospectus supplement, and we undertake no obligation to update these forward-looking statements in the future, except as required by applicable law.

A number of important factors could cause actual results to differ materially from those indicated by the forward-looking statements, including, without limitation, those factors described under the caption Risk Factors in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, which is incorporated by reference in this prospectus supplement and the accompanying prospectus, and under similar headings in our subsequently filed quarterly reports on Form 10-Q, as well as the other risks and uncertainties described herein and in the other documents incorporated by reference in this prospectus supplement. Some of the key factors that could cause actual results to differ from our expectations include the following:

we have 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, including, without limitation, recent lawsuits against us and our Chairman and CEO by the SEC, as well as related class action and derivative lawsuits;

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;

the success of our relationship with Pfizer;

that we may fail to obtain regulatory approval for hGH-CTP or successfully commercialize *Rayaldee* and hGH-CTP;

that we may not generate profits or cash flow from our laboratory operations or substantial revenue from *Rayaldee* and our 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 to build a successful pharmaceutical sales and marketing infrastructure;

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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 CEO;

integration challenges for Transition, BioReference Laboratories or BioReference, EirGen and other acquired businesses;

availability of insurance coverage with respect to material litigation matters;

changes in regulation and policies in the 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 Blues 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 the *4Kscore* test;

failure to timely or accurately bill and collect for our services;

failure in our information technology systems, including cybersecurity attacks or other data security or privacy incidents;

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;

failure to obtain and maintain regulatory approval outside the U.S.;

legal, economic, political, regulatory, currency exchange and other risks associated with international operations; and

our ability to finance and successfully complete construction of a research, development and manufacturing center in Waterford, Ireland.

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**USE OF PROCEEDS**

We estimate that the net proceeds to us from this offering of notes will be approximately \$192.3 million (or \$221.3 million if the underwriter exercises its over-allotment option in full), after deducting the underwriter's discount and commission and our estimated expenses relating to the offering.

We intend to use the net proceeds we receive from sales of securities offered hereby to fund research and development to further develop and commercialize our portfolio of proprietary pharmaceutical and diagnostic products and for working capital, capital expenditures, acquisitions and other general corporate purposes, which will include the repayment or repurchase of indebtedness or debt securities outstanding from time to time, including \$28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit with an affiliate of Dr. Frost.

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**DIVIDEND POLICY**

We have not declared or paid any cash dividends on our common stock and do not intend to pay cash dividends on our common stock in the near future.

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**Table of Contents****CAPITALIZATION**

The following table sets forth our cash and cash equivalents and consolidated capitalization as of September 30, 2018:

on an actual basis reflecting our consolidated cash and cash equivalents and capitalization; and

on an as-adjusted basis reflecting our consolidated cash and cash equivalents and capitalization to give effect to this offering and the use of the net proceeds from this offering.

The information in this table should be read in conjunction with Use of Proceeds, included elsewhere in this prospectus supplement, and Management's Discussion and Analysis of Financial Condition and Results of Operations and the consolidated financial statements and the related notes contained in our Form 8-K filed with the SEC on January 28, 2019 and our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2018, which are incorporated by reference into this prospectus supplement and the accompanying prospectus, as well as the other financial information incorporated by reference into this prospectus supplement and the accompanying prospectus.

	<b>As of September 30, 2018</b>	
	<b>Actual</b>	<b>As Adjusted</b>
	<i>(unaudited) (in millions)</i>	
Cash and Cash Equivalents	\$ 43.7	\$ 207.2(6)
Debt:		
4.5% Convertible Senior Notes Due 2025 offered hereby(1)		192.3
3.0% Senior Notes Due 2033(2)	31.0	3.1
5.0% Convertible Promissory Notes due 2023(3)	56.6	56.6
BioReference Credit Agreement(4)	105.0	105.0
Other local lines of credit	4.7	4.7
Other indebtedness	8.3	8.3
<b>Total</b>	<b>\$ 205.6</b>	<b>\$ 370.0</b>
Equity:		
Common shares, par value \$0.01 per share; 750,000,000 shares authorized; 560,377,422 shares issued at September 30, 2018(5)	\$ 5.6	\$ 5.6
Treasury Stock 549,907 shares at September 30, 2018	(1.8)	(1.8)
Additional paid-in capital	2,907.0	2,907.0
Accumulated other comprehensive loss	(13.1)	(13.1)
Accumulated deficit	(1,109.0)	(1,109.0)
<b>Total shareholders' equity</b>	<b>\$ 1,789.0</b>	<b>\$ 1,789.0</b>
<b>Total capitalization</b>	<b>\$ 1,994.6</b>	<b>\$ 2,159.0</b>

- (1) In accordance with Financial Accounting Standards Board Accounting Standards Codification 470-20, Debt with Conversion and Other Options ( ASC 470-20 ), convertible debt that may be entirely or partially, settled in cash (such as the notes) is required to be separated into a liability and an equity component, such that interest expense reflects the issuer's non-convertible debt interest cost. We expect that on the issuance date, the value of the conversion option of the notes, representing the equity component, will be recorded as additional paid-in capital within stockholders' equity and as an original issue discount to the notes, which reduces their initial carrying value. We expect that the carrying value of the notes, net of the discount recorded, will be accreted up to the principal amount of the notes from the issuance date until maturity. ASC 470-20 does not affect the actual amount that we are required to repay. The amount shown in the table above for the notes is the aggregate principal amount of the notes, without reflecting the debt discount for the value of the conversion option, and is net of the underwriters' discounts and our estimated offering expenses related to this offering.

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- (2) Holders of the 2033 Senior Notes may require us to repurchase the 2033 Senior Notes for 100% of their principal amount, plus accrued and unpaid interest, on February 1, 2019, February 1, 2023 and February 1, 2028 under the indenture governing the 2033 Senior Notes. We anticipate using a portion of the net proceeds of this offering to repurchase such amount of 2033 Senior Notes as we were required to repurchase on February 1, 2019 pursuant to the terms of the indenture governing the 2033 Senior Notes. On February 1, 2019, approximately \$28.8 million aggregate principal amount of 2033 Senior Notes were tendered by holders thereof pursuant to such holders option to require us to repurchase such 2033 Senior Notes pursuant to the terms of the indenture governing the 2033 Senior Notes. The aggregate repurchase price for such 2033 Senior Notes was the aggregate principal amount of such 2033 Senior Notes, plus accrued and unpaid interest thereon to, but not including, the date of repurchase. Following the repurchase, approximately \$3.1 million aggregate principal amount of the 2033 Senior Notes will remain outstanding, as reflected in the As Adjusted column.
- (3) The amount shown in the table above for the notes is the aggregate principal amount of the notes, including accrued interest.
- (4) As of September 30, 2018, the total availability under the Credit Agreement with CB and our lines of credit with financial institutions in Chile and Spain was \$138.0 million, of which \$109.7 million was used and outstanding as of September 30, 2018. The weighted average interest rate on these lines of credit is approximately 4.7%. See Description of Other Indebtedness .
- (5) Does not include 33,011,848 shares of our common stock issuable under our stock option plans based on outstanding awards as of September 30, 2018 or up to 644,330 shares of our common stock that may be issuable to the sellers of Claros Diagnostics Inc. in connection with the approval of the Sangia Total PSA Test using the Claros Analyzer.
- (6) Reflects the use of proceeds to repay \$28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit with an affiliate of Dr. Frost as described in Subsequent Events below.

## **Subsequent Events**

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 the line of credit will bear interest at a rate of 10% 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 November 8, 2023.

On February 1, 2019, we borrowed \$28.8 million under the line of credit; no amounts were previously outstanding under the line of credit. We intend to use the proceeds of the \$28.8 million borrowing to repurchase the 2033 Senior Notes (as defined below) tendered by holders thereof pursuant to such holders option to require us to repurchase such 2033 Senior Notes pursuant to the terms of the indenture governing the 2033 Senior Notes. We intend to use a portion of the proceeds of this offering to repay the \$28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit and to terminate the line of credit thereafter.

**Table of Contents****SELECTED FINANCIAL DATA**

The following selected historical consolidated statement of operations data for the years ended December 31, 2017, 2016, 2015, 2014 and 2013 and the consolidated balance sheet data as of December 31, 2017, 2016, 2015, 2014 and 2013, below are derived from our audited consolidated financial statements and related notes thereto. The following selected historical consolidated statement of operations data for the period January 1, 2018 through September 30, 2018, and the consolidated balance sheet data as of September 30, 2018, are derived from our unaudited condensed consolidated financial statements and related notes thereto. This data should be read in conjunction with our

Management's Discussion and Analysis of Financial Condition and Results of Operations and the consolidated financial statements and the related notes contained in our Form 8-K filed with the SEC on January 28, 2019 and our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2018.

Effective January 1, 2018, we adopted Accounting Standards Codification Topic 606, Revenue from Contracts with Customers, using the full retrospective transition method. The information contained in the table below for the nine months ended September 30, 2017, and the years ended December 31, 2017, 2016 and 2015 has been adjusted to reflect our retrospective adoption of Topic 606. The information for the years ended December 31, 2014 and 2013 has not been adjusted to reflect the impact of the adoption of ASC 606.

