UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the fiscal year ended: December 31, 2021

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

Commission file number 001-35092

EXACT SCIENCES CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**02-0478229**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
5505 Endeavor Lane, Madison, Wisconsin	**53719**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(608) 284-5700**

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

Common Stock, $0.01 Par Value	**EXAS**	**The Nasdaq Stock Market LLC**

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such report(s), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

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

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

Large accelerated filer ☒	Accelerated filer ☐	Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting compan ☐	Emerging growth ☐

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, as of the last business day of the Registrant's most recently completed second fiscal quarter was approximately 21,211,910,456 (based on the closing price of the Registrant's Common Stock on June 30, 2021 of $124.31 per share).

The number of shares outstanding of the Registrant's $0.01 par value Common Stock as of February 21, 2022 was 174,116,598.

DOCUMENT INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days after the end of the fiscal year ended December 31, 2021. Portions of such proxy statement are incorporated by reference into Part III of this Form 10-K.

EXACT SCIENCES CORPORATION
ANNUAL REPORT ON FORM 10-K
YEAR ENDED DECEMBER 31, 2021

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PART I

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that are intended to be covered by the "safe harbor" created by those sections. Forward-looking statements, which are based on certain assumptions and describe our future plans, strategies and expectations, can generally be identified by the use of forward-looking terms such as "believe," "expect," "may," "will," "should," "would," "could," "seek," "intend," "plan," "goal," "project," "estimate," "anticipate" or other comparable terms. All statements other than statements of historical facts included in this Annual Report on Form 10-K regarding our strategies, prospects, expectations, financial condition, operations, costs, plans and objectives are forward-looking statements. Examples of forward-looking statements include, among others, statements we make regarding expected future operating results; our strategies, positioning, resources, capabilities and expectations for future events or performance; and the anticipated benefits of our acquisitions, including estimated synergies and other financial impacts. Forward-looking statements are neither historical facts nor assurances of future performance or events. Instead, they are based only on current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Actual results, conditions and events may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause actual results, conditions and events to differ materially from those indicated in the forward-looking statements include, among others, the following: uncertainties associated with the coronavirus (COVID-19) pandemic, including its possible effects on our operations, including our supply chain and clinical studies, and the demand for our products and services; our ability to efficiently and flexibly manage our business amid uncertainties related to COVID-19; our ability to raise additional capital in amounts and on terms satisfactory to us, if at all; our ability to successfully and profitably market our products and services; the acceptance of our products and services by patients and healthcare providers; our ability to meet demand for our products and services; the willingness of health insurance companies and other payers to cover our products and services and adequately reimburse us for such products and services; the amount and nature of competition for our products and services; the effects of any judicial, executive or legislative action affecting us or the healthcare system; recommendations, guidelines and quality metrics issued by various organizations regarding cancer screening or our products and services; our ability to successfully develop new products and services and assess potential market opportunities; our ability to effectively enter into and utilize strategic partnerships and acquisitions; our success establishing and maintaining collaborative, licensing and supplier arrangements; our ability to obtain and maintain regulatory approvals and comply with applicable regulations; our ability to manage an international business and our expectations regarding our international expansion and opportunities; the potential effects of foreign currency exchange rate fluctuations and our efforts to hedge such effects; the possibility that the anticipated benefits from our business acquisitions will not be realized in full or at all or may take longer to realize than expected; the possibility that costs or difficulties related to the integration of acquired businesses' operations will be greater than expected and the possibility that integration efforts will disrupt our business and strain management time and resources; the outcome of any litigation, government investigations, enforcement actions or other legal proceedings, including in connection with acquisitions; our ability to retain and hire key personnel including employees at businesses we acquire; and the other risks and uncertainties described in the Risk Factors and in Management's Discussion and Analysis of Financial Condition and Results of Operations sections in this Annual Report on Form 10-K and our subsequently filed Quarterly Reports on Form 10-Q. You are further cautioned not to place undue reliance upon any such forward-looking statements, which speak only as of the date made. Except as otherwise required by the federal securities laws, we undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

Item 1. Business

Overview

Exact Sciences Corporation (together with its subsidiaries, "Exact," "we," "us," "our" or the "Company") is a leading, global, advanced cancer diagnostics company. We have developed some of the most impactful tests in cancer diagnostics, and we are currently working to develop additional tests, with the goal of bringing new, innovative cancer tests to patients throughout the world.

We are committed to making earlier cancer detection a routine part of medical care. From screening to treatment guidance, we seek to help people get the answers they need to make more informed decisions across the cancer continuum. Our revenues are primarily generated by our laboratory testing services from our Cologuard® colorectal cancer screening test, our Oncotype DX® cancer diagnostic tests and services, and our COVID-19 test.

We recently executed a number of significant and transformative projects and acquisitions to enhance shareholder value and bring new, innovative cancer tests to patients.

Significant recent developments include:

- Acquisition of PreventionGenetics — In December 2021, we acquired PreventionGenetics LLC ("PreventionGenetics"), a Clinical Laboratory Improvement Amendments ("CLIA") certified and College of American Pathologists ("CAP") accredited DNA testing laboratory, providing more than 5,000 predefined genetic tests for nearly all clinically relevant genes, additional custom panels, and comprehensive germline whole exome and whole genome sequencing tests. We intend to use PreventionGenetics' capabilities to expand the use of hereditary cancer testing ("HCT") in the U.S. and globally.
- Exclusive License of OncXerna Xerna™ TME Panel — In December 2021, we acquired an exclusive license to bring OncXerna Therapeutics, Inc.'s ("OncXerna") Xerna TME Panel lab services to U.S. patients. The Xerna TME Panel is an innovative gene expression score that helps identify patients likely to respond to anti-angiogenic- and immunotherapies.
- Pfizer — In September 2021, we completed an expedited hiring process and onboarded approximately 400 former Pfizer, Inc. ("Pfizer") sales representatives to increase adoption of our Cologuard test and our pipeline of innovative screening tests. Prior to late August 2021, when Pfizer announced a decrease in the number of sales positions supporting its Internal Medicine therapeutic area, these employees had been promoting our Cologuard test under our promotion agreement (the "Promotion Agreement") with Pfizer. Pursuant to a November 2021 amendment to our promotion agreement with Pfizer, Pfizer ceased promoting our Cologuard test on November 30, 2021.
- Acquisition of PFS Genomics — In May 2021, we acquired PFS Genomics Inc. ("PFS"), a healthcare company focused on personalizing treatment for breast cancer patients to improve outcomes and reduce unnecessary treatment.
- Acquisition of Ashion — In April 2021, we acquired Ashion Analytics, LLC ("Ashion"), a CLIA certified and CAP accredited sequencing lab and its developed oncomap™ ExTra test, also known as the GEM ExTra® test, one of the most comprehensive genomic cancer tests available. Ashion provides advanced whole exome, matched germline, and transcriptome sequencing capabilities.
- Exclusive License of TARDIS Technology — In January 2021, we acquired an exclusive license to The Translational Genomics Research Institute's ("TGen") proprietary Targeted Digital Sequencing ("TARDIS") technology for use in minimal residual disease ("MRD"). We are currently seeking to utilize TARDIS's compelling and technically distinct approach to develop a test to detect small amounts of tumor DNA that may remain in cancer patients' blood after they have undergone initial treatment.
- Acquisition of Thrive — In January 2021, we acquired Thrive Earlier Detection Corp. ("Thrive"), a healthcare company dedicated to developing a blood-based, multi-cancer early detection ("MCED") test. An early version of Thrive's MCED test achieved promising results with very few false positives in a 10,000-patient, prospective, interventional study. It detected 10 different types of cancer, including seven with no recommended screening tests available today.

Our Products and Services

With a leading portfolio of products for earlier cancer detection and treatment guidance, we provide patients with earlier, smarter answers. Our current products and services focus on screening and precision oncology tests.

Our Cologuard Test

Our flagship screening product, the Cologuard test, is a patient-friendly, non-invasive, stool-based DNA ("sDNA") screening test that utilizes a multi-target approach to detect DNA and hemoglobin biomarkers associated with colorectal cancer and pre-cancer. Eleven biomarkers are targeted that have been shown to be strongly associated with colorectal cancer and pre-cancer. Methylation, mutation, and hemoglobin results are combined in the laboratory analysis through a proprietary algorithm to provide a single positive or negative reportable result.

We believe the large underserved population of unscreened and inadequately screened patients represents a significant opportunity for our Cologuard test. It is widely accepted that colorectal cancer is among the most preventable, yet least prevented cancers. Colorectal cancer can take up to 10-15 years to progress from a pre-cancerous lesion to metastatic cancer and death. Patients who are diagnosed early in the progression of the disease — with pre-cancerous lesions or early-stage cancer — are more likely to have a complete recovery and to be treated less expensively. Colorectal cancer is the second leading cause of cancer deaths in the United States ("U.S.") and the leading cause of cancer deaths in the U.S. among non-smokers. Each year in the U.S. there are approximately 150,000 new cases of colorectal cancer and approximately 53,000 deaths.

Upon approval by the U.S. Food and Drug Administration ("FDA") in August 2014, our Cologuard test became the first and only FDA-approved sDNA non-invasive colorectal cancer screening test. In September 2019, the FDA expanded its indication to include average-risk individuals ages 45-49. Our Cologuard test is now indicated for average risk adults 45 years of age and older.

Our peer-reviewed study, "Multi-target Stool DNA Testing for Colorectal-Cancer Screening," published in the New England Journal of Medicine in April 2014, highlighted the performance of the Cologuard test in its 10,000 patient Deep-C clinical trial:

- Cancer Sensitivity: 92%
- Stage I and II Cancer Sensitivity: 94%
- High-Grade Dysplasia Sensitivity: 69%
- Specificity: 87%

We believe the competitive advantages of sDNA screening provide a significant market opportunity. There are nearly 110 million Americans between the ages of 45 and 85 who are at average risk for colorectal cancer. At a three-year screening interval and an average revenue per test of approximately $500, this represents a potential $18 billion market for our Cologuard test.

Approximately 45% of Americans between the ages of 45 and 85 who are at average risk for colorectal cancer are not up-to-date with screening according to the American Cancer Society's ("ACS") colorectal cancer screening guidelines. We believe our Cologuard test helps more people get screened for colorectal cancer. Internal studies have shown that approximately 40% of surveyed Cologuard users were previously unscreened for colorectal cancer.