(In thousands, except share and per share information)	For the periods January 1 through September 30,			For the years ended December 31,			
	2018	2017	2017	2016	2015	2014	2013
<b>Statement of operations data:</b>							
Revenues	\$ 768,412	\$ 805,022	\$ 966,006	\$ 1,117,494	\$ 447,517	\$ 91,125	\$ 96,530
Costs and expenses:							
Cost of revenue	455,105	463,511	620,130	611,482	235,239	48,009	48,860
Operating expenses	394,491	460,322	622,318	602,563	332,858	188,931	127,302
Total costs and expenses	849,596	923,833	1,242,448	1,214,045	568,097	236,940	176,162
Operating loss	(81,184)	(118,811)	(276,442)	(96,551)	(120,580)	(145,815)	(79,632)
Other income and (expense), net	5,320	937	4,518	(271)	(39,517)	(25,212)	(24,586)

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Income tax benefit (provision)	10,437	42,309	(18,855)	56,115	113,675	(24)	(1,672)
Net loss	(76,969)	(87,336)	(305,250)	(48,359)	(53,527)	(174,638)	(117,346)
Net loss attributable to common shareholders	\$ (76,969)	\$ (87,336)	\$ (305,250)	\$ (48,359)	\$ (52,127)	\$ (171,666)	\$ (114,827)
Loss per share, basic and undiluted:							
Net loss per share, basic	\$ (0.14)	\$ (0.16)	\$ (0.55)	\$ (0.09)	\$ (0.11)	\$ (0.41)	\$ (0.32)
Net loss per share, diluted	\$ (0.14)	\$ (0.16)	\$ (0.55)	\$ (0.10)	\$ (0.11)	\$ (0.41)	\$ (0.32)
Weighted average number of common shares outstanding basic:	559,601,097	559,065,232	559,160,565	550,846,553	488,065,908	422,014,039	355,095,701
Weighted average number of common shares outstanding diluted:	559,601,097	559,065,232	559,160,565	555,605,448	488,065,908	422,014,039	355,095,701
<b>Balance sheet data:</b>							
Total assets	\$ 2,480,994	\$ 2,721,990	\$ 2,589,956	\$ 2,766,619	\$ 2,799,188	\$ 1,267,664	\$ 1,391,516
Long-term liabilities	\$ 374,521	\$ 390,008	\$ 434,304	\$ 480,166	\$ 614,423	\$ 348,812	\$ 426,687
Total shareholders equity	\$ 1,788,643	\$ 2,057,882	\$ 1,843,623	\$ 2,046,433	\$ 1,957,695	\$ 835,741	\$ 872,979

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**DESCRIPTION OF NOTES**

We will issue the 4.50% Convertible Senior Notes due 2025 (the **notes** ) under a base indenture (the **base indenture** ) to be dated as of February 7, 2019, the date of initial issuance of the notes, between us and U.S. Bank, National Association, as trustee (the **trustee** ), as supplemented by a supplemental indenture (the **supplemental indenture** ), to be dated as of February 7, 2019, with respect to the notes. In this section, and throughout this prospectus supplement, we refer to the base indenture, as supplemented by the supplemental indenture, as the **indenture**. This description of notes supplements the description of the general provisions of the notes and the base indenture in the accompanying prospectus. The terms of the notes include those expressly set forth in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as amended (the **Trust Indenture Act** ).

The following description is a summary of the material provisions of the notes and the indenture and does not purport to be complete. This summary is subject to and is qualified by reference to all of the provisions of the notes and the indenture, including the definitions of certain terms used in the indenture. We urge you to read these documents because they, and not this description, define your rights as a holder of the notes.

You may request a copy of the indenture from us as described under **Where You Can Find More Information**.

For purposes of this description, references to **OPKO**, the **Company**, **we**, **our** and **us** refer only to **OPKO Health**, and not to our subsidiaries, unless the context otherwise requires.

**General**

The notes will:

be our general unsecured, senior obligations;

initially be limited to an aggregate principal amount of \$200.0 million (or \$230.0 million if the underwriter's overallotment option to purchase additional notes is exercised in full);

bear cash interest from February 7, 2019 at an annual rate of 4.50%, payable semiannually on February 15 and August 15 of each year, beginning on August 15, 2019;

be subject to redemption 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 conversion price for the notes then in effect 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;

be subject to repurchase by us at the option of the holders following a fundamental change (as defined below under **Fundamental Change Permits Holders to Require Us to Repurchase 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;

mature on February 15, 2025, unless earlier converted, redeemed or repurchased;

be issued in denominations of \$1,000 and integral multiples of \$1,000; and

be represented by one or more registered notes in global form, but in certain limited circumstances may be represented by notes in definitive form. See Book-Entry, Settlement and Clearance.

Subject to satisfaction of certain conditions and during the periods described below, the notes may be converted at an initial conversion rate of 236.7424 shares of common stock per \$1,000 principal amount of notes

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(equivalent to an initial conversion price of approximately \$4.22 per share of common stock). The conversion rate is subject to adjustment if certain events occur.

We will settle conversions of notes by paying or delivering, 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, as described under **Conversion Rights Settlement upon Conversion**. You will not receive any separate cash payment for interest, if any, accrued and unpaid to the conversion date except under the limited circumstances described below.

The indenture does not limit the amount of debt that may be issued by us or our subsidiaries under the indenture or otherwise. The indenture does not contain any financial covenants and does not restrict us from paying dividends or issuing or repurchasing our other securities. Other than restrictions described under **Fundamental Change Permits Holders to Require Us to Repurchase Notes** and **Consolidation, Merger or Sale of Assets** below and except for the provisions set forth under **Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption**, the indenture does not contain any covenants or other provisions designed to afford holders of the notes protection in the event of a highly leveraged transaction involving us or in the event of a decline in our credit rating as the result of a takeover, recapitalization, highly leveraged transaction or similar restructuring involving us that could adversely affect such holders.

We may, without the consent of the holders, reopen the indenture for the notes and issue additional notes under the indenture with the same terms as the notes offered hereby (other than differences in the issue price and interest accrued prior to the issue date of such additional notes) in an unlimited aggregate principal amount; *provided* that if any such additional notes are not fungible with the notes initially offered hereby for U.S. federal income tax or securities law purposes, such additional notes will have one or more separate CUSIP numbers.

We do not intend to list the notes on any securities exchange or any automated dealer quotation system.

References in this prospectus supplement to a holder or holders of notes that are held through DTC are references to owners of beneficial interests in such notes, unless the context otherwise requires. However, we and the trustee will treat the person in whose name the notes are registered (Cede & Co., in the case of notes held through DTC) as the owner of such notes for all purposes. References herein to the close of business refer to 5:00 p.m., New York City time, and to the open of business refer to 9:00 a.m., New York City time.

**Purchase and Cancellation**

The registrar, paying agent and conversion agent (if other than the trustee) will forward to the trustee all notes surrendered for payment, repurchase (including as described below), redemption, registration of transfer or exchange or conversion. All notes delivered to the trustee shall be cancelled promptly by the trustee. Except for any notes surrendered for registration of transfer or exchange, no notes shall be authenticated in exchange for any notes cancelled as provided in the indenture.

We may, to the extent permitted by law, and without the consent of holders, directly or indirectly (regardless of whether such notes are surrendered to us), repurchase notes in the open market or otherwise, whether by us or our subsidiaries or through a private or public tender or exchange offer or through counterparties to private agreements, including by cash-settled swaps or other derivatives. We will cause any notes so repurchased (other than notes repurchased pursuant to cash-settled swaps or other derivatives) to be surrendered to the trustee for cancellation, and they will no longer be considered outstanding under the indenture upon their repurchase.



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### **Payments on the Notes; Paying Agent and Registrar; Transfer and Exchange**

We will pay or cause the paying agent to pay the principal of, and interest on, notes in global form registered in the name of or held by DTC or its nominee by wire transfer in immediately available funds to DTC or its nominee, as the case may be, as the registered holder of such global note.

We will pay or cause the paying agent to pay the principal of any certificated notes at the office or agency designated by us for that purpose. We have initially designated the trustee as our paying agent and registrar and its agency in the continental United States as a place where notes may be presented for payment or for registration of transfer. We may, however, change the paying agent or registrar without prior notice to the holders of the notes, and we may act as paying agent or registrar. Interest on certificated notes will be payable (i) to holders having an aggregate principal amount of \$1,000,000 or less, by check mailed to the holders of these notes and (ii) to holders having an aggregate principal amount of more than \$1,000,000, either by check mailed to each holder or, upon application by such a holder to the registrar not later than the relevant regular record date, by wire transfer in immediately available funds to that holder's account within the United States if such holder has provided us, the trustee or the paying agent (if other than the trustee) with the requisite information necessary to make such wire transfer, which application shall remain in effect until the holder notifies, in writing, the registrar of the notes to the contrary.

A holder of notes may transfer or exchange notes at the office of the registrar in accordance with the indenture. The registrar and the trustee may require a holder, among other things, to furnish appropriate endorsements and transfer documents. No service charge will be imposed by us, the trustee or the registrar for any registration of transfer or exchange of notes, but we may require a holder to pay a sum sufficient to cover any transfer tax or other similar governmental charge required by law or permitted by the indenture. We are not required to transfer or exchange any note selected for redemption or surrendered for conversion or required repurchase.

The registered holder of a note will be treated as its owner for all purposes.

### **Interest**

The notes will bear cash interest at a rate of 4.50% per year until maturity of the notes. Interest on the notes will accrue from February 7, 2019 or from the most recent date on which interest has been paid or duly provided for. Interest will be payable semiannually in arrears on February 15 and August 15 of each year, beginning on August 15, 2019.

Interest will be paid to the person in whose name a note is registered at the close of business on February 1 or August 1, as the case may be, immediately preceding the relevant interest payment date (each, a regular record date). Interest on the notes will be computed on the basis of a 360-day year composed of twelve 30-day months, and, for partial months, on the basis of the number of days actually elapsed in a 30-day month.

If any interest payment date, the maturity date or any earlier required repurchase date upon a fundamental change repurchase date of a note falls on a day that is not a business day, the required payment will be made on the next succeeding business day and no interest on such payment will accrue in respect of the delay. The term business day means, with respect to any note, any day other than a Saturday, a Sunday or a day on which the Federal Reserve Bank of New York is authorized or required by law or executive order to close or be closed.

Unless the context otherwise requires, all references to interest in this prospectus supplement include additional interest, if any, payable at our election as the sole remedy relating to the failure to comply with our reporting obligations as described under Events of Default.