Our Cologuard test is included in key guidelines and quality measures that many healthcare providers rely on when making screening recommendations.

- In its updated guidelines released in May 2021, the U.S. Preventive Services Task Force (“USPSTF”) gave an "A" grade to colorectal cancer screening starting at age 50 and continuing until age 75 and a "B" grade to colorectal cancer screening for ages 45 to 49. The updated guidelines include our Cologuard test (referred to in their statement as sDNA-FIT) as a recommended screening method for all average-risk patients in the 45-75 age group.
- The American Cancer Society has specifically included our Cologuard test as a recommended colorectal cancer screening test in average-risk, asymptomatic individuals. The ACS recommends colorectal cancer screening beginning at age 45 for people at average risk of colorectal cancer.
- The National Comprehensive Cancer Network (“NCCN”) includes sDNA screening at a once-every-three-years interval in its Colorectal Cancer Screening Guidelines.
- The National Committee for Quality Assurance (“NCQA”) includes sDNA testing on a three-year interval as one of the methods permitted for colorectal cancer screening in its most recent Healthcare Effectiveness Data and Information Set (“HEDIS”) quality measures.
- The Centers for Medicare & Medicaid Services (“CMS”) includes our Cologuard test in its most recent Medicare Advantage Star Ratings program.

Our Precision Oncology Tests

With our portfolio of Oncotype tests, we apply our world-class scientific and commercial expertise and infrastructure to lead the translation of clinical and genomic data into actionable results for treatment planning throughout the cancer patient's journey. We believe our Oncotype tests improve the quality of treatment decisions and the health economics of cancer care.

Our portfolio of Oncotype tests is currently comprised of:

- our flagship line of Oncotype DX gene expression tests for breast, prostate and colon cancers,
- Oncotype DX AR-V7 Nucleus Detect® test, a liquid-based test for advanced stage prostate cancer,
- Oncotype MAP™ Pan-Cancer Tissue test (“oncomap” test), a test delivering rapid, comprehensive tumor profiling to aid therapy selection for patients with advanced, metastatic, refractory or recurrent cancer, and
- GEM ExTra test, one of the most comprehensive genomic (DNA) and transcriptomic (RNA) panels available today that provides a complete biological picture of certain refractory, rare, or aggressive cancers.

Oncotype MAP Pan-Cancer Tissue test and GEM ExTra will be rebranded to oncomap and oncomap ExTra, respectively, in 2022.

Oncotype DX Breast Recurrence Score® Test

Our Oncotype DX Breast Recurrence Score test has been demonstrated to identify patients who are most likely to benefit from chemotherapy as well as those who may receive no clinical benefit from chemotherapy.

Among women, breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death. In 2022, nearly 288,000 women are expected to be diagnosed with invasive breast cancer in the U.S. according to ACS, and more than 51,000 women are expected to be diagnosed with non-invasive (in situ) breast cancer. Worldwide, it is estimated that there are approximately 2.3 million newly diagnosed cases of breast cancer each year.

The Oncotype DX breast cancer test examines the activity of 21 genes in a patient’s breast tumor tissue to provide personalized information for tailoring treatment based on the biology of the patient's individual disease. The test is supported by multiple rigorous clinical validation studies, including the landmark TAILORx and RxPONDER studies, confirming the test’s ability to predict the likelihood of chemotherapy benefit as well as the chance of cancer recurrence in certain common types of early-stage breast cancer.

As the only test proven to predict chemotherapy benefit, the Oncotype DX Breast Recurrence Score test is included in all major cancer guidelines worldwide, and is considered a standard of care for women with early-stage breast cancer.

Oncotype DX Breast DCIS Score® Test

Our Oncotype DX DCIS test provides ductal carcinoma in situ ("DCIS") patients an individualized prediction of the 10-year risk of local recurrence (DCIS or invasive carcinoma), represented by a DCIS Score® result. This test helps guide treatment decision-making in women with DCIS treated by local excision, with or without tamoxifen. Development of our Oncotype DX Breast DCIS Score test was based on published results for the Oncotype DX Breast Recurrence Score test that showed similarity in the expression profiles of genes between DCIS and invasive breast cancer when both are present within the same patient tumor.

Oncotype DX Colon Recurrence Score® Test

In patients with stage II and stage III colon cancer, the decision to treat with chemotherapy following surgery is based on an assessment of the likelihood of cancer recurrence and as a result, it is critical for clinicians to accurately assess a patient's risk of recurrence. Our Oncotype DX Colon Recurrence Score test is a multi-gene test for predicting recurrence risk in patients with stage II and stage III A/B colon cancer to enable an individualized approach to treatment planning. By evaluating specific genes within a patient’s colon tumor, the test can determine the likelihood that the cancer cells will spread and cause the disease to return after surgery. Based on this information, healthcare providers and patients can make more informed treatment decisions. The Oncotype DX colon cancer test is supported by three rigorous clinical validation studies confirming the test’s ability to provide additional and independent value beyond the currently used measures for determining colon cancer recurrence risk.

Oncotype DX Genomic Prostate Score® Test

Worldwide, prostate cancer ranks as the second most frequent cancer and the fifth leading cause of cancer death in men. Our Oncotype DX Genomic Prostate Score (“GPS™”) test helps men newly diagnosed with early-stage prostate cancer make the most informed treatment decision for their individual disease, including active surveillance. Our prostate needle biopsy-based, multi-gene test has been clinically validated to predict aggressive cancer at the time of diagnosis, helping to identify those men who need immediate surgery or radiation therapy versus those who can confidently choose active surveillance. The result is a more precise and accurate assessment of risk, which helps more men avoid the lifelong complications associated with treatments they do not need, while directing aggressive therapy to those men who require immediate treatment.

Oncotype DX AR-V7 Nucleus Detect Test

Our Oncotype DX AR-V7 Nucleus Detect test is a blood-based test designed to guide treatment decisions for men with metastatic castration-resistant prostate cancer (“mCRPC”), an advanced stage of the disease in which the cancer continues to grow and spread despite androgen deprivation therapy. mCRPC is often treated with androgen receptor-signaling inhibitor (“ARSI”) therapies. However, one in three patients become resistant to ARSI therapy after two rounds of treatment, leading to poor outcomes and unnecessary treatment costs. Epic Sciences developed and performs the Oncotype DX AR-V7 Nucleus Detect test. We commercialize the test pursuant to an exclusive license and distribution agreement with Epic Sciences.

Oncomap Pan-Cancer Tissue Test

In October 2020, we introduced the oncomap test, previously known as Oncotype MAP, a rapid, comprehensive tumor profiling panel that aids therapy selection for patients with advanced, metastatic, refractory, or recurrent cancer. The oncomap test utilizes next generation sequencing and immunohistochemistry to provide in-depth insights into genomic alterations in hundreds of cancer-related genes. The oncomap test report supports clinical decision making by showing actionable biomarkers associated with more than 100 evidence-based therapies, over 45 combination therapies, and more than 650 active clinical trial associations. The identification of these biomarkers helps inform treatment options for a breadth of solid tumor types.

Oncomap ExTra Test

In April 2021, we began performing and selling the oncomap ExTra test, also known as GEM ExTra, as a result of our acquisition of Ashion. The oncomap ExTra test provides physicians with vital information to understand changes to a patient's genomic profile. This information can provide a more complete biological picture of certain refractory, rare, or aggressive cancers, helping patients and physicians make informed choices when considering therapeutic treatment plans. The oncomap ExTra is a comprehensive sequencing test, including both genomic and transcriptomic panels and approximately 20,000 genes and 169 introns.

COVID-19 Testing

In late March 2020, we began providing COVID-19 testing. We have partnered with various customers, including the State of Wisconsin Department of Health, to administer testing. Customers are responsible for employing trained personnel to collect specimens. Specimens are sent to our laboratory in Madison, Wisconsin, where we run the assay in our laboratories and provide test results to ordering providers. In light of the uncertainty surrounding the COVID-19 pandemic, we intend to periodically reassess offering COVID-19 testing. Although we expect that demand for our COVID-19 testing services will decline as the pandemic abates, as discussed below, demand for these services remained relatively strong during the year ended December 31, 2021, particularly during times when there were higher COVID-19 caseloads in Wisconsin.

Pipeline Research and Development

Our research and development efforts are focused on developing new products and enhancing existing products to address unmet cancer needs and expand the clinical utility and addressable patient populations for our existing tests. We are focused on enhancing our Cologuard test's performance characteristics and developing blood and other liquid-based ("liquid biopsy") tests. These development efforts may lead to a variety of new products, including risk assessment, screening and prevention, early disease diagnosis, adjuvant and/or neoadjuvant disease treatment, metastatic disease treatment selection, and patient monitoring.

Through our collaboration with the Mayo Foundation for Medical Education and Research ("Mayo"), we have successfully performed validation studies involving multiple types of cancer using tissue, blood, and other samples. In September 2020, Mayo agreed to make available certain personnel to provide us research development assistance through January 2025. Through recent business development activities, we have also acquired exclusive access to technologies developed by The Johns Hopkins University, TGen, Oxford University, and the Ludwig Institute for Cancer Research.

We expect to advance liquid biopsy through biomarker discovery and validation in tissue, blood, or other fluids and to leverage recent business development activities to accelerate our leadership in earlier cancer detection and treatment guidance. We are pursuing the following opportunities:

- *Colorectal Cancer Screening.* We are seeking opportunities to improve upon our Cologuard test's performance characteristics. In January 2022, we and Mayo presented at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium findings from a study including prospectively collected samples that showed overall sensitivity of 95% for colorectal cancer at specificity of 92%. Subgroup analyses showed 83% sensitivity for high-grade dysplasia, the most dangerous pre-cancerous lesions, and 57% for all advanced pre-cancerous lesions. To establish the performance of an enhanced multi-target stool DNA test, we expect to enroll at least 20,000 patients 40 years of age and older in our multi-center, prospective BLUE-C study. The timing of any such enhancements to our Cologuard test is unknown and would be subject to FDA approval. We are also working to develop a blood-based screening test for colorectal cancer.
- *Multi-Cancer Early Detection Test Development.* We are currently seeking to develop a blood-based, MCED test. In January 2021, we completed the acquisition of Thrive, a healthcare company dedicated to developing a blood-based, MCED test. An early version of Thrive's test achieved promising results in a 10,000-patient, prospective, interventional study detecting 10 different types of cancer, including seven with no current recommended screening test available, with very few false positives. We intend to combine Thrive's expertise with our scientific capabilities, clinical organization, and commercial infrastructure to bring an accurate blood-based, multi-cancer early detection test to patients faster.
- *Minimal Residual Disease and Recurrence Monitoring Test Development.* In January 2021, we acquired an exclusive license to TGen's proprietary TARDIS technology. We are currently seeking to utilize this compelling and technically distinct approach to develop a tumor-informed test to detect small amounts of tumor DNA that may remain in patients' blood after they have undergone initial treatment. In a 2019 study published in Science Translational Medicine, TARDIS demonstrated high accuracy in assessing molecular response and residual disease during neoadjuvant therapy to treat breast cancer. The study reported that TARDIS achieved up to 100-fold improvement over alternative circulating tumor DNA detection methods. We are also working on a tumor-naive approach to MRD and recurrence monitoring in order to support patients where there is no access to the tumor tissue to inform patient-specific biomarker targets. We have published data showing the ability of cancer-associated methylation markers to reliably detect distantly recurrent colorectal cancer from a blood draw with promising accuracy.
- *Hereditary Cancer Testing.* In December 2021, we acquired PreventionGenetics, a DNA testing laboratory that provides more than 5,000 predefined genetic tests for nearly all clinically relevant genes, additional custom panels, and comprehensive germline whole exome and whole genome sequencing tests. We intend to use PreventionGenetics' capabilities to expand the use of hereditary cancer testing in the U.S. and globally.
- *Hepatocellular Carcinoma ("HCC") Test Development.* We are currently developing a blood-based biomarker test to serve as an alternative to ultrasound and alpha-fetoprotein ("AFP") for use in HCC testing. HCC is the most common type of liver cancer. Our goal is to provide a patient-friendly test that performs better than the current guideline-recommended testing options. In August 2021, the performance of our Oncoguard™ Liver liquid biopsy test was published in the peer-reviewed journal, Clinical Gastroenterology and Hepatology. The test delivers 82% early-stage sensitivity and an overall 88% sensitivity for HCC at 87% specificity with a novel combination of six blood-based biomarkers for HCC. The study compared performance to the AFP test, which demonstrated 40% sensitivity for early stage HCC at 100% specificity. Our test was made available on a limited basis beginning in the second quarter of 2021.
- *Development Studies for Oncotype DX Products.* We may also conduct or fund clinical studies that could support additional opportunities for our Oncotype DX products. For example, we are exploring clinical studies to expand the use of genomic testing to address additional populations, including higher-risk patients. In addition, we are using technology from our acquisition of PFS Genomics to better personalize treatment for breast cancer patients, improve outcomes, and reduce unnecessary treatment.

Research and development, which includes our clinical study programs, accounts for a material portion of our operating expenses. As we seek to enhance our current product portfolio and expand our product pipeline by developing additional cancer screening and diagnostic tests, we expect that our research and development expenditures will continue to increase.

Commercial Operations

We operate within a single business segment, with commercial teams focused on screening, precision oncology, and international markets. The COVID-19 pandemic has disrupted our commercial operations, including the suspension of face-to-face interactions between sales representatives and healthcare providers. The severity of the pandemic and its effects on our operations has varied over time and from region to region. Although our sales force has resumed field-based interactions, access to healthcare providers remains limited.

Cologuard Test Commercial Operations

We promote our Cologuard test through our primary care, gastroenterology, women's health, and health systems field sales teams, as well as through an inside sales team. Pfizer previously promoted our Cologuard test and provided certain sales, marketing, analytical, and other commercial operations support pursuant to the Promotion Agreement. Effective November 30, 2021, we and Pfizer entered into an amendment to the Promotion Agreement, which terminated Pfizer's services, other than Pfizer's advertisement purchasing services, which will continue through September 2022.

Our sales team actively engages with healthcare providers and their staff to emphasize the need for colorectal cancer screening, educate them on the value of our Cologuard test, and facilitate their ability to order the test. We focus on specific healthcare providers based on a combination of Cologuard order history and ordering potential data. We also focus on healthcare provider groups and larger regional and national health systems.

A critical part of the value proposition of our Cologuard test is its adherence program, which involves active engagement with patients and providers by our adherence team. This customer-oriented support activity is focused on encouraging and helping patients complete Cologuard tests that have been ordered for them by their providers. We undertake a variety of activities to promote patient adherence including letters, text messages, online chat, emails, and phone calls.

We have undertaken a significant public relations effort to engage patients in the U.S., and launched demographically-targeted, direct-to-patient advertising campaigns in digital, social, print, and other channels. We promote our Cologuard test through a national television advertising campaign, with a majority of placements in national cable and syndicated programming widely viewed by our target patient demographic. During 2021, in response to COVID-19, we deepened our investment in virtual resources, including strengthening our telehealth option for patients, which can be found on Cologuard.com. We also built new capabilities to market our Cologuard test to health systems, with a focus on health information technologies. Following the FDA's September 2019 expansion and the USPSTF's updated guidelines in May 2021 of Cologuard's indication to average risk individuals ages 45-49, we updated our direct-to-consumer efforts to educate and motivate this younger population to screen with our Cologuard test.

Oncotype Commercial Operations

We promote our Oncotype tests through our precision oncology sales force. Our commercial infrastructure, including our sales force, managed care group, and patient support network, is critical to the success of our Oncotype products. In our domestic sales, marketing and reimbursement efforts, we interact directly with medical, radiation, and surgical oncologists, urologists, pathologists, and payers. We employ a direct sales approach that targets oncologists, cancer surgeons and urologists, and utilizes medical education and scientific liaisons who target key opinion leaders. We also plan to continue conducting clinical studies with the objective of having results published in peer-reviewed journals. We believe the combination of these approaches is our best means to increase patient and healthcare provider awareness of our Oncotype products and services and the number of favorable reimbursement coverage decisions by third-party payers.

International Commercial Operations

We now commercialize our Oncotype tests internationally through employees in Canada, Japan, and eight European countries, as well as through exclusive distribution agreements. We do not offer our Cologuard test outside of the U.S. We have provided our Oncotype tests in more than 90 countries outside of the U.S.

Inclusion of our products in guidelines and quality measures will be critical to our international success. The Oncotype DX breast cancer test is recognized in international guidelines issued by the St. Gallen International Breast Cancer Expert Panel and European Society for Medical Oncology. Our Oncotype DX breast cancer test has been recommended to guide certain patients' chemotherapy treatment decisions by the National Institute for Health and Care Excellence in England, the Gynecologic Oncology Working Group in Germany, and the Japan Breast Cancer Society. Our Oncotype DX breast cancer test is reimbursed for certain patients in the public health systems in more than ten countries, including Germany, the United Kingdom ("U.K."), and Canada.

We are exploring opportunities to establish local laboratories in certain locations outside of the U.S. and have started to establish local testing capacity in Germany. Certain countries have severe restrictions on reimbursing tests performed abroad or exporting tissue samples or patient health data. These restrictions limit our ability to offer our tests in those countries without local laboratories or a method of test delivery that does not require samples to be transported to our U.S. laboratory.

Reimbursement for our Tests

Reimbursement for our Cologuard Test

Our Cologuard test has broad reimbursement coverage from Medicare and most private payers. As outlined in CMS's National Coverage Determination ("NCD"), Medicare Part B covers our Cologuard test once every three years for beneficiaries who meet all of the following criteria:

- age 50 to 85 years,
- asymptomatic (no signs or symptoms of colorectal disease including, but not limited to, lower gastrointestinal pain, blood in stool, positive guaiac fecal occult blood test or fecal immunochemical test), and
- at average risk for developing colorectal cancer (e.g., no personal history of adenomatous polyps, colorectal cancer, or inflammatory bowel disease, including Crohn's Disease and ulcerative colitis; no family history of colorectal cancers or adenomatous polyps, familial adenomatous polyposis or hereditary non-polyposis colorectal cancer).

In addition to Medicare reimbursement, most commercial payers have issued positive coverage decisions for our Cologuard test, and we continue to negotiate contracts with payers to include our Cologuard test as an in-network service. In-network agreements with payers have varying terms and conditions, including reimbursement rate, term, and termination. Some payers may apply various medical management requirements, including a requirement that they give prior authorization for a Cologuard test before they are willing to pay for it. Other payers may perform post-payment reviews or audits, which may lead to payment recoupments.

The following laws and regulations establish coverage requirements relevant to our Cologuard test.

- Section 2713 of the Patient Protection and Affordable Care Act ("ACA") mandates that certain health insurers cover, without imposing any patient cost-sharing, evidence-based items or services that have in effect a rating of "A" or "B" in the current recommendations of USPSTF ("ACA Mandate").
- Federal regulations require that Medicare Advantage plans cover "A" or "B" rated preventive services without patient cost-sharing, and CMS has issued a notice affirming that Medicare Advantage plans must include coverage of our Cologuard test every three years without patient cost-sharing.
- We believe the laws of approximately 30 states currently mandate coverage of our Cologuard test by certain health insurance plans.

The federal laws and regulations referenced above currently mandate coverage for individuals beginning at age 50. However, new USPSTF colorectal cancer screening guidelines became final in May 2021 and after a transition period, will mandate coverage of our Cologuard test beginning at age 45 for ACA covered health plans beginning as early as June 2022. While most of the state mandates apply beginning at age 50, we believe some should be interpreted to require coverage beginning at age 45.

Reimbursement for our Oncotype Tests

We depend on government insurance plans, managed care organizations, and private insurance plans for reimbursement of our Oncotype tests.

Medicare coverage for our Oncotype tests is currently subject to the discretion of the local Medicare Administrative Contractors ("MAC"). Palmetto, the MAC that establishes the coverage and coding policies for most of our tests under Medicare, developed the Molecular Diagnostic Services Program ("MolDx"), to identify and establish Medicare coverage for molecular diagnostic tests that fall within the scope of its Molecular Diagnostic Test local coverage decision ("LCD"). To obtain coverage under the MolDx program, developers of molecular diagnostic tests must submit a detailed dossier of analytical and clinical data to substantiate that a test meets Medicare's requirements for coverage. We have received positive coverage decisions under the MolDx program for our invasive breast, colon, prostrate, and oncomap tests.