## **Ranking**

The notes will be our senior unsecured obligations that rank senior in right of payment to all of our indebtedness that is expressly subordinated in right of payment to the notes. The notes will rank equal in right of

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payment to all of our unsecured indebtedness that is not so subordinated. The notes will effectively rank junior to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness. The notes will be structurally junior to all existing and future indebtedness and other liabilities of our current or future subsidiaries (including trade payables). In the event of our bankruptcy, liquidation, reorganization or other winding up, our assets that secure secured debt will be available to pay obligations on the notes only after all indebtedness under such secured debt has been repaid in full from such assets. We advise you that there may not be sufficient assets remaining to pay amounts due on any or all the notes then outstanding.

As of September 30, 2018, we had \$205.6 million of outstanding indebtedness for borrowed money (excluding intercompany debt) and our subsidiaries had \$486.8 million of indebtedness and other liabilities (including trade payables but excluding intercompany obligations and liabilities of a type not required to be reflected on a balance sheet of such subsidiaries in accordance with U.S. GAAP) to which the notes would have been structurally subordinated. After giving effect to the issuance of the notes (assuming no exercise of the underwriter's overallotment option to purchase additional notes, our and our subsidiaries' total indebtedness for borrowed money as of September 30, 2018 (excluding intercompany debt) would have been \$405.6 million.

A substantial portion of our operations is conducted through our subsidiaries. The notes will not be guaranteed by any of our current or future subsidiaries. Our subsidiaries are separate and distinct legal entities and have no obligation, contingent or otherwise, to pay amounts due with respect to the notes or to make any funds available therefor, whether by dividends, loans or other payments. Our right to receive any assets of any of our subsidiaries upon such subsidiary's bankruptcy, liquidation or reorganization, and, therefore, the rights of the holders of notes to participate in those assets, will be subject to prior claims of creditors of the subsidiary, including trade creditors, and such subsidiary may not have sufficient assets remaining to make any payments to us as a stockholder or otherwise. The ability of our subsidiaries to pay dividends and make other payments to us is restricted by, among other things, applicable corporate and other laws and regulations and may be restricted by agreements to which our subsidiaries may become a party.

We may not be able to pay the cash portions of any settlement amount upon conversion of the notes, or to pay cash for the fundamental change repurchase price upon a fundamental change if a holder requires us to repurchase notes as described below. See **Risk Factors** **Additional Risks Related to this Offering and the Notes**. We may not have the ability to raise the funds necessary to settle conversions of the notes or to repurchase the notes upon a fundamental change, and our future debt may contain limitations on our ability to repurchase the notes.

**Optional Redemption**

No sinking fund is provided for the notes, which means that we are not required to redeem or retire the notes periodically. Prior to February 15, 2022, the notes will not be redeemable. On or after February 15, 2022, we may redeem for cash any or all of the notes, at our option, if the last reported sale price of our common stock has been at least 130% of the conversion price then in effect 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. In the case of any optional redemption, we will provide not less than 30 scheduled trading days nor more than 60 calendar days' notice before the redemption date to the trustee, the conversion agent (if other than the trustee), the paying agent (if other than the trustee) and each holder of notes, and the redemption price will be equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date (unless the redemption date falls after a regular record date but on or prior to the immediately succeeding interest payment date, in which case we will pay the full amount of accrued and unpaid interest to the holder of record as of the close of business on such regular record date, and the redemption price will be equal to 100% of the principal amount of the notes to be redeemed). The redemption date must be a business day. We may not specify a redemption date that falls on or after

the 26th scheduled trading day immediately preceding the maturity date.

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If less than all of the outstanding notes are to be redeemed, the trustee will select the notes to be redeemed in principal amounts of \$1,000 or multiples of \$1,000 by lot, pro rata or by another method the trustee in its discretion considers reasonable. If only a portion of a note is subject to redemption and that note is converted in part, then the converted portion of that note will be deemed to be from the portion of that note that was subject to redemption.

No notes may be optionally redeemed if the principal amount of the notes has been accelerated, and such acceleration has not been rescinded, on or prior to the redemption date (except in the case of an acceleration resulting from a default by us in the payment of the redemption price).

## **Conversion Rights**

### ***General***

Prior to the close of business on the business day immediately preceding November 15, 2024, the notes will be convertible only upon satisfaction of one or more of the conditions described under the headings **Conversion upon Satisfaction of Sale Price Condition**, **Conversion upon Satisfaction of Trading Price Condition**, **Conversion upon Notice of Redemption**, and **Conversion upon Specified Corporate Events**. On or after November 15, 2024, until the close of business on the business day immediately preceding the maturity date, holders may convert all or any portion of their notes at the conversion rate at any time irrespective of the foregoing conditions.

The conversion rate for the notes will initially be 236.7424 shares of common stock per \$1,000 principal amount of notes (equivalent to an initial conversion price of approximately \$4.22 per share of common stock). Upon conversion of a note, we will satisfy our conversion obligation by paying or delivering, 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, all as set forth below under **Settlement upon Conversion**. If we satisfy our conversion obligation solely in cash or through payment and delivery, as the case may be, of a combination of cash and shares of our common stock, the amount of cash and shares of common stock, if any, due upon conversion will be based on a daily conversion value (as defined below) calculated on a proportionate basis for each trading day in a 25 trading-day observation period (as defined below under **Settlement upon Conversion**). The trustee will initially act as the conversion agent.

A holder may convert fewer than all of such holder's notes so long as the notes converted are a multiple of \$1,000 principal amount.

If we call the notes for redemption, a holder of notes may convert all or any portion of such holder's notes only until the close of business on the scheduled trading day immediately preceding the redemption date, unless we fail to pay the redemption price (in which case a holder of notes may convert such holder's notes until the redemption price has been paid or duly provided for).

Upon conversion, you will not receive any separate cash payment for accrued and unpaid interest, if any, except as described below. We will not issue fractional shares of our common stock upon conversion of notes. Instead, we will pay cash in lieu of delivering any fractional share as described under **Settlement upon Conversion**. Our payment and delivery, as the case may be, to you of the cash, shares of our common stock, or a combination thereof, as the case may be, into which a note is convertible will be deemed to satisfy in full our obligation to pay:

the principal amount of the note; and

accrued and unpaid interest, if any, to, but not including, the relevant conversion date.

As a result, accrued and unpaid interest, if any, to, but not including, the relevant conversion date will be deemed to be paid in full rather than cancelled, extinguished or forfeited. Upon a conversion of notes into a

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combination of cash and shares of our common stock, accrued and unpaid interest will be deemed to be paid first out of the cash paid upon such conversion.

Notwithstanding the immediately preceding paragraph, if notes are converted after 5:00 p.m., New York City time, on a regular record date for the payment of interest, holders of such notes at 5:00 p.m., New York City time, on such regular record date will receive the full amount of interest payable on such notes on the corresponding interest payment date notwithstanding the conversion. Notes surrendered for conversion during the period from 5:00 p.m., New York City time, on any regular record date to 9:00 a.m., New York City time, on the immediately following interest payment date must be accompanied by funds equal to the amount of interest payable on the notes so converted; *provided* that no such payment need be made:

for conversions of notes following the regular record date immediately preceding the maturity date;

if we have specified a redemption date that is after a regular record date and on or prior to the business day immediately following the corresponding interest payment date;

if we have specified a fundamental change repurchase date that is after a regular record date and on or prior to the business day immediately following the corresponding interest payment date; or

to the extent of any overdue interest, if any overdue interest exists at the time of conversion with respect to such note.

Therefore, for the avoidance of doubt, all record holders on the regular record date immediately preceding the maturity date, any fundamental change repurchase date or redemption date, in each case, described above, will receive the full interest payment due on the maturity date or other applicable interest payment date in cash, regardless of whether their notes have been converted following such regular record date.

If a holder converts notes, we will pay any documentary, stamp or similar issue or transfer tax due on any issuance of any shares of our common stock upon the conversion, unless the tax is due because the holder requests any such shares to be issued in a name other than the holder's name, in which case the holder will pay that tax.

Holders may surrender their notes for conversion only under the following circumstances:

***Conversion upon Satisfaction of Sale Price Condition***

Prior to the close of business on the business day immediately preceding November 15, 2024, a holder of notes may surrender all or a portion of its notes for conversion 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 the period of 30 consecutive trading days ending on, and including, 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.

The last reported sale price of our common stock (or other security for which a closing sale price must be determined) on any date means the closing sale price per share (or if no closing sale price is reported, the average of the bid and

ask prices or, if more than one in either case, the average of the average bid and the average ask prices) on that date as reported in composite transactions for the principal U.S. national or regional securities exchange on which our common stock (or such other security) is traded. If our common stock (or such other security) is not listed for trading on a U.S. national or regional securities exchange on the relevant date, the last reported sale price will be the last quoted bid price for our common stock (or such other security) in the over-the-counter market on the relevant date as reported by OTC Markets Group Inc. or a similar organization. If our common stock (or such other security) is not so quoted, the last reported sale price will be the average of the mid-point of the last bid and ask prices for our common stock (or such other security) on the relevant date from each of at least three nationally recognized independent investment banking firms selected by us for this purpose. The last reported sale price will be determined without regard to after-hours trading or any other trading outside of the regular trading session hours.

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Except for purposes of determining amounts due upon conversion, **trading day** means a day on which (i) trading in our common stock (or other security for which a closing sale price must be determined) generally occurs on the Nasdaq Global Select Market or, if our common stock (or such other security) is not then listed on the Nasdaq Global Select Market, on the principal other U.S. national or regional securities exchange on which our common stock (or such other security) is then listed or, if our common stock (or such other security) is not then listed on a U.S. national or regional securities exchange, on the principal other market on which our common stock (or such other security) is then traded and (ii) a last reported sale price for our common stock (or closing sale price for such other security) is available on such securities exchange or market. If our common stock (or such other security) is not so listed or traded, **trading day** means a business day.

***Conversion upon Satisfaction of Trading Price Condition***

Prior to the close of business on the business day immediately preceding November 15, 2024, a holder of notes may surrender all or any portion of its notes for conversion at any time 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 notes, as determined following a request by a holder of notes in accordance with the procedures described below, 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 (the **trading price condition**).

The **trading price** of the notes on any date of determination means the average of the secondary market bid quotations obtained by the bid solicitation agent for \$2,000,000 principal amount of notes at approximately 3:30 p.m., New York City time, on such determination date from three independent nationally recognized securities dealers we select for this purpose; *provided* that if three such bids cannot reasonably be obtained by the bid solicitation agent but two such bids are obtained, then the average of the two bids shall be used, and if only one such bid can reasonably be obtained by the bid solicitation agent, that one bid shall be used. If, on any date, the bid solicitation agent cannot reasonably obtain at least one bid for \$2,000,000 principal amount of notes on such date from a nationally recognized securities dealer, then the trading price per \$1,000 principal amount of notes will be deemed to be less than 98% of the product of the last reported sale price of our common stock and the conversion rate. If (x) we are not acting as bid solicitation agent, and we do not, when we are required to, instruct the bid solicitation agent in writing to obtain bids, or if we give such written instruction to the bid solicitation agent, and the bid solicitation agent fails to make such determination, or (y) we are acting as bid solicitation agent and we fail to obtain such bids, then, in either case, the trading price per \$1,000 principal amount of notes will be deemed to be less than 98% of the product of the last reported sale price of our common stock and the conversion rate on each trading day of such failure.

The bid solicitation agent (if other than us) shall have no obligation to determine the trading price per \$1,000 principal amount of notes unless we have requested such determination in writing; and we will have no obligation to make such request (or, if we are acting as bid solicitation agent, we shall have no obligation to determine the trading price) unless a holder provides us with reasonable evidence that the trading price per \$1,000 principal amount of notes would be less than 98% of the product of the last reported sale price of our common stock and the conversion rate. At such time, we will (i) instruct the three independent nationally recognized securities dealers to deliver bids to the bid solicitation agent and (ii) instruct the bid solicitation agent (if other than us) to determine, or if we are acting as bid solicitation agent, we shall determine, the trading price per \$1,000 principal amount of notes in each case, beginning on the next trading day and on each successive trading day until the trading price per \$1,000 principal amount of notes is greater than or equal to 98% of the product of the last reported sale price of our common stock and the conversion rate. If the trading price condition has been met, we will so notify the holders, the trustee and the conversion agent (if other than the trustee) in writing. If, at any time after the trading price condition has been met, the trading price per \$1,000 principal amount of notes is greater than or equal to 98% of the product of the last reported sale price of our common stock



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and the conversion rate for such date, we will so notify the holders, the trustee and the conversion agent (if other than the trustee) in writing.

We will initially act as the bid solicitation agent.

### ***Conversion upon Notice of Redemption***

If we call the notes for redemption, holders may convert all or any portion of their notes at any time prior to the close of business on the scheduled trading day prior to the redemption date, even if the notes are not otherwise convertible at such time. After that time, the right to convert notes on account of our delivery of the notice of redemption will expire, unless we default in the payment of the redemption price, in which case a holder of notes may convert all or any portion of its notes until the close of business on the scheduled trading day immediately preceding the date on which the redemption price has been paid or duly provided for.

### ***Conversion upon Specified Corporate Events***

#### ***Certain Distributions***

If, prior to the close of business on the business day immediately preceding November 15, 2024, we elect to:

issue to all or substantially all holders of our common stock any rights, options or warrants (other than in connection with a stockholder rights plan so long as such rights have not separated from the shares of common stock) entitling them, for a period of not more than 60 calendar days after the announcement date of such issuance, to subscribe for or purchase shares of our common stock at a price per share that is less than the average of the last reported sale prices of our common stock for the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the date of announcement of such issuance; or

distribute to all or substantially all holders of our common stock our assets, securities or rights to purchase our securities, which distribution has a per share value, as determined by our board of directors or a committee thereof, exceeding 10% of the last reported sale price of our common stock on the trading day preceding the date of announcement for such distribution,

then, in either case, we must notify the holders of the notes, the trustee and the conversion agent (if other than the trustee) in writing at least 30 scheduled trading days prior to the ex-dividend date (as defined below) for such issuance or distribution (or, if later in the case of any such separation of rights issued pursuant to a stockholder rights plan, as soon as reasonably practicable after we become aware that such separation or triggering event has occurred or will occur). Once we have given such notice, holders may surrender all or any portion of their notes for conversion at any time until the earlier of 5:00 p.m., New York City time, on the business day immediately preceding the ex-dividend date for such issuance or distribution and our announcement that such issuance or distribution will not take place (or in the case of a separation or triggering event, until the 20th trading day following the date of our notice), even if the notes are not otherwise convertible at such time.

Holders of the notes may not convert their notes pursuant to this provision if they participate, at the same time and upon the same terms as holders of our common stock and solely as a result of holding the notes, in any of the transactions described above without having to convert their notes as if they held a number of shares of common stock

equal to the conversion rate, multiplied by the principal amount (expressed in thousands) of notes held by such holder.

*Certain Corporate Events*

If (i) a transaction or event that constitutes (x) a fundamental change (as defined under Fundamental Change Permits Holders to Require Us to Repurchase Notes ) or (y) a make-whole fundamental change (as

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defined under "Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption") occurs prior to the close of business on the business day immediately preceding November 15, 2024, regardless of whether a holder has the right to require us to repurchase the notes as described under

Fundamental Change Permits Holders to Require Us to Repurchase Notes or (ii) we are a party to a share exchange event (as defined under "Recapitalizations, Reclassifications and Changes of Our Common Stock") (other than a share exchange event that is solely for the purpose of changing our jurisdiction of organization that (x) does not constitute a fundamental change or a make-whole fundamental change and (y) results in a reclassification, conversion or exchange of outstanding shares of our common stock solely into shares of common stock of the surviving entity and such common stock becomes reference property for the notes) that occurs prior to the close of business on the business day immediately preceding November 15, 2024 (each such fundamental change, make-whole fundamental change or share exchange event, a corporate event), all or any portion of a holder's notes may be surrendered for conversion at any time after the effective date for such corporate event until the earlier of (x) 35 trading days after the actual effective date of such corporate event or, if such corporate event also constitutes a fundamental change, until the close of business on the business day immediately preceding the related fundamental change repurchase date and (y) the scheduled trading day immediately preceding the maturity date. We will notify holders, the trustee and the conversion agent (if other than the trustee) in writing within three business days following the date we publicly announce such corporate event but in no event later than the actual effective date of such corporate event.

***Conversions during the Three Months Immediately Preceding the Maturity Date***

On or after November 15, 2024, a holder may convert all or any portion of its notes at any time prior to the close of business on the business day immediately preceding the maturity date regardless of the foregoing conditions.

***Conversion Procedures***

If you hold a beneficial interest in a global note (as defined below), to convert you must comply with DTC's procedures for converting a beneficial interest in a global note and, if required, pay funds equal to interest payable on the next interest payment date to which you are not entitled.

If you hold a certificated note (as defined below), to convert you must:

complete and manually sign the conversion notice on the back of the note, or a facsimile of the conversion notice;

deliver the conversion notice, which is irrevocable, and the note to the conversion agent;

if required, furnish appropriate endorsements and transfer documents; and

if required, pay funds equal to interest payable on the next interest payment date to which you are not entitled.

We will pay any documentary, stamp or similar issue or transfer tax on the issuance of any shares of our common stock upon conversion of the notes, unless the tax is due because the holder requests such shares to be issued in a name other than the holder's name, in which case the holder will pay the tax.

We refer to the date you comply with the relevant procedures for conversion described above as the conversion date.

If a holder has already delivered a repurchase notice as described under Fundamental Change Permits Holders to Require Us to Repurchase Notes with respect to a note, the holder may not surrender that note for conversion until the holder has validly withdrawn the repurchase notice in accordance with the relevant provisions of the indenture. If a holder submits its notes for required repurchase, the holder's right to withdraw the repurchase notice and convert the notes that are subject to repurchase will terminate at the close of business on the business day immediately preceding the fundamental change repurchase date.

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***Settlement upon Conversion***

Upon conversion, we may choose to pay or deliver, as the case may be, either cash ( cash settlement ), shares of our common stock ( physical settlement ) or a combination of cash and shares of our common stock ( combination settlement ), as described below. We refer to each of these settlement methods as a settlement method.

All conversions for which the relevant conversion date occurs on or after November 15, 2024, and all conversions for which the conversion date occurs after our issuance of a notice of redemption and prior to the related redemption date, will be settled using the same settlement method. Except for any conversions that occur after our issuance of a notice of redemption, but prior to the related redemption date, and any conversions for which the relevant conversion date occurs on or after November 15, 2024, we will use the same settlement method for all conversions occurring on the same conversion date, but we will not have any obligation to use the same settlement method with respect to conversions that occur on different conversion dates. That is, we may choose for notes converted on one conversion date to settle conversions in physical settlement, and choose for notes converted on another conversion date cash settlement or combination settlement.

If we elect a settlement method, we will inform holders of the notes so converting, the trustee and the conversion agent (if other than the trustee) of the settlement method we have selected no later than the close of business on the trading day immediately following the related conversion date (or in the case of any conversions occurring (i) after the date of issuance of a notice of redemption as described under Optional Redemption and prior to the related redemption date, in such notice of redemption or (ii) on or after November 15, 2024, no later than the close of business on the scheduled trading day immediately preceding November 15, 2024). If we do not timely elect a settlement method, we will no longer have the right to elect cash settlement or physical settlement and we will be deemed to have elected combination settlement in respect of our conversion obligation, as described below, and the specified dollar amount (as defined below) per \$1,000 principal amount of notes will be equal to \$1,000. If we elect combination settlement, but we do not timely notify converting holders, the trustee and the conversion agent (if other than the trustee) in writing of the specified dollar amount per \$1,000 principal amount of notes, such specified dollar amount will be deemed to be \$1,000. It is our current intent to settle conversions through combination settlement with a specified dollar amount per \$1,000 principal amount of notes of \$1,000.