Reimbursement of our Oncotype tests by third-party payers is essential to our commercial success. Where there is a payer policy, contract or agreement in place, we bill the third-party payer, the hospital or referring laboratory and/or the patient (for deductibles and coinsurance or copayments, where applicable) in accordance with established policy, contract or agreement terms. Where there is no payer policy in place, we pursue third-party reimbursement on behalf of each patient on a case-by-case basis. Our efforts on behalf of these patients involve a substantial amount of time and expense, and bills may not be paid for many months, if at all. Furthermore, if a third-party payer denies coverage after final appeal, it may take a substantial amount of time to collect from the patient, if we are able to collect at all.

State Medicaid agencies generally assign a reimbursement rate for our Oncotype tests equal to or less than the prevailing Medicare rate, often determined by state law as a percentage of the Medicare reimbursement rate.

International Reimbursement

In many countries, governments are primarily responsible for financing and establishing reimbursement for diagnostic tests. The majority of our international Oncotype test revenues come from reimbursement, payments from our distributors, and patient self-pay. We have obtained coverage for our invasive breast cancer test outside of the U.S., including coverage for certain patients in Canada, France, Spain, Germany, Italy, Ireland, Israel, Netherlands, Saudi Arabia, Sweden, Switzerland, and the U.K.

We expect that our international sales will be heavily dependent on the availability of reimbursement, and broadening coverage and reimbursement for our Oncotype and other tests outside of the United States will take years.

Reimbursement for Future Products

Successful commercialization of our newly developed products and products in development will also depend on our ability to obtain adequate reimbursement from government insurance plans, managed care organizations and private insurance plans for such products.

Our Clinical Laboratory and Manufacturing Facilities

We process our Cologuard test at two state of the art, high throughput clinical laboratories in Madison, Wisconsin that are certified pursuant to federal CLIA and accredited by CAP. Our total lab capacity at both facilities is approximately seven million Cologuard tests per year, with the opportunity to add additional capacity, if needed.

We currently manufacture our Cologuard test at two facilities in Madison, Wisconsin. We are committed to manufacturing and providing medical devices and related products that meet customer expectations and applicable regulatory requirements. We adhere to manufacturing and safety standards required by federal, state, and local laws and regulations and operate our manufacturing facilities under a quality management system. We purchase certain components for our Cologuard test from third-party suppliers and manufacturers.

Beginning in March 2020, we allocated space at our clinical laboratories in Madison, Wisconsin to process our COVID-19 tests. Throughout 2020 and 2021, we manufactured and assembled our COVID-19 test kits at our manufacturing facilities in Madison, Wisconsin. In 2022, we will continue to manufacture COVID-19 reagents out of our manufacturing facilities, and will now provide all the components for the test kits to be assembled with a third-party vendor.

All internally developed Oncotype tests for domestic and international patients are currently processed in our CLIA-certified and CAP-accredited clinical reference laboratory facilities in Redwood City, California. Our oncomap and oncomap ExTra tests are processed in our CLIA-certified and CAP-accredited clinical reference laboratory facilities in Phoenix, Arizona. The Oncotype DX AR-V7 Nucleus Detect test, which was designed and validated by Epic Sciences, Inc. (“Epic Sciences”), is performed in its CLIA-accredited, CAP-certified clinical reference laboratory facility in San Diego, California. Beginning in 2022, a portion of our international Oncotype tests will be processed in our newly constructed facility in Trier, Germany, which is operated by a third-party partner.

As part of the acquisition of PreventionGenetics in December 2021, we acquired a CLIA-certified and CAP-accredited DNA testing laboratory in Marshfield, Wisconsin. PreventionGenetics' laboratory provides more than 5,000 predefined genetic tests for nearly all clinically relevant genes, additional custom panels, and comprehensive germline whole exome and whole genome sequencing tests.

We believe that we currently have sufficient capacity to process all of our tests. We are in the process of constructing additional facilities as we expand our business.

Competition

We operate in a rapidly evolving and highly competitive industry. There are a number of private and public companies that offer products or have announced that they are developing products that compete with ours. Some of our current and potential competitors may have significant competitive advantage over us, which may make them more attractive to hospitals, clinics, group purchasing organizations and physicians, including:

- greater brand recognition;
- larger or more established distribution networks and customer bases;
- a broader product portfolio, resulting in greater ability to market their products;
- ore extensive research, development, sales, marketing, and manufacturing capabilities and greater financial resources; and
- greater technical resources positioning them to continue to improve their technology in order to compete in an evolving industry.

The U.S. market for colorectal cancer screening is large, consisting of nearly 110 million eligible individuals between the ages of 45 and 85, and has attracted numerous competitors. Our Cologuard test faces competition from procedure-based detection technologies such as colonoscopy, flexible sigmoidoscopy, “virtual” colonoscopy - a radiological imaging approach that visualizes the inside of the bowel by CT scan (spiral computerized axial tomography) - as well as other common screening tests, such as the fecal occult blood test ("FOBT") and the fecal immunochemical test (“FIT”), and other screening technologies. Newer screening technologies include liquid biopsy tests, such as Epi proColon, which was approved by the FDA in April 2016, and pill-based imaging solutions like PillCam COLON, which was cleared by the FDA in February 2014, and C-Scan, which obtained a CE Mark in early 2019. As noted below, a number of companies are developing liquid biopsy tests for colorectal cancer screening, as well as other applications.

We also are aware of at least three companies, DiaTech Pharmacogenetics, Prescient Metabiomics, and Geneoscopy, that are seeking to develop stool-based colorectal cancer tests in the United States. Our competitors may also be developing additional methods of detecting colorectal cancer and pre-cancer that have not yet been announced.

Notwithstanding that the market for colorectal cancer screening is highly competitive, we believe that our Cologuard test, as the first and only sDNA-based non-invasive colorectal cancer screening test on the market today, compares favorably to other available products and services. All other colorectal cancer detection methods in use today are constrained by some combination of poor sensitivity, poor adherence, or high cost. For example, colonoscopy requires advanced dietary restrictions and bowel cleansing and can be uncomfortable, time-consuming, hazardous, and expensive. Colonoscopy requires sedation, potential lost time from work, and someone to drive the patient home from the procedure. A 2010 study shows that 7 out of 10 people age 50 and older who were told they should get a colonoscopy did not do so primarily due to fear. Fecal blood testing, including FIT testing, suffers from poor sensitivity, with only a 74% detection rate for cancer and 24% detection rate for pre-cancer. The blood-based DNA tests currently available are also disadvantaged by relatively low sensitivity. Epigenomics AG has reported that the Epi proColon test has an overall cancer sensitivity rate of 68%, and only 59% for early-stage cancer. Additionally, FIT testing suffers from low adherence over time. One study published in the American Journal of Managed Care demonstrated that only 3 out of every 1,000 patients studied adhered to fecal test screening guidelines during a continuous 10-year observation period.

Our Oncotype products compete against a number of companies that offer products or have conducted research to profile genes and gene expression in breast, colon, and prostate cancer. These companies include Agendia Inc., BioTheranostics, GenomeDx Biosciences Inc., Guardant Health, Inc., Hologic Inc., Myriad Genetics Inc. (and its Sividon Diagnostics subsidiary), NanoString Technologies Inc., NeoGenomics, Inc., OPKO Health, Inc. (and its Bio-Reference Laboratories, Inc. subsidiary), Pacific Edge Limited, Qiagen N.V. and Veracyte, Inc. Historically, our principal competition for our Oncotype tests has also come from existing diagnostic methods used by pathologists and oncologists, and such traditional diagnostic methods can be difficult to compete with or supplement. Our Oncotype tests also face competition from commercial laboratories with strong distribution networks for diagnostic tests, such as Laboratory Corporation of America Holdings and Quest Diagnostics Incorporated. Other potential competitors include companies that develop diagnostic tests such as Roche Diagnostics, a division of Roche Holding, Ltd, and Siemens AG, as well as other companies and academic and research institutions.

For our prostate cancer tests, we face comparatively greater competition than for our breast cancer tests, including competition from products that were on the market prior to our product launch and that are supported by clinical studies and published data. This existing direct and indirect competition for tests and procedures may make it difficult to gain market share, impact our ability to obtain reimbursement or result in a substantial increase in resources necessary to successfully commercialize our Oncotype DX GPS prostate test and the Oncotype DX AR-V7 Nucleus Detect test.

We believe that our Oncotype tests compete primarily on the basis of the value of the quantitative information they provide, the clinical validation of the utility of our tests, the level of adoption and reimbursement coverage for our tests, the inclusion of our tests in clinical practice guidelines, our ability to commercialize products through our clinical development platform, our ability to expand our sales efforts into new areas of medical practice as we launch new products, our collaborations with clinical study groups, the quality of our clinical laboratory, and the level of customer service we provide. While we believe that our Oncotype tests compete favorably with respect to these factors, to continue to do so we must innovate and adopt advanced technology, successfully market, sell and enhance our tests, obtain peer-reviewed publications of our clinical studies in a timely manner, continue to obtain positive reimbursement determinations, continue to expand in countries outside of the U.S., continue to develop our technological and clinical operations, encourage healthcare provider participation in Medicare-required information collection efforts, and successfully expand our reach into additional product markets including through collaborations with third parties.

In addition to our on-market products, we intend to offer additional liquid biopsy tests that:

- screen for colorectal cancer,
- screen for multiple types of cancers using a single test,
- provide diagnostic information for liver cancer,
- provide prognostic information, guide therapy selection, or measure minimal residual disease or cancer recurrence.

We are aware of a number of companies — including Bioprognos, Bluestar Genomics, Burning Rock, Caris Life Sciences, CellMax, Inc., Clinical Genomics, DiaCarta, EarlyDx, Epigenomics AG, Foundation Medicine, Freenome Inc., Glycotest, GRAIL, Inc., Guardant Health, Inc., Helio Health, Immunovia AB, Inivata, Invitae, JBS Science, Natera Inc., Nucleix Ltd., Singlera Genomics, Sysmex Ignostics, and Tempus — that have developed, or are developing, liquid biopsy tests for the detection of cancer, based on the detection of proteins, tumor cells, nucleic acids, epigenetic markers, or other biomarkers. These tests could represent significant competition for our current tests, including our Cologuard and Oncotype tests, as well as other tests that we currently are developing or in the future may develop. Guardant Health, Inc. and Freenome Inc.are conducting prospective colorectal cancer screening clinical trials intended to support FDA approval for their liquid biopsy tests, and other companies may do so in the future. Geneoscopy is also conducting a prospective colorectal cancer screening clinical trial intended to support FDA approval for its stool-based colorectal cancer screening test.