Settlement amounts will be computed as follows:

if we elect physical settlement, we will deliver to the converting holder in respect of each \$1,000 principal amount of notes being converted a number of shares of common stock equal to the conversion rate;

if we elect cash settlement, we will pay to the converting holder in respect of each \$1,000 principal amount of notes being converted cash in an amount equal to the sum of the daily conversion values for each of the 25 consecutive trading days during the related observation period; and

if we elect (or are deemed to have elected) combination settlement, we will pay or deliver, as the case may be, to the converting holder in respect of each \$1,000 principal amount of notes being converted a settlement amount equal to the sum of the daily settlement amounts for each of the 25 consecutive trading days during the related observation period.

If more than one note is surrendered for conversion at any one time by the same holder, the conversion obligation with respect to such notes shall be computed on the basis of the aggregate principal amount of the notes surrendered.

The daily settlement amount, for each of the 25 consecutive trading days during the observation period, will consist of:

cash equal to the lesser of (i) the maximum cash amount per \$1,000 principal amount of notes to be received upon conversion as specified in the notice specifying our chosen settlement method (or

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deemed specified as set forth above) (the specified dollar amount ), if any, divided by 25 (such quotient the daily measurement value ) and (ii) the daily conversion value; and

if the daily conversion value exceeds the daily measurement value, a number of shares equal to (i) the difference between the daily conversion value and the daily measurement value, divided by (ii) the daily VWAP for such trading day.

The daily conversion value means, for each of the 25 consecutive trading days during the observation period, 4.0% of the product of (1) the conversion rate on such trading day and (2) the daily VWAP on such trading day.

The daily VWAP means, for each of the 25 consecutive trading days during the relevant observation period, the per share volume-weighted average price as displayed under the heading Bloomberg VWAP on Bloomberg page OPK <equity> AQR (or its equivalent successor if such page is not available) in respect of the period from the scheduled open of trading until the scheduled close of trading of the primary trading session on such trading day (or if such volume-weighted average price is unavailable, the market value of one share of our common stock on such trading day reasonably determined, using a volume-weighted average method, by a nationally recognized independent investment banking firm retained for this purpose by us). The daily VWAP will be determined without regard to after-hours trading or any other trading outside of the regular trading session trading hours.

The observation period with respect to any note surrendered for conversion means:

subject to the immediately succeeding bullet, if the relevant conversion date occurs prior to November 15, 2024, the 25 consecutive trading-day period beginning on, and including, the second trading day immediately succeeding such conversion date;

if the relevant conversion date occurs on or after the date of our issuance of a notice of redemption with respect to the notes as described under Optional Redemption and prior to the relevant redemption date, the 25 consecutive trading days beginning on, and including, the 26th scheduled trading day immediately preceding such redemption date; and

subject to the immediately preceding bullet, if the relevant conversion date occurs on or after November 15, 2024, the 25 consecutive trading days beginning on, and including, the 26th scheduled trading day immediately preceding the maturity date.

For the purposes of determining amounts due upon conversion only, trading day means a day on which (i) there is no market disruption event (as defined below) and (ii) trading in our common stock generally occurs on the Nasdaq Global Select Market or, if our common stock is not then listed on the Nasdaq Global Select Market, on the principal other U.S. national or regional securities exchange on which our common stock is then listed or, if our common stock is not then listed on a U.S. national or regional securities exchange, on the principal other market on which our common stock is then listed or admitted for trading. If our common stock is not so listed or admitted for trading, trading day means a business day.

Scheduled trading day means a day that is scheduled to be a trading day on the principal U.S. national or regional securities exchange or market on which our common stock is listed or admitted for trading. If our common stock is not so listed or admitted for trading, scheduled trading day means a business day.



For the purposes of determining amounts due upon conversion, market disruption event means (i) a failure by the primary U.S. national or regional securities exchange or market on which our common stock is listed or admitted for trading to open for trading during its regular trading session or (ii) the occurrence or existence prior to 1:00 p.m., New York City time, on any scheduled trading day for our common stock for more than one half-hour period in the aggregate during regular trading hours of any suspension or limitation imposed on trading (by reason of movements in price exceeding limits permitted by the relevant stock exchange or otherwise) in our common stock or in any options contracts or future contracts relating to our common stock.

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Except as described under **Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption and Recapitalizations, Reclassifications and Changes of Our Common Stock**, we will deliver the consideration due in respect of conversion on the second business day immediately following the relevant conversion date, if we elect physical settlement (*provided* that, with respect to any conversion date occurring after November 15, 2024, settlement will occur on the maturity date), or on the second business day immediately following the last trading day of the relevant observation period, in the case of any other settlement method.

We will pay cash in lieu of delivering any fractional share of common stock issuable upon conversion based on the daily VWAP on the relevant conversion date (in the case of physical settlement) or based on the daily VWAP on the last trading day of the relevant observation period (in the case of combination settlement).

Each conversion will be deemed to have been effected as to any notes surrendered for conversion on the conversion date; *provided, however*, that the person in whose name any shares of our common stock shall be issuable upon such conversion will become the holder of record of such shares as of the close of business on the conversion date (in the case of physical settlement) or the last trading day of the relevant observation period (in the case of combination settlement).

### ***Conversion Rate Adjustments***

The conversion rate will be adjusted as described below, except that we will not make any adjustments to the conversion rate if holders of the notes participate (other than in the case of a share split or share combination or a tender or exchange offer), at the same time and upon the same terms as holders of our common stock and solely as a result of holding the notes, in any of the transactions described below without having to convert their notes as if they held a number of shares of common stock equal to the conversion rate, *multiplied by* the principal amount (expressed in thousands) of notes held by such holder.

(1) If we exclusively issue shares of our common stock as a dividend or distribution on shares of our common stock, or if we effect a share split or share combination, the conversion rate will be adjusted based on the following formula:

$$CR_1 = CR_0 \times \frac{OS_1}{OS_0}$$

where,

$CR_0$  = the conversion rate in effect immediately prior to the open of business on the ex-dividend date of such dividend or distribution, or immediately prior to the open of business on the effective date of such share split or share combination, as applicable;

$CR_1$  = the conversion rate in effect immediately after the open of business on such ex-dividend date or effective date;

$OS_0$  = the number of shares of our common stock outstanding immediately prior to the open of business on such ex-dividend date or effective date (before giving effect to any such dividend, distribution, split or combination); and

$OS_1$  =

the number of shares of our common stock outstanding immediately after giving effect to such dividend, distribution, share split or share combination.

Any adjustment made under this clause (1) shall become effective immediately after the open of business on the ex-dividend date for such dividend or distribution, or immediately after the open of business on the effective date for such share split or share combination, as applicable. If any dividend or distribution of the type described

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in this clause (1) is declared but not so paid or made, the conversion rate shall be immediately readjusted, effective as of the date our board of directors or a committee thereof determines not to pay such dividend or distribution, to the conversion rate that would then be in effect if such dividend or distribution had not been declared.

(2) If we issue to all or substantially all holders of our common stock any rights, options or warrants (other than in connection with a stockholder rights plan) entitling them, for a period of not more than 60 calendar days after the announcement date of such issuance, to subscribe for or purchase shares of our common stock at a price per share that is less than the average of the last reported sale prices of our common stock for the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the date of announcement of such issuance, the conversion rate will be increased based on the following formula:

$$CR_1 = CR_0 \times \frac{OS_0 + Y}{OS_0 + Z}$$

where,

$CR_0$  = the conversion rate in effect immediately prior to the open of business on the ex-dividend date for such issuance;

$CR_1$  = the conversion rate in effect immediately after the open of business on such ex-dividend date;

$OS_0$  = the number of shares of our common stock outstanding immediately prior to the open of business on such ex-dividend date;

$Y$  = the total number of shares of our common stock issuable pursuant to such rights, options or warrants; and

$Z$  = the number of shares of our common stock equal to the aggregate price payable to exercise such rights, options or warrants, *divided* by the average of the last reported sale prices of our common stock over the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the date of announcement of the issuance of such rights, options or warrants.

Any increase made under this clause (2) will be made successively whenever any such rights, options or warrants are issued and shall become effective immediately after the open of business on the ex-dividend date for such issuance. To the extent that shares of common stock are not delivered after the expiration of such rights, options or warrants, the conversion rate shall be decreased to the conversion rate that would then be in effect had the increase with respect to the issuance of such rights, options or warrants been made on the basis of delivery of only the number of shares of common stock actually delivered. If such rights, options or warrants are not so issued, the conversion rate shall be decreased to the conversion rate that would then be in effect if such ex-dividend date for such issuance had not occurred.

For the purpose of this clause (2) and for the purpose of the first bullet point under Conversion upon Specified Corporate Events Certain Distributions, in determining whether any rights, options or warrants entitle the holders to subscribe for or purchase shares of our common stock at less than such average of the last reported sale prices for the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the date of announcement of such issuance, and in determining the aggregate offering price of such shares of common stock, there shall be taken into account any consideration received by us for such rights, options or warrants and any amount payable on exercise or conversion thereof, the value of such consideration, if other than cash, to be determined by our board of directors or a committee thereof.