The hereditary cancer testing market is becoming increasingly competitive, and we expect this competition to intensify in the future. We face competition from a variety of sources, including Ambry Genetics, a subsidiary of Konica Minolta Inc.; Myriad Genetics, Inc.; Invitae; Natera, Inc.; Color Health, Inc.; and Sema4 Genomics; a few large, established general testing companies such as Laboratory Corporation of America Holdings and Quest Diagnostics Incorporated; and clinical laboratories in an academic or healthcare provider setting that perform clinical genetic testing on behalf of their affiliated institutions.

Competitors may develop their own versions of our tests in countries where we did not apply for patents, where our patents have not issued or where our intellectual property rights are not recognized and compete with us in those countries, including encouraging healthcare providers or patients to use their tests in other countries. We are aware of at least one company that is offering or intends to offer in China a test that appears similar to our Cologuard test. Competitors also may be able to design around our intellectual property.

We may be unable to compete effectively against our competitors either because their products and services are superior or because they are more effective in developing or commercializing competing products and services are more effective in developing or commercializing competing products and services. Furthermore, even if we do develop new marketable products or services, our current and future competitors may develop products and services that are more clinically or commercially attractive than ours, and they may bring those products and services to market earlier or more effectively than us. If we are unable to compete successfully against current or future competitors, we may be unable to increase market acceptance for and sales of our tests, which could prevent us from increasing or sustaining our revenues or achieving sustained profitability and could cause the market price of our common stock to decline.

Seasonality

We are continuing to learn how seasonal factors may affect our business. Based on our experience to date, we expect some seasonal variations in our financial results due to a variety of factors, such as the year-end holiday period and other major holidays, vacation patterns of both patients and healthcare providers, climate and weather conditions in our markets, seasonal conditions that may affect medical practices and provider activity, including for example influenza outbreaks that may reduce the percentage of patients that can be seen, and other factors relating to the timing of patient deductibles and co-insurance limits.

Regulation

Certain of our activities are subject to regulatory oversight by the FDA under provisions of the Federal Food, Drug, and Cosmetic Act ("FDCA") and regulations thereunder, including regulations governing the development, marketing, labeling, promotion, manufacturing, distribution, and export of diagnostic products. Our clinical laboratory facilities are subject to oversight by CMS pursuant to CLIA, as well as agencies in various states, including New York. We are subject to many other federal, state and foreign laws, including anti-fraud and abuse, anti-kickback and patient privacy. Failure to comply with applicable requirements can lead to sanctions, including withdrawal of products from the market, recalls, refusal to authorize government contracts, product seizures, exclusion from participation in federal and state healthcare programs, civil money penalties, injunctions, and criminal prosecution.

U.S. Food and Drug Administration

Devices subject to FDA regulation must undergo premarket review prior to commercialization unless the device is exempt from such review. The FDA granted premarket approval ("PMA") for our Cologuard test in August 2014. The regulations governing Cologuard's approval place substantial restrictions on how our Cologuard test is marketed and sold, specifically, by prescription only. In addition, as a condition of our FDA approval, we were required to conduct a post-approval study. The post-approval study concluded in 2020 and final results were submitted to the FDA in late 2020. There can be no assurance that the results of this study will be satisfactory and will not cause the FDA to modify or withdraw our approval for the Cologuard test.

Additionally, manufacturers of medical devices must comply with various regulatory requirements under the FDCA and regulations thereunder, including, but not limited to, quality system regulations, unless they are exempt, facility registration, product listing, labeling requirements, and certain post-market surveillance requirements. Entities that fail to comply with FDA requirements can be liable for criminal or civil penalties, such as recalls, detentions, orders to cease manufacturing, and restrictions on labeling and promotion, among other potential sanctions. In 2017, we recalled one of the components of our Cologuard test kit and circumstances may arise that cause us to recall other products or components used in connection with our Cologuard test.

Certain of our products in development or additional diagnostic products and services that we seek to develop may be regulated by the FDA as medical devices. The regulatory review and approval process for medical devices can be costly, timely, and uncertain. This process may involve, among other things, successfully completing additional clinical trials and submitting a premarket clearance notice or filing a premarket approval application with the FDA. If premarket review is required by the FDA, there can be no assurance that our tests will be cleared or approved on a timely basis, if at all. In addition, there can be no assurance that the labeling claims cleared or approved by the FDA will be consistent with our current claims or adequate to support continued adoption of and reimbursement for our products. Ongoing compliance with FDA regulations could increase the cost of conducting our business, subject us to FDA inspections and other regulatory actions, and potentially subject us to penalties in the event we fail to comply with such requirements.

Laboratory Developed Tests ("LDTs")

Our Oncotype tests and oncomap ExTra test are regulated as LDTs and we may seek to commercialize certain of our products in development as LDTs. LDTs are clinical laboratory tests that are developed and validated by a laboratory for its own use. Historically, LDTs have been regulated under CLIA while the FDA has exercised enforcement discretion and not required approvals or clearances for many LDTs performed by CLIA-certified laboratories. The FDA has traditionally chosen not to exercise its authority to regulate LDTs because LDTs were limited in number, were relatively simple tests, and were typically used to diagnose rare diseases and uncommon conditions.

At various times since 2006, the FDA has issued documents outlining its intent to require varying levels of FDA oversight of many LDTs, including our tests. The FDA has yet to implement any form of oversight requirements with respect to LDTs, and it is unclear at this time if or when the FDA ends enforcement discretion for LDTs. It is also unclear whether the FDA may decide to regulate certain LDTs on a case-by-case basis at any time. Action by the FDA to exercise enforcement discretion over LDTs may materially impact our development and commercialization of LDTs, including without limitation our Oncotype tests.

Laboratory Certification, Accreditation, and Licensing

We are also subject to U.S. and state laws and regulations regarding the operation of clinical laboratories. CLIA requirements and laws of certain states, including those of California, New York, Maryland, Pennsylvania, and Rhode Island, impose certification requirements for clinical laboratories, and establish standards for quality assurance and quality control, among other things. CLIA provides that a state may adopt different or more stringent regulations than federal law and permits states to apply for exemption from CLIA if the state's laboratory laws are equivalent to or more stringent than CLIA. For example, the State of New York's clinical laboratory regulations, which have received an exemption from CLIA, contain provisions that are in certain respects more stringent than federal law. Therefore, as long as New York maintains a licensure program that is CLIA-exempt, we will need to comply with New York's clinical laboratory regulations in order to offer our clinical laboratory products and services in New York.

We have current certificates to perform clinical laboratory testing. Clinical laboratories are subject to inspection by regulators and to sanctions for failing to comply with applicable requirements. Sanctions available under CLIA and certain state laws include prohibiting a laboratory from running tests, requiring a laboratory to implement a corrective plan, and imposing civil monetary penalties. If we fail to meet any applicable requirements of CLIA or state law, that failure could adversely affect any future CMS consideration of our technologies, prevent their approval entirely, and/or interrupt the commercial sale of any products and services and otherwise cause us to incur significant expense.

HIPAA and Other Privacy Laws

The Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act ("HIPAA") established comprehensive protection for the privacy and security of health information. The HIPAA standards apply to three types of organizations, or "Covered Entities": health plans, healthcare clearinghouses, and healthcare providers that conduct certain healthcare transactions electronically. Covered Entities and their business associates must have in place administrative, physical, and technical standards to guard against the misuse of individually identifiable health information. We perform activities that may implicate HIPAA, such as providing clinical laboratory testing services and entering into specific kinds of relationships with Covered Entities and business associates of Covered Entities. Penalties for violations of HIPAA include civil money and criminal penalties.

Our activities must also comply with other applicable privacy laws, which impose restrictions on the access, use and disclosure of personal information. More state and international privacy laws are being adopted. Many state laws are not preempted by HIPAA because they are more stringent or are broader in scope than HIPAA including the California Consumer Privacy Act of 2018, which protects personal information other than health information covered by HIPAA and allows certain data access and erasure rights to California consumers. Further, we are required to comply with international personal data protection laws and regulations, including the European Union's General Data Protection Regulation ("GDPR"). The GDPR is a prescriptive, detailed regulation that provides extensive powers to public authorities to sanction and stop use of personal data. While companies are afforded some flexibility in determining how to comply with the GDPR's various requirements, the GDPR has and will continue to require significant effort and expense to ensure compliance. All of these laws may impact our business and may change periodically, which could adversely affect our business operations. Our failure to comply with these privacy laws or significant changes in the laws restricting our ability to obtain stool, tissue, blood, and other patient samples and associated patient information could significantly impact our business and our future business plans, including potentially a temporary inability to provide tests to patients in the European Union.

Federal and State Billing and Fraud and Abuse Laws

Anti-fraud Laws/Overpayments. We are subject to numerous federal and state anti-fraud and abuse laws, including the Federal False Claims Act. Many of these anti-fraud laws are broad in scope, and neither the courts nor government agencies have extensively interpreted these laws. Prohibitions under some of these laws include:

- the submission of false claims or false information to government programs,
- the retention of any overpayments by governmental payers,
- deceptive or fraudulent conduct,
- excessive or unnecessary services or services at excessive prices, and
- defrauding private sector health insurers.

We may be subject to substantial penalties for violations of anti-fraud and abuse laws, including denial of payment and refunds or recoupments, suspension of payments from Medicare, Medicaid or other federal healthcare programs, and exclusion from participation in federal and state healthcare programs, as well as civil monetary and criminal penalties and imprisonment. Numerous federal and state agencies enforce the anti-fraud and abuse laws. In addition, private insurers may also bring private actions. In some circumstances, private whistleblowers are authorized to bring fraud suits on behalf of the government against providers and are entitled to receive a portion of any final recovery.

In addition, amendments to the False Claims Act impose severe penalties for the knowing and improper retention of overpayments collected from governmental payers. Within 60 days of identifying and quantifying an overpayment, a provider is required to notify CMS or the Medicare contractor of the overpayment and the reason for it and return the overpayment. These amendments could subject our procedures for identifying and processing payments to greater scrutiny. Overpayments may occur from time to time in the healthcare industry without any fraudulent intent. For example, overpayments may result from mistakes in reimbursement claim forms or from improper processing by governmental payers. We maintain protocols intended to identify any overpayments. From time to time we have identified overpayments and made refunds to government payers.

To avoid liability, we must carefully and accurately code claims for reimbursement, proactively monitor the accuracy and appropriateness of Medicare claims and payments received, diligently investigate any credible information indicating that we may have received an overpayment, and promptly return any overpayments.

Federal and State "Self-Referral" and "Anti-Kickback" Restrictions

If we or our operations are found to be in violation of applicable laws and regulations prohibiting improper referrals for healthcare services or products, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in U.S. federal or state healthcare programs, and the curtailment or restructuring of our operations.

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering, or paying remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs, unless an exception applies. The term "remuneration" is not defined in the federal Anti-Kickback Statute and has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. Sanctions for violations of the federal Anti-Kickback Statute may include imprisonment and other criminal penalties, civil monetary penalties, and exclusion from participation in federal healthcare programs. Many states have also adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs, and do not contain identical safe harbors.

In addition to the Anti-Kickback Statute, in October 2018, Congress enacted the Eliminating Kickbacks in Recovery Act of 2018 ("EKRA") as a component of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act. EKRA is an anti-kickback law similar to the federal Anti-Kickback Statute that, subject to several exceptions, makes it a criminal offense to pay any remuneration to induce referrals to, or in exchange for, patients using the services of a recovery home, a substance use clinical treatment facility, or laboratory. Although it appears that EKRA was intended to reach patient brokering and similar arrangements to induce patronage of substance use recovery and treatment, the language in EKRA is broadly written and can apply to laboratory services covered under public or private payer arrangements. That said, an interpretation of EKRA that prohibits certain incentive compensation payments to sales employees or other forms of remuneration that would otherwise be permissible under a safe harbor to the federal Anti-Kickback Statute would directly conflict with the intent of the federal Anti-Kickback Statute and regulations and would prohibit a number of practices that are common throughout the industry. Significantly, EKRA permits the U.S. Department of Justice "DOJ") to issue regulations clarifying EKRA's exceptions or adding additional exceptions, but no such regulations or applicable guidance have yet been issued.

Self-Referral Law. The federal "self-referral" law, commonly referred to as the "Stark" law, provides that healthcare providers who, personally or through a family member, have ownership interests in or compensation arrangements with a laboratory are prohibited from making a referral to that laboratory for laboratory tests reimbursable by Medicare, and also prohibits laboratories from submitting a claim for Medicare payments for laboratory tests referred by healthcare providers who, personally or through a family member, have ownership interests in or compensation arrangements with the testing laboratory. The Stark law contains a number of specific exceptions which, if met, permit healthcare providers who have ownership or compensation arrangements with a testing laboratory to make referrals to that laboratory and permit the laboratory to submit claims for Medicare payments for laboratory tests performed pursuant to such referrals. We are subject to comparable state laws, some of which apply to all payers regardless of source of payment, and do not contain identical exceptions to the Stark law.

Any action against us for violation of these or similar foreign laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

Sunshine Act

In 2010, Congress enacted a statute commonly known as the Sunshine Act, which aims to promote transparency. The Sunshine Act requires manufacturers of drugs, devices, biologicals, and medical supplies covered by Medicare, Medicaid, or the Children's Health Insurance Program to report annually to CMS any payments or other transfers of value made to healthcare providers and teaching hospitals, unless an exception applies. Manufacturers must also disclose to CMS any healthcare provider ownership or investment interests. Some states have similar transparency laws. Our failure to comply with any applicable transparency reporting requirements may subject us to substantial penalties.

International

When marketing our tests outside of the U.S., we are subject to foreign regulatory requirements governing human clinical testing, export of tissue, marketing approval for our products, and performance and reporting of tests in each market. These requirements vary by jurisdiction, differ from those in the U.S., and may require us to perform additional pre-clinical or clinical testing. In many countries outside of the U.S., coverage, pricing, and reimbursement approvals are also required in order for our tests to be made available to patients in substantial volume.

Many countries in which we offer our tests have anti-inducement laws or regulations prohibiting providers, as well as medical and in vitro diagnostic device manufacturers, from offering, paying, soliciting, or receiving remuneration, directly or indirectly, or providing a benefit to a healthcare professional in order to induce business. In situations involving healthcare providers employed by public or state-funded institutions or national healthcare services, violation of the local anti-corruption or anti-gift laws may also constitute a violation of the U.S. Foreign Corrupt Practices Act ("FCPA").

The FCPA prohibits any U.S. individual, business entity, or employee of a U.S. business entity from offering or providing, directly or through a third party, including the distributors we rely on in certain markets, anything of value to a foreign government official with corrupt intent to influence an award or continuation of business or to gain an unfair advantage, whether or not such conduct violates local laws. In addition, it is illegal for a company that reports to the Securities and Exchange Commission ("SEC") to have false or inaccurate books or records or to fail to maintain a system of internal accounting controls. We are also required to maintain accurate information and control over sales and distributors' activities that may fall within the purview of the FCPA, its books and records provisions, and its anti-bribery provisions.

Other Laws

Occupational Safety and Health. In addition to its comprehensive regulation of health and safety in the workplace in general, the Occupational Safety and Health Administration has established extensive requirements aimed specifically at laboratories and other healthcare-related facilities. In addition, because our operations require employees to use certain hazardous chemicals, we also must comply with regulations on hazard communication and hazardous chemicals in laboratories. These regulations require us, among other things, to develop written programs and plans, which must address methods for preventing and mitigating employee exposure, the use of personal protective equipment, and training.

Specimen Transportation. Our commercialization activities subject us to regulations of the Department of Transportation, the U.S. Postal Service, and the Centers for Disease Control and Prevention that apply to the surface and air transportation of clinical laboratory specimens.

Environmental. The cost of compliance with federal, state, and local provisions related to the protection of the environment has had no material effect on our business. There were no material capital expenditures for environmental control facilities in the year ended December 31, 2021, and there are no material expenditures planned for such purposes for the year ended December 31, 2022.

Intellectual Property

We rely on a combination of patents, patent applications, copyrights and trademarks, as well as contracts, such as confidentiality, material data transfer, and license and invention assignment agreements to protect our intellectual property rights. We also rely upon trade secret laws to protect unpatented know-how and continuing technological innovation.

We have intellectual property rights pertaining to sample type, sample preparation, sample preservation, biomarkers, gene expression and sequencing technology, and related methods and formulations.

Our success depends upon our ability to protect our technologies through patent coverage. As of December 31, 2021, we had 144 issued patents in the U.S. and 765 issued patents outside of the U.S., which includes validated patents issued by the European Patent Office in key European Union countries, covering genes and methods that are components of the Cologuard test, Oncotype DX breast, colon and prostate cancer tests, pipeline technologies or research methods, and platform technologies. In addition, we have a number of pending patent applications in the U.S. and in other countries, including provisional and non-provisional filings. Our issued U.S. patents expire at various times between 2022 and 2039. Some of these U.S. patent applications also have corresponding pending or granted applications under the Patent Cooperation Treaty in Canada, Europe, Japan, Australia, and other jurisdictions. In these patent applications, we have either sole or joint ownership positions. In certain cases where joint ownership positions were created, we have negotiated contractual provisions providing us with the opportunity to acquire exclusive rights under the patent applications. Under some patent applications, we have elected to allow exclusive options to lapse without exercising the option. The joint ownership agreements generally are in the form of material data transfer agreements that were executed at the onset of our collaborations with third parties.

License Agreements

We license certain technologies that are, or may be, incorporated into our technology under several license agreements, as well as the rights to commercialize certain diagnostic tests through collaboration agreements. Generally, the license agreements require us to pay single-digit royalties based on certain net revenues received using the technologies and may require minimum royalty amounts, milestone payments, or maintenance fees.

Mayo

In June 2009, we entered into a license agreement with Mayo, which was most recently amended in September 2020. Under the license agreement, Mayo granted us an exclusive, worldwide license to certain Mayo patents and patent applications, as well as a non-exclusive, worldwide license with regard to certain Mayo know-how. The scope of the license covers any screening, surveillance, or diagnostic test or tool for use in connection with any type of cancer, pre-cancer, disease, or condition.

The licensed Mayo patents and patent applications contain both method and composition claims that relate to sample processing, analytical testing, and data analysis associated with nucleic acid screening for cancers and other diseases. The jurisdictions covered by these patents and patent applications include the U.S., Australia, Canada, the European Union, China, Japan, and Korea. Under the license agreement, we assumed the obligation and expense of prosecuting and maintaining the licensed Mayo patents and are obligated to make commercially reasonable efforts to bring to market products using the licensed Mayo intellectual property.

Pursuant to our license agreement with Mayo, we are required to pay Mayo various single-digit royalty rates on net sales of current and future products using the licensed Mayo intellectual property during the term of the Mayo agreement.

In addition to the royalties described above, we are also required to pay Mayo cash of $0.2 million, $0.8 million, and $2.0 million upon each product using the licensed Mayo intellectual property reaching $5.0 million, $20.0 million, and $50.0 million in cumulative net sales, respectively.

As part of the September 2020 amendment, we agreed to pay Mayo an additional $6.3 million, payable in five annual installments, through 2024.

The license agreement will remain in effect, unless earlier terminated by the parties in accordance with the agreement, until the last of the licensed patents expires in 2039 (or later, if certain licensed patent applications are issued). However, if we are still using the licensed Mayo know-how or certain Mayo-provided biological specimens or their derivatives on such expiration date, the term shall continue until the earlier of the date we stop using such know-how and materials and the date that is five years after the last licensed patent expires. The license agreement contains customary termination provisions and permits Mayo to terminate the license agreement if we sue Mayo or its affiliates, other than any such suit claiming an uncured material breach by Mayo of the license agreement.

In addition to granting us a license to the covered Mayo intellectual property, Mayo provides us with research and development assistance pursuant to the license agreement and other collaborative arrangements. In September 2020, Mayo also agreed to make available certain personnel to provide such assistance through January 2025.

Johns Hopkins University ("JHU")

Through the acquisition of Thrive, we acquired a worldwide exclusive license agreement with JHU for use of several JHU patents and licensed know-how. We are seeking to utilize the JHU licensed technology to develop and commercialize a blood-based MCED test. The agreement terms include single-digit sales-based royalties and sales-based milestone payments of $10.0 million, $15.0 million, and $20.0 million upon achieving calendar year licensed product revenue using JHU proprietary data of $0.50 billion, $1.00 billion, and $1.50 billion, respectively.