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(3) If we distribute shares of our capital stock, evidences of our indebtedness, other assets or property of ours or rights, options or warrants to acquire our capital stock or other securities, to all or substantially all holders of our common stock, excluding:

dividends, distributions or issuances (including share splits) as to which an adjustment was effected pursuant to clause (1) or (2) above;

dividends or distributions paid exclusively in cash as to which the provisions set forth in clause (4) below shall apply;

except as otherwise described below, rights issued pursuant to a stockholder rights plan of ours;

distributions of reference property in a transaction described in Recapitalizations, Reclassifications, and Changes of Our Common Stock; and

spin-offs as to which the provisions set forth below in this clause (3) shall apply;  
then the conversion rate will be increased based on the following formula:

$$CR_1 = CR_0 \times \frac{SP_0}{SP_0 + FMV}$$

where,

$CR^0$  = the conversion rate in effect immediately prior to the open of business on the ex-dividend date for such distribution;

$CR_1$  = the conversion rate in effect immediately after the open of business on such ex-dividend date;

$SP_0$  = the average of the last reported sale prices of our common stock over the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the ex-dividend date for such distribution; and

$FMV$  = the fair market value (as determined by our board of directors or a committee thereof) of the shares of capital stock, evidences of indebtedness, assets, property, rights, options or warrants distributed with respect to each outstanding share of our common stock on the ex-dividend date for such distribution.

Any increase made under the portion of this clause (3) above will become effective immediately after the open of business on the ex-dividend date for such distribution. If such distribution is not so paid or made, the conversion rate shall be decreased to be the conversion rate that would then be in effect if such distribution had not been declared. If we issue rights, options or warrants that are only exercisable upon the occurrence of certain triggering events, then we will not adjust the conversion rate pursuant to the clauses above until the earliest of these triggering events occurs, and

we will readjust the conversion rate to the extent that any of these rights, options or warrants are not exercised before they expire. In the case of any distribution of rights, options or warrants, to the extent any such rights, options or warrants expire unexercised, the conversion rate shall be immediately readjusted to the conversion rate that would then be in effect had the increase made for the distribution of such rights, options or warrants been made on the basis of delivery of only the number of shares of our common stock actually delivered upon exercise of such rights, options or warrants.

Notwithstanding the foregoing, if FMV (as defined above) is equal to or greater than  $\frac{1}{10}$  of the FMV (as defined above), in lieu of the foregoing increase, each holder of a note shall receive, in respect of each \$1,000 principal amount thereof, at the same time and upon the same terms as holders of our common stock, the amount and kind of our capital stock, evidences of our indebtedness, other assets or property of ours or rights, options or warrants to acquire our capital stock or other securities that such holder would have received if such holder owned a number of shares of common stock equal to the conversion rate in effect on the ex-dividend date for the distribution.

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With respect to an adjustment pursuant to this clause (3) where there has been a payment of a dividend or other distribution on our common stock of shares of capital stock of any class or series, or similar equity interest, of or relating to a subsidiary or other business unit, that are, or, when issued, will be, listed or admitted for trading on a U.S. national securities exchange, which we refer to as a spin-off, the conversion rate will be increased based on the following formula:

$$CR_1 = CR_0 \times \frac{FMV_0 + MP_0}{MP_0}$$

where,

$CR_0$  = the conversion rate in effect immediately prior to the end of the valuation period (as defined below);

$CR_1$  = the conversion rate in effect immediately after the end of the valuation period;

$FMV_0$  = the average of the last reported sale prices of the capital stock or similar equity interest distributed to holders of our common stock applicable to one share of our common stock (determined by reference to the definition of last reported sale price set forth under Conversion upon Satisfaction of Sale Price Condition as if references therein to our common stock were to such capital stock or similar equity interest) over the first 10 consecutive trading day period after, and including, the ex-dividend date of the spin-off (the valuation period); *provided* that if there is no last reported sale price of the capital stock or similar equity interest distributed to the holders of our common stock on such ex-dividend date, the valuation period shall be the first ten consecutive trading day period after, and including, the first date such last reported sale price is available; and

$MP_0$  = the average of the last reported sale prices of our common stock over the valuation period.

The increase to the conversion rate under the preceding paragraph will occur at the close of business on the last trading day of the valuation period; provided that (x) in respect of any conversion of notes for which physical settlement is applicable, if the relevant conversion date occurs during the valuation period, the reference to 10 in the preceding paragraph shall be deemed replaced with such lesser number of trading days as have elapsed from, and including, the ex-dividend date for such spin-off to, and including, such conversion date in determining the conversion rate and (y) in respect of any conversion of notes for which cash settlement or combination settlement is applicable, for any trading day that falls within the relevant observation period for such conversion and within the valuation period, the reference to 10 in the preceding paragraph shall be deemed replaced with such lesser number of trading days as have elapsed from, and including, the ex-dividend date for such spin-off to, and including, such trading day in determining the conversion rate as of such trading day of such observation period. If any dividend or distribution that constitutes a spin-off is declared but not so paid or made, the conversion rate shall be immediately decreased, effective as of the date our board of directors or a committee thereof determines not to pay or make such dividend or distribution, to the conversion rate that would then be in effect if such dividend or distribution had not been declared or announced.

(4) If any cash dividend or distribution is made to all or substantially all holders of our common stock, the conversion rate will be adjusted based on the following formula:



$$CR_1 = CR_0 \times \frac{SP_0}{SP_0 - C}$$

where,

$CR_0$  = the conversion rate in effect immediately prior to the open of business on the ex-dividend date for such dividend or distribution;

$CR_1$  = the conversion rate in effect immediately after the open of business on the ex-dividend date for such dividend or distribution;

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$SP_0$  = the last reported sale price of our common stock on the trading day immediately preceding the ex-dividend date for such dividend or distribution; and

$C$  = the amount in cash per share we distribute to all or substantially all holders of our common stock. Any increase made under this clause (4) shall become effective immediately after the open of business on the ex-dividend date for such dividend or distribution. If such dividend or distribution is not so paid, the conversion rate shall be decreased, effective as of the date our board of directors or a committee thereof determines not to make or pay such dividend or distribution, to be the conversion rate that would then be in effect if such dividend or distribution had not been declared.

Notwithstanding the foregoing, if  $C$  (as defined above) is equal to or greater than  $SP_0$  (as defined above), in lieu of the foregoing increase, each holder of a note shall receive, for each \$1,000 principal amount of notes, at the same time and upon the same terms as holders of shares of our common stock, the amount of cash that such holder would have received if such holder owned a number of shares of our common stock equal to the conversion rate in effect on the ex-dividend date for such cash dividend or distribution.

(5) If we or any of our subsidiaries make a payment in respect of a tender or exchange offer for our common stock that is subject to the then-applicable tender offer rules under the Exchange Act, other than an odd lot tender offer, to the extent that the cash and value of any other consideration included in the payment per share of common stock exceeds the average of the last reported sale prices of our common stock over the 10 consecutive trading day period commencing on, and including, the trading day next succeeding the last date on which tenders or exchanges may be made pursuant to such tender or exchange offer, the conversion rate will be increased based on the following formula:

$$CR_1 = CR_0 \times \frac{AC + (SP_1 \times OS_1)}{OS \times SP_1}$$

where,

$CR_0$  = the conversion rate in effect immediately prior to the close of business on the 10th trading day immediately following, and including, the trading day next succeeding the date such tender or exchange offer expires;

$CR_1$  = the conversion rate in effect immediately after the close of business on the 10th trading day immediately following, and including, the trading day next succeeding the date such tender or exchange offer expires;

$AC$  = the aggregate value of all cash and any other consideration (as determined by our board of directors or a committee thereof) paid or payable for shares purchased in such tender or exchange offer;

$OS_0$  = the number of shares of our common stock outstanding immediately prior to the date such tender or exchange offer expires (prior to giving effect to the purchase of all shares accepted for purchase or exchange in such tender or exchange offer);

$OS_1$  = the number of shares of our common stock outstanding immediately after the date such tender or exchange offer expires (after giving effect to the purchase of all shares accepted for purchase or exchange in such tender or exchange offer); and

$SP_1$  = the average of the last reported sale prices of our common stock over the 10 consecutive trading day period commencing on, and including, the trading day next succeeding the date such tender or exchange offer

expires.

The increase to the conversion rate under the preceding paragraph will occur at the close of business on the 10th trading day immediately following, and including, the trading day immediately following the date such

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tender or exchange offer expires; provided that (x) in respect of any conversion of notes for which physical settlement is applicable, if the relevant conversion date occurs during the 10 trading days immediately following, and including, the trading day next succeeding the expiration date of any tender or exchange offer, references to 10 or 10th in the preceding paragraph shall be deemed replaced with such lesser number of trading days as have elapsed from, and including, the trading day next succeeding the expiration date of such tender or exchange offer to, and including, such conversion date in determining the conversion rate and (y) in respect of any conversion of notes for which cash settlement or combination settlement is applicable, for any trading day that falls within the relevant observation period for such conversion and within the 10 trading days immediately following, and including, the trading day immediately following the expiration date of any tender or exchange offer, references to 10 or 10th in the preceding paragraph shall be deemed replaced with such lesser number of trading days as have elapsed from, and including, the trading day next succeeding such expiration date of such tender or exchange offer to, and including, such trading day in determining the conversion rate as of such trading day.

If we are or one of our subsidiaries is obligated to purchase our common stock pursuant to any such tender or exchange offer described in this clause (5) but we are, or such subsidiary is, permanently prevented by applicable law from effecting any such purchase or all such purchases are rescinded, the conversion rate will be decreased to be the conversion rate that would then be in effect if such tender or exchange offer had not been made or had been made only in respect of the purchases that have been effected.

Notwithstanding the foregoing, if a conversion rate adjustment becomes effective on any ex-dividend date as described above, and a holder that has converted its notes on or after such ex-dividend date and on or prior to the related record date would be treated as the record holder of shares of our common stock as of the related conversion date as described under Settlement upon Conversion based on an adjusted conversion rate for such ex-dividend date, then, notwithstanding the foregoing conversion rate adjustment provisions, the conversion rate adjustment relating to such ex-dividend date will not be made for such converting holder. Instead, such holder will be treated as if such holder were the record owner of the shares of our common stock on an unadjusted basis and participate in the related dividend, distribution or other event giving rise to such adjustment.