In addition to granting us a license to the covered JHU intellectual property, JHU provides us with research and development assistance pursuant to other collaboration arrangements.

Human Capital

Our vision to pursue smarter solutions that provide the clarity to take life-changing action earlier drives us to find ambitious, dynamic individuals who thrive in a team-based environment. To facilitate talent attraction and retention, we strive to make Exact Sciences a diverse and inclusive workplace, with opportunities for our employees to grow and develop in their careers, supported by strong compensation, benefits, and health and wellness programs.

At December 31, 2021, we had approximately 6,500 full-time, part-time and temporary employees, 6,420 of which were full-time employees. More than 97% of our employees are located in the United States and none of our employees are represented by a labor union. During fiscal year 2021, our voluntary turnover rate was approximately 12%, below the healthcare industry benchmark, which is comprised of certain of our key competitors (Aon, 2021 Salary Increase and Turnover Study — Second Edition, December 2021).

Diversity and Inclusion

We believe diversity in thought, experience, perspective, and background within our team is necessary to support our core value of innovation. We are firmly committed to providing equal opportunity in all aspects of employment and will not discriminate in any employment decision because of a person's race, color, sex, religion, national origin, age, disability, sexual orientation, gender identity, genetic information, veteran status, or any other basis prohibited by applicable law. In order to increase the pool of diverse candidates for open positions, we partner with community resource groups and participate in diversity-focused career fairs.

Our Executive VP of Human Resources is part of the executive leadership team and has direct responsibility for our diversity and inclusion program. We track and monitor workforce diversity data to ensure we are fulfilling our diversity and inclusion aspiration – to be known as a great place to work for all. Thanks, in part, to our competitive benefits and the positive results of our diversity and inclusion program, women make up approximately 54% of total employees (full-time and part-time), and 49% of management positions. Our nine-member Board of Directors includes four female members to support diversity of opinion and perspective at the board level as well. In addition, we have been awarded with a Great Place to Work® Certification™ in 2021, Fortune's Best Workplaces in Health Care & Biopharma™ in 2021, and Fortune's Best Workplaces for Millennials™ in 2021. We were also recognized as one of Glassdoor's Best Places to Work for 2022.

Compensation and Benefits

Attracting the best talent starts with offering industry-leading compensation and benefits. We want our compensation and benefits to give our employees a sense of ownership in our company, and pride and determination to achieve our mission. To help our employees achieve financial well being and share in the success they create, we offer competitive base pay, a company-sponsored 401(k) plan with employer matching, retirement planning resources, employee stock purchase plan opportunities, stock awards upon hire and annually thereafter, and annual cash bonus programs. To help our employees get and stay healthy, we offer our employees generous health benefits, including among others, medical, dental, and vision care coverage for employees and their dependents; family formation benefits (such as adoption assistance, (in)fertility treatments, etc.), life, disability, and accident insurance and critical illness benefits; health care and dependent care flexible spending account programs and employer contributions to health savings accounts (for specific medical plans). To enable our employees to take the time they need to re-energize and focus on what matters most, we offer a parental leave program and ample time away benefits (vacation, sick, holidays, volunteer time, voting time, other leaves). To foster a culture of care and compassion, we offer an employee assistance program with employer-paid counseling coverage for employee and household members, charitable donation matches, commuter benefits, family care assistance, wellness programs, including fitness and mental health/ well being, and more.

Training and Development

We invest significant resources to develop the talent needed to achieve long-term success. We have implemented a comprehensive employee training program that applies to all employees, including full-time, part-time, and temporary employees. Senior leadership, in conjunction with Human Resources, is responsible for ensuring that all staff, including contractors and consultants, have the appropriate education, training, competency, and credentials.

We create opportunities for personal growth, professional growth, and career mobility for all employees. From facilitated workshops and podcasts to eLearning modules, individual development plans, mentoring and coaching, we have invested in developmental capabilities to meet our employees at any stage of their career to help them grow. We have a variety of tools to facilitate developmental feedback. In 2021, we launched a mentoring program aimed to support the growth and development journey of employees, increase talent retention, enhance our inclusive culture, and increase partnership and collaboration across the business. We also hosted our first leadership summit in 2021, bringing leaders across the Company for two and a half days of dedicated development and enrichment activities. Thanks, in large part, to our training and development investments, in 2021 we were able to fill 33% of our open positions with internal candidates.

Financial Information

See our consolidated financial statements included elsewhere in this Form 10-K and accompanying notes to the consolidated financial statements.

Available Information

We were incorporated in the State of Delaware on February 10, 1995. Our corporate headquarters are located at 5505 Endeavor Lane, Madison, Wisconsin 53719. Our telephone number is 608-284-5700. Our Internet website address is *www.exactsciences.com*. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 are available free of charge through the investor relations page of our Internet website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission. Our Internet website and the information contained therein or connected thereto are not intended to be incorporated into this Annual Report on Form 10-K.

Item 1A. Risk Factors

We operate in a rapidly changing environment that involves a number of risks that could materially affect our business, financial condition or future results, some of which are beyond our control. This discussion highlights some of the risks that may affect future operating results. These are the risks and uncertainties we believe are most important for you to consider. We cannot be certain that we will successfully address these risks. If we are unable to address these risks, our business may not grow, our stock price may suffer, and we may be unable to stay in business. Additional risks and uncertainties not presently known to us, which we currently deem immaterial or which are similar to those faced by other companies in our industry or business in general, may also impair our business operations.

Risk Factors Summary

The following is a summary of the principal risks that could adversely affect our business, operations and financial results.

Risks Related to our Business and Business Strategy

- We may never become profitable.
- We may need additional capital to execute our business plan.
- Our success depends heavily on our Cologuard and Oncotype tests and the successful commercialization of our tests in development.
- Our operating results could be subject to significant fluctuation, which could increase the volatility of our stock price.
- We face intense competition from other companies and may not be able to compete successfully.
- If any of our facilities or our laboratory equipment were damaged or destroyed, or if we experience a significant disruption in our operations for any reason, our ability to continue to operate our business could be materially harmed.
- We heavily rely upon certain suppliers, including suppliers that are the sole source of certain products; the loss or interruption of supply from our suppliers could have a disruptive effect on our business.
- Failure in our information technology, storage systems, or our clinical laboratory equipment could significantly disrupt our operations and our research and development efforts.
- If the courier delivery services we use in connection with our tests are disrupted or become significantly more expensive, customer satisfaction and our business could be negatively impacted.
- The success of our business is substantially dependent upon the efforts of our senior management team and our ability to attract and retain personnel.
- Our business and reputation will suffer if we are unable to establish and comply with stringent quality standards to assure that the highest level of quality is observed in the performance of our tests.
- Our inability to manage growth could harm our business.
- We may engage in acquisitions that are not successful and which could disrupt our business, cause dilution to our stockholders and reduce our financial resources.
- International expansion of our business exposes us to business, regulatory, political, operational, financial, compliance and economic risks associated with doing business outside of the U.S.
- The COVID-19 outbreak has and may further materially and adversely affect our business and financial results.
- We currently offer COVID-19 testing, but there can be no assurance that we will continue to be able to successfully offer, perform, or generate revenues from the test.
- Our results of operations can be adversely affected by labor shortages, turnover, and labor cost increases.
- We may be a party to litigation in the normal course of business or otherwise, which could affect our business and financial position.

Risks Relating to Governmental Regulation and Reimbursement

- We face uncertainty related to healthcare reform, pricing, coverage, and reimbursement.
- If third-party payers, including managed care organizations, do not approve and maintain reimbursement for our tests at adequate reimbursement rates, our commercial success could be compromised.
- Because of Medicare billing rules or changes in Medicare billing rules and processes, we may not receive reimbursement for all tests provided to Medicare patients or may experience delays in receiving payments.
- If we are unable to obtain or maintain adequate reimbursement for our Oncotype tests outside of the U.S., our ability to expand internationally will be compromised.
- If we fail to meet any applicable requirements of CLIA or similar state laws, that failure could adversely affect any future payer consideration of our technologies, prevent their approval entirely, and/or interrupt the commercial sale and/or marketing of any products and services and otherwise cause us to incur significant expense.
- Failure to maintain compliance with FDA requirements may prevent or delay the development, marketing or manufacturing of our Cologuard test, or future improvements to that test.
- Delays in obtaining regulatory clearances or approvals for new tests, products, or services, or improvements to or expanded indications for our current offerings, could prevent, delay, or adversely impact future product commercialization.
- If the FDA were to change its position with respect to its regulation of the laboratory developed tests we offer or plan to offer, we could incur substantial costs and time delays and decreased demand for or reimbursement of our tests.
- We are subject to numerous U.S. and foreign laws and governmental regulations, and any governmental enforcement action may materially affect our financial condition and business operations.

- Our business is subject to various complex laws and regulations applicable to clinical diagnostics. We could be subject to significant fines and penalties if we or our partners fail to comply with these laws and regulations.
- Due to billing complexities in the diagnostic and laboratory service industry, we may not be able to collect payment for the tests we perform.
- Some of our activities may subject us to risks under federal, state, and foreign laws prohibiting 'kickbacks' and false or fraudulent claims as well as the Foreign Corrupt Practices Act.
- Compliance with the privacy laws and regulations may increase our costs.
- We expect to rely on third parties to conduct any future studies of our technologies that may be required by the FDA or other U.S. or foreign regulatory bodies, and those third parties may not perform satisfactorily.
- We are subject to increasingly complex taxation rules and practices.
- Our business is subject to complex and evolving laws, as well as customer and patient expectations, regarding data privacy, protection, and security.
- We are subject to evolving corporate governance and public disclosure expectations and regulations that impact compliance costs and risks of noncompliance.

Risks Relating to Product Development, Commercialization and Sales of our Products

- We have finite resources, which may restrict our success in commercializing our products, and we may be unsuccessful in entering into or maintaining third-party arrangements to support our internal efforts.
- If we are unable to deploy and maintain effective sales, marketing and medical affairs capabilities, we will have difficulty achieving market awareness and selling our products and services.
- The success of our Cologuard test, our Oncotype tests, and any other screening or diagnostic product or service we may offer or develop will depend on the degree of market acceptance by healthcare providers, patients, healthcare payers, and others in the medical community.
- Recommendations, guidelines, and quality metrics issued by various organizations may significantly affect payers' willingness to cover, and healthcare providers' willingness to prescribe, our products.
- We expect to make significant investments to research and develop new cancer tests, which may not be successful.
- Our dependence on distributors for sales outside of the U.S. could limit or prevent us from selling our tests in foreign markets and impact our revenue.
- Our research and development efforts will be hindered if we are not able to obtain samples, contract with third parties for access to samples, or complete timely enrollment in future clinical studies.