Except as stated herein, we will not adjust the conversion rate for the issuance of shares of our common stock or any securities convertible into or exchangeable for shares of our common stock or the right to purchase shares of our common stock or such convertible or exchangeable securities.

As used in this section, ex-dividend date means the first date on which the shares of our common stock trade on the applicable exchange or in the applicable market, regular way, without the right to receive the issuance, dividend or distribution in question, from us or, if applicable, from the seller of our common stock on such exchange or market (in the form of due bills or otherwise) as determined by such exchange or market, and effective date means the first date on which the shares of our common stock trade on the applicable exchange or in the applicable market, regular way, reflecting the relevant share split or share combination, as applicable. For the avoidance of doubt, any alternative trading convention on the applicable exchange or market in respect of shares of our common stock under a separate ticker symbol or CUSIP number will not be considered regular way for this purpose.

As used in this section, record date means, with respect to any dividend, distribution or other transaction or event in which the holders of our common stock (or other applicable security) have the right to receive any cash, securities or other property or in which our common stock (or such other security) is exchanged for or converted into any combination of cash, securities or other property, the date fixed for determination of holders of our common stock (or such other security) entitled to receive such cash, securities or other property (whether such date is fixed by our board of directors or a duly authorized committee thereof, statute, contract or otherwise).

Subject to the applicable listing standards of the Nasdaq Global Select Market or the principal U.S. national or regional securities exchange on which our common stock is then traded if not the Nasdaq Global Select

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Market, we are permitted to increase the conversion rate of the notes by any amount for a period of at least 20 business days if our board of directors or a committee thereof determines that such increase would be in our best interest. Subject to the applicable listing standards of the Nasdaq Global Select Market or the principal U.S. national or regional securities exchange on which our common stock is then traded if not the Nasdaq Global Select Market, we may also (but are not required to) increase the conversion rate to avoid or diminish income tax to holders of our common stock or rights to purchase shares of our common stock in connection with a dividend or distribution of shares (or rights to acquire shares) or similar event.

A holder may, in some circumstances, including a distribution of cash dividends to holders of shares of our common stock, be deemed to have received a distribution subject to U.S. federal income tax as a result of an adjustment or the nonoccurrence of an adjustment to the conversion rate. For a discussion of the U.S. federal income tax treatment of an adjustment to the conversion rate, see U.S. Federal Income Tax Considerations.

If we have a rights plan in effect upon conversion of the notes into common stock, you will receive, in addition to any shares of common stock received in connection with such conversion, the rights under the rights plan. However, if, prior to any conversion, the rights have separated from the shares of common stock in accordance with the provisions of the applicable rights plan, the conversion rate will be adjusted at the time of separation as if we distributed to all or substantially all holders of our common stock, shares of our capital stock, evidences of indebtedness, assets, property, rights, options or warrants as described in clause (3) above, subject to readjustment in the event of the expiration, termination or redemption of such rights.

Notwithstanding any of the foregoing, the conversion rate will not be adjusted:

upon the issuance of any shares of our common stock pursuant to any present or future plan providing for the reinvestment of dividends or interest payable on our securities and the investment of additional optional amounts in shares of our common stock under any plan;

upon the issuance of any shares of our common stock or options or rights to purchase those shares pursuant to any present or future employee, director or consultant benefit or incentive plan or program of or assumed by us or any of our subsidiaries;

upon the issuance of any shares of our common stock pursuant to any option, warrant, right or exercisable, exchangeable or convertible security not described in the preceding bullet and outstanding as of the date the notes were first issued;

upon the repurchase of any shares of our common stock pursuant to an open-market share repurchase program or other buy-back transaction (including, without limitation, through any structured or derivative transactions such as accelerated share repurchase transactions or similar forward derivatives), or other buy-back transaction, that is not a tender offer or exchange offer of the nature described under clause (5) above;

solely for a change in the par value (or lack of par value) of our common stock; or

for accrued and unpaid interest, if any.

We will not adjust the conversion rate pursuant to the clauses above unless the adjustment would result in a change of at least 1% in the then effective conversion rate. However, we will carry forward any adjustment to the conversion rate that we would otherwise have to make and take that adjustment into account in any subsequent adjustment. Notwithstanding the foregoing, all such carried-forward adjustments shall be made with respect to the notes (i) in connection with any subsequent adjustment to the conversion rate of at least 1% of the conversion rate, (ii) regardless of whether the aggregate adjustment is less than 1% of the conversion rate, (x) on the conversion date (in the case of physical settlement) or (y) on each trading day of any observation period (in the case of cash settlement or combination settlement) and (iii) on the effective date of any make-whole fundamental change, in each case, unless the adjustment has already been made. Adjustments to the conversion rate will be calculated to the nearest 1/10,000th of a share.

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***Recapitalizations, Reclassifications and Changes of Our Common Stock***

In the case of:

any recapitalization, reclassification or change of our common stock (other than changes resulting from a subdivision or combination),

any consolidation, merger or combination involving us,

any sale, lease or other transfer to a third party of the consolidated assets of ours and our subsidiaries substantially as an entirety, or

any statutory share exchange,

in each case, as a result of which our common stock would be converted into, or exchanged for, stock, other securities, other property or assets (including cash or any combination thereof) (any such event, a share exchange event), then we or the successor or purchasing company, as the case may be, will execute with the trustee and without the consent of the holders a supplemental indenture providing that at and after the effective time of the share exchange event, the right to convert each \$1,000 principal amount of notes will be changed into a right to convert such principal amount of notes into the kind and amount of shares of stock, other securities or other property or assets (including cash or any combination thereof) that a holder of a number of shares of common stock equal to the conversion rate immediately prior to such share exchange event would have owned or been entitled to receive (the reference property) upon such share exchange event. The supplemental indenture providing that the notes will be convertible into reference property will provide for anti-dilution and other adjustments that are as nearly equivalent as possible to the adjustments described under Conversion Rate Adjustments above. If the reference property in respect of any transaction includes shares of stock, securities or other property or assets of a company other than us or the successor or purchasing corporation, as the case may be, in such transaction, such other company will also execute such supplemental indenture, and such supplemental indenture will contain such additional provisions to protect the interests of the holders, including the right of holders to require us to repurchase their notes upon a fundamental change as described under Fundamental Change Permits Holders to Require Us to Repurchase Notes below, as the board of directors reasonably considers necessary by reason of the foregoing. At and after the effective time of the share exchange event, (i) we will continue to have the right to determine the form of consideration to be paid or delivered, as the case may be, upon conversion of notes, as set forth under Settlement upon Conversion and (ii)(x) any amount payable in cash upon conversion of the notes as set forth under Settlement upon Conversion will continue to be payable in cash, (y) any shares of our common stock that we would have been required to deliver upon conversion of the notes as set forth under Settlement upon Conversion will instead be deliverable in the amount and type of reference property that a holder of that number of shares of our common stock would have received in such share exchange event and (z) the daily VWAP will be calculated based on the value of a unit of reference property that a holder of one share of our common stock would have received in such share exchange event. If the share exchange event causes our common stock to be converted into, or exchanged for, the right to receive more than a single type of consideration (determined based in part upon any form of stockholder election), the reference property into which the notes will be convertible will be deemed to be (i) the weighted average of the types and amounts of consideration received by the holders of our common stock that affirmatively make such an election or (ii) if no holders of our common stock affirmatively make such an election, the types and amount of consideration actually received by such holders. We will notify holders, the



trustee and the conversion agent (if other than the trustee) in writing of the weighted average as soon as practicable after such determination is made. If the holders of our common stock receive only cash in such share exchange event, then for all conversions that occur after the effective date of such share exchange event (i) the consideration due upon conversion of each \$1,000 principal amount of notes shall be solely cash in an amount equal to the conversion rate in effect on the conversion date (as may be increased as described under Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption ), multiplied by the price paid per share of common stock in such share exchange event and (ii) we will satisfy our conversion obligation by paying cash to converting holders on the second business day immediately following the conversion date.

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Whenever any provision of the indenture requires us to calculate the last reported sale prices, the daily VWAPs, the daily conversion values or the daily settlement amounts over a span of multiple days (including an observation period and the stock price for purposes of a make-whole fundamental change or redemption), we will make appropriate adjustments without duplication in respect of any adjustment made pursuant to the provisions described under

Conversion Rate Adjustments above) to each to account for any adjustment to the conversion rate that becomes effective, or any event requiring an adjustment to the conversion rate where the ex-dividend date, effective date or expiration date of the event occurs, at any time during the period when such last reported sale prices, daily VWAPs, daily conversion values or daily settlement amounts are to be calculated.

***Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption***

If (i) the effective date (as defined below) of a fundamental change (as defined below and determined after giving effect to any exceptions to or exclusions from such definition, but without regard to subclause (a) of the proviso in clause (2) of the definition thereof, a make-whole fundamental change ) occurs prior to the maturity date of the notes or (ii) we give a notice of optional redemption with respect to the notes as provided for under Optional Redemption and, in each case, a holder elects to convert its notes in connection with such make-whole fundamental change or redemption notice, as applicable, we will, under certain circumstances, increase the conversion rate for the notes so surrendered for conversion by a number of additional shares of common stock (the additional shares ), as described below. A conversion of notes will be deemed for these purposes to be in connection with such make-whole fundamental change if the relevant notice of conversion of the notes is received by the conversion agent from, and including, the effective date of the make-whole fundamental change up to, and including, the business day immediately prior to the related fundamental change repurchase date (or, in the case of a make-whole fundamental change that would have been a fundamental change but for subclause (a) of the proviso in clause (2) of the definition thereof, the 30th trading day immediately following the effective date of such make-whole fundamental change). A conversion of notes will be deemed for these purposes to be in connection with a redemption notice if the notice of conversion of the notes is received by the conversion agent from, and including, the date of the redemption notice until the close of business on the business day immediately preceding the redemption date.

Upon surrender of notes for conversion in connection with a make-whole fundamental change or optional redemption, we will, at our option, satisfy our conversion obligation by physical settlement, cash settlement or combination settlement, based on the conversion rate as increased to reflect the additional shares pursuant to the table set forth below, as described under Settlement upon Conversion. However, if the consideration for our common stock in any make-whole fundamental change described in clause (2) of the definition of fundamental change is composed entirely of cash, for any conversion of notes following the effective date of such make-whole fundamental change, the conversion obligation will be calculated based solely on the stock price (as defined below) for the transaction and will be deemed to be an amount of cash per \$1,000 principal amount of converted notes equal to the conversion rate (including any increase to reflect the additional shares as described in this section), *multiplied by* such stock price. In such event, the conversion obligation will be determined and paid to holders in cash on the second business day following the conversion date. We will notify holders, the trustee and the conversion agent (if other than the trustee) in writing of the effective date of any make-whole fundamental change no later than five business days after such effective date.

The number of additional shares, if any, by which the conversion rate will be increased will be determined by reference to the table below, based on the date on which the make-whole fundamental change occurs or becomes effective, or the date of the redemption notice, as the case may be (in each case, the effective date ) and the price paid

(or deemed to be paid) per share of our common stock in the make-whole fundamental change or with respect to the optional redemption, as the case may be (the stock price ). If the holders of our common stock receive in exchange for their common stock only cash in a make-whole fundamental change described in

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clause (2) of the definition of fundamental change, the stock price will be the cash amount paid per share. Otherwise, the stock price will be the average of the last reported sale prices of our common stock over the five trading-day period ending on, and including, the trading day immediately preceding the effective date of the make-whole fundamental change or the date of the redemption notice, as the case may be.

The stock prices set forth in the column headings of the table below will be adjusted as of any date on which the conversion rate of notes is otherwise adjusted. The adjusted stock prices will equal the stock prices immediately prior to such adjustment, *multiplied by* a fraction, the numerator of which is the conversion rate immediately prior to the adjustment giving rise to the stock price adjustment and the denominator of which is the conversion rate as so adjusted. The number of additional shares as set forth in the table below will be adjusted in the same manner and at the same time as the conversion rate as set forth under Conversion Rate Adjustments.

The following table sets forth the number of additional shares by which the conversion rate for the notes will be increased per \$1,000 principal amount of notes for each stock price and effective date set forth below:

Effective Date	Stock Price											
	\$3.52	\$4.00	\$4.22	\$4.75	\$5.49	\$6.50	\$8.00	\$10.00	\$12.00	\$15.00	\$20.00	\$25.00
February 7, 2019	47.3485	47.3485	47.3485	47.3485	37.5692	27.0730	17.6326	10.6176	6.6409	3.3309	0.8926	0.0050
February 15, 2020	47.3485	47.3485	47.3485	46.4997	35.0015	24.8268	15.8576	9.3776	5.7826	2.8243	0.6926	0.0000
February 15, 2021	47.3485	47.3485	47.3485	42.8787	31.6142	21.9038	13.6451	7.8776	4.7659	2.2576	0.4826	0.0000
February 15, 2022	47.3485	47.3485	47.3485	37.9313	27.0615	18.1038	10.8576	6.0876	3.6076	1.6443	0.2876	0.0000
February 15, 2023	47.3485	47.3485	42.5426	31.0471	20.8698	13.1038	7.4326	4.0476	2.3659	1.0443	0.1126	0.0000
February 15, 2024	47.3485	38.5076	31.7708	20.6260	11.9828	6.5499	3.4701	1.9376	1.1659	0.5043	0.0026	0.0000
February 15, 2025	47.3485	13.2576	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

The exact stock prices and effective dates may not be set forth in the table above, in which case

If the stock price is between two stock prices in the table or the effective date is between two effective dates in the table, the number of additional shares by which the conversion rate for the notes will be increased will be determined by a straight-line interpolation between the number of additional shares set forth for the higher and lower stock prices and the earlier and later effective dates, as applicable, based on a 365-day year.

If the stock price is greater than \$25.00 per share (subject to adjustment in the same manner as the stock prices set forth in the column headings of the table above), no additional shares will be added to the conversion rate for the notes.

If the stock price is less than \$3.52 per share (subject to adjustment in the same manner as the stock prices set forth in the column headings of the table above), no additional shares will be added to the conversion rate for the notes.

Notwithstanding the foregoing, in no event will the conversion rate per \$1,000 principal amount of notes exceed 284.0909 shares of common stock, subject to adjustment in the same manner as the conversion rate as set forth under Conversion Rate Adjustments.

Our obligation to increase the conversion rate for notes converted in connection with a make-whole fundamental change could be considered a penalty, in which case the enforceability thereof would be subject to general principles of reasonableness and equitable remedies.

#### **Fundamental Change Permits Holders to Require Us to Repurchase Notes**

If a fundamental change (as defined below in this section) occurs at any time prior to the maturity date of the notes, holders will have the right, at their option, to require us to repurchase for cash all of their notes, or any

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portion of the principal thereof that is equal to \$1,000 or a multiple of \$1,000. The fundamental change repurchase date will be a date specified by us that is not less than 20 or more than 35 business days following the date of our fundamental change notice as described below.

The fundamental change repurchase price we are required to pay will be 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 (unless the fundamental change repurchase date falls after a regular record date but on or prior to the interest payment date to which such regular record date relates, in which case we will instead pay the full amount of accrued and unpaid interest to the holder of record on such regular record date, and the fundamental change repurchase price will be equal to 100% of the principal amount of the notes to be repurchased).

A fundamental change will be deemed to have occurred at the time after the notes are originally issued if any of the following occurs:

(1) a person or group within the meaning of Section 13(d) of the Exchange Act, other than us, our wholly-owned subsidiaries and our and their employee benefit plans and other than Phillip Frost, M.D. or entities directly or indirectly controlled by him or established for the benefit of him or his descendants or spouses or charities (collectively, the permitted owners), has become the direct or indirect beneficial owner, as defined in Rule 13d-3 under the Exchange Act, of our common equity representing more than 50% of the voting power of our common equity or the permitted owners have (or any group within the meaning of Section 13(d) of the Exchange Act including any permitted owner has) become the direct or indirect beneficial owners, as defined in Rule 13d-3 under the Exchange Act, of our common equity representing more than 70% of the voting power of our common equity;

(2) the consummation of (A) any recapitalization, reclassification or change of our common stock (other than changes resulting from a subdivision, a combination or merely a change in par value) as a result of which our common stock would be converted into, or exchanged for, stock, other securities, other property or assets; (B) any share exchange, consolidation or merger of us pursuant to which our common stock will be converted into cash, securities or other property or assets; or (C) any sale, lease or other transfer in one transaction or a series of related transactions of all or substantially all of the consolidated assets of us and our subsidiaries, taken as a whole, to any person other than one or more of our subsidiaries; *provided, however*, that neither (a) a transaction described in clause (B) in which the holders of all classes of our common equity immediately prior to such transaction own, directly or indirectly, more than 50% of all classes of common equity of the continuing or surviving corporation or transferee or the parent thereof immediately after such transaction in substantially the same proportions as such ownership immediately prior to such transaction or (b) any merger of us solely for the purpose of changing our jurisdiction of incorporation that results in a reclassification, conversion or exchange of outstanding shares of common stock solely into shares of common stock of the surviving entity shall be a fundamental change pursuant to this clause (2);

(3) our stockholders approve any plan or proposal for the liquidation or dissolution of us; or

(4) our common stock (or other common stock underlying the notes) ceases to be listed or quoted on any of the New York Stock Exchange, the Nasdaq Global Select Market or the Nasdaq Global Market (or any of their respective successors).

A transaction or transactions described in clause (2) above will not constitute a fundamental change, however, if at least 90% of the consideration received or to be received by our common stockholders, excluding cash payments for fractional shares or pursuant to statutory appraisal rights, in connection with such transaction or transactions consists of shares of common stock or other common equity that are listed or quoted on any of the New York Stock Exchange, the Nasdaq Global Select Market or the Nasdaq Global Market (or any of their respective successors) or will be so

listed or quoted when issued or exchanged in connection with such

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transaction or transactions and as a result of such transaction or transactions the notes become convertible into such consideration, excluding cash payments for fractional shares or pursuant to statutory appraisal rights (subject to the provisions set forth above under **Conversion Rights Settlement upon Conversion** ).

If any transaction in which our common stock is replaced by the securities of another entity occurs, following the effective date of such transaction, references to us in the definition of **fundamental change** above shall instead be references to such other entity.

For purposes of the definition of **fundamental change** above, any transaction that constitutes a fundamental change pursuant to both clause (1) and clause (2) of such definition (without giving effect to the proviso to clause (2)) shall be deemed a fundamental change solely under clause (2) of such definition (subject to the proviso to clause (2)).

Notwithstanding the foregoing, we will not be required to repurchase, or to make an offer to repurchase, the notes upon a fundamental change if a third party makes such an offer in the same manner, at the same time and otherwise in compliance with the requirements for an offer made by us as set forth above and such third party purchases all notes properly surrendered and not validly withdrawn under its offer in the same manner, at the same time and otherwise in compliance with the requirements for an offer made by us as set forth above.

On or before the 20th business day after the occurrence of a fundamental change, we will provide to all holders of the notes and the trustee and paying agent a written notice of the occurrence of the fundamental change and of the resulting repurchase right. Such notice shall state, among other things:

the events causing a fundamental change;

the effective date of the fundamental change;

the last date on which a holder may exercise the repurchase right;

the fundamental change repurchase price;

the fundamental change repurchase date;

the name and address of the paying agent and the conversion agent, if applicable;

if applicable, the conversion rate and any adjustments to the conversion rate;

that the notes with respect to which a fundamental change repurchase notice has been delivered by a holder may be converted only if the holder validly withdraws the fundamental change repurchase notice in accordance with the terms of the indenture; and