Risks Relating to our Intellectual Property

- We rely on strategic collaborative and licensing arrangements with third parties to develop critical intellectual property. We may not be able to successfully establish and maintain such intellectual property.
- We may be subject to substantial costs and liability, or be prevented from using technologies incorporated in our tests, as a result of litigation or other proceedings relating to patent or other intellectual property rights.
- If we are unable to protect or enforce our intellectual property effectively, we may be unable to prevent third parties from using our intellectual property, which would impair any competitive advantage we may otherwise have.

Risks Relating to our Securities

- We are required to assess our internal control over financial reporting on an annual basis and any future adverse results from such assessment could result in a loss of investor confidence and an adverse effect on our stock price.
- We face risks associated with currency exchange rate fluctuations, which could adversely affect our operating results.
- Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.
- Our stock price has fluctuated widely and is likely to continue to be volatile.
- Our balance sheet includes significant amounts of goodwill and intangible assets. The impairment of a significant portion of these assets would negatively affect our results of operations.
- Our management has broad discretion over the use of our available cash and marketable securities and might not spend available cash and marketable securities in ways that increase the value of your investment.
- Our indebtedness could adversely affect our business, financial condition, and results of operations.
- Servicing our debt will require a significant amount of cash, and we may not have sufficient cash flow from our business to pay amounts due under our indebtedness, including the convertible notes.

Risks Related to our Business and Business Strategy

We may never become profitable.

We have incurred losses since we were formed. From our date of inception on February 10, 1995 through December 31, 2021, we have accumulated a total deficit of approximately $2.64 billion. We expect to continue investing significantly toward development and commercialization of our colorectal cancer screening technology, our Oncotype tests, our blood-based multi-cancer early detection test and other products and services. If our revenue does not grow faster than our operating expenses, we will not be profitable. We cannot be certain that the revenue from the sale of any products or services based on our technologies will be sufficient to make us profitable.

We may need additional capital to execute our business plan.

Although we believe that we have sufficient capital to fund our operations for at least the next twelve months, we may require additional capital to fully fund our current strategic plan, which includes successfully commercializing our Cologuard and Oncotype tests and developing a pipeline of future products and services. Additional financing may not be available in amounts or on terms satisfactory to us or at all. Our success in raising additional capital may be significantly affected by general market conditions, the market price of our common stock, our financial condition, uncertainty about the future commercial success of our current products and services, the development and commercial success of future products or services, regulatory developments, the status and scope of our intellectual property, any ongoing litigation, our compliance with applicable laws and regulations and other factors. If we raise additional funds through the sale of equity, convertible debt or other equity-linked securities, our stockholders' ownership will be diluted, and the market price of our common stock could be depressed. We may issue securities that have rights, preferences and privileges senior to our common stock. If we raise additional funds through collaborations, licensing arrangements or other structured financing transactions, we may relinquish rights to our technologies or products or services, grant security interests in our assets or grant licenses to third parties on terms that are unfavorable to us.

Our success depends heavily on our Cologuard colorectal cancer screening test and our Oncotype DX breast cancer test and the successful commercialization of our tests in development.

For at least the next 12 months, our ability to generate revenues will depend very substantially on the commercial success of our Cologuard and Oncotype DX breast cancer tests. There can be no assurance that we will develop or commercialize any other products or services that will generate significant revenue. The commercial success of our tests and our ability to generate revenues will depend on a variety of factors, including the following:

- acceptance in the medical community;
- inclusion in healthcare guidelines and recommendations, such as those developed by ACS, USPSTF, American Society of Clinical Oncology, and NCCN and similar guidelines and recommendations outside the United States;
- inclusion in quality measures including the HEDIS measures and the CMS Medicare Advantage Star Ratings;
- recommendations and studies that may be published by government agencies, companies, professional organizations, academic or medical journals or other key opinion leaders;
- patient acceptance and demand;
- patient compliance with orders for our tests by healthcare providers, and patient adherence to recommendations regarding periodic re-testing;
- successful sales, marketing, and educational programs, including successful direct-to-patient marketing such as television advertising and social media;
- the number of patients screened for colorectal cancer, as well as the number of patients who use our Cologuard test for that purpose;
- the number of women diagnosed with breast cancer;
- sufficient coverage and reimbursement by third-party payers within and outside the U.S.;
- the existence of federal or state laws that mandate coverage for colorectal cancer and other types of screening, the extent to which those laws mandate coverage of our tests and the enforcement of those laws;
- the amount and nature of competition from other products and procedures;
- maintaining regulatory approvals to legally market;
- the ease of use of our ordering process for healthcare providers;
- maintaining and defending patent protection for the intellectual property relevant to our products and services; and
- our ability to establish and maintain adequate commercial manufacturing, distribution, sales and CLIA laboratory testing capabilities.

If we are unable to continue to grow sales of our Cologuard and Oncotype DX breast cancer tests or if we are delayed or limited in doing so, our business prospects, financial condition and results of operations would be adversely affected.

Additionally, we are devoting significant resources to the development of an improved version of our Cologuard test, a MCED test, minimal residual disease test, as well as other new products. The successful commercialization of these tests will also be subject to the factors listed above, among others. If we are unable to successfully commercialize these tests in development, our business prospects, financial condition and results of operations would be adversely affected.

Our operating results could be subject to significant fluctuation, which could increase the volatility of our stock price and cause losses to our stockholders.

Our revenues and results of operations may fluctuate significantly, depending on a variety of factors, including the following:

- the impact of the COVID-19 pandemic on our business and operations;
- our success in marketing and selling, and changes in demand for, our Cologuard and Oncotype tests, and the level of reimbursement and collection obtained for such tests;
- seasonal variations affecting healthcare provider recommendations for our tests and patient compliance with healthcare provider recommendations, including without limitation holidays, weather events, and circumstances such as the outbreak of influenza that may limit patient access to medical practices for diagnostic tests and preventive services;
- our success in collecting payments from third-party payers, patients and collaborative partners, variation in the timing of these payments and recognition of these payments as revenues;
- the pricing of our tests, including potential changes in CMS or other reimbursement rates;
- circumstances affecting our ability to provide our tests, including weather events, supply shortages, or regulatory or other circumstances that adversely affect our ability to manufacture our tests or process tests in our clinical laboratories;
- fluctuations in the amount and timing of our selling and marketing costs and our ability to manage costs and expenses and effectively implement our business; and
- our research and development activities, including the timing, size, complexity, and cost of clinical studies.

We face intense competition from other companies and may not be able to compete successfully.

We operate in a rapidly evolving and highly competitive industry. There are a number of private and public companies that offer products or have announced that they are developing products that compete with ours. Some of our current and potential competitors may have significant competitive advantage over us, which may make them more attractive to hospitals, clinics, group purchasing organizations and physicians, including:

- greater brand recognition;
- larger or more established distribution networks and customer bases;
- a broader product portfolio, resulting in greater ability to market their products;
- more extensive research, development, sales, marketing, and manufacturing capabilities and greater financial resources; and
- greater technical resources positioning them to continue to improve their technology in order to compete in an evolving industry.

We may be unable to compete effectively against our competitors either because their products and services are superior or because they are more effective in developing or commercializing competing products and services. Furthermore, even if we do develop new marketable products or services, our current and future competitors may develop products and services that are more clinically or commercially attractive than ours, and they may bring those products and services to market earlier or more effectively than us. If we are unable to compete successfully against current or future competitors, we may be unable to increase market acceptance for and sales of our tests, which could prevent us from increasing or sustaining our revenues or achieving sustained profitability and could cause the market price of our common stock to decline.

If any of our facilities or our laboratory equipment were damaged or destroyed, or if we experience a significant disruption in our operations for any reason, our ability to continue to operate our business could be materially harmed.

We currently perform our Cologuard and COVID-19 tests in laboratory facilities in Madison, Wisconsin. We manufacture the Cologuard test in two facilities in Madison, Wisconsin. Our headquarters are also located in Madison, Wisconsin. We perform our Oncotype DX tests out of our clinical laboratory facilities in Redwood City, California. Redwood City is situated near active earthquake fault lines and we do not have a redundant facility where we can perform our Oncotype DX tests. We also operate laboratories in Phoenix, Arizona, Marshfield, Wisconsin, and provide a testing facility in Trier, Germany. If our present, or any future facilities, were to be damaged, destroyed or otherwise unable to operate, whether due to fire, floods, storms, tornadoes, earthquakes, other inclement weather events or natural disasters, employee malfeasance, terrorist acts, power outages, or otherwise, it may render it difficult or impossible for us to perform our tests for some period of time and our business could be severely disrupted. Our facilities and the equipment we use to perform our tests would be costly to replace and could require substantial lead time to repair or replace. The inability to perform our tests or the backlog of tests that could develop if any of our facilities become inoperable for even a short period of time may result in the loss of customers or harm our reputation, and we may be unable to regain those customers in the future. Although we possess insurance for damage to our property and the disruption of our business, this insurance may not be sufficient to cover all of our potential losses and may not continue to be available to us on acceptable terms, if at all.

In order to rely on a third party to perform certain of our tests, we could only use another facility with established state licensure and CLIA accreditation under the scope of which Oncotype DX tests could be performed following validation and other required procedures. We cannot assure you that we would be able to find another CLIA certified facility willing to comply with the required procedures, that this laboratory would be willing to perform the tests for us on commercially reasonable terms, or that it would be able to meet our quality or regulatory standards. In order to establish a redundant clinical reference laboratory outside of our Redwood City, California facilities, we would have to spend considerable time and money securing adequate space, constructing the facility, recruiting and training employees, and establishing the additional operational and administrative infrastructure necessary to support a second facility. We may not be able, or it may take considerable time, to replicate our testing processes or results in a new facility. Additionally, any new clinical reference laboratory facility opened by us would be subject to certification under CLIA and licensing by several states, including California and New York, which could take a significant amount of time and result in delays in our ability to resume operations.

We heavily rely upon certain suppliers, including suppliers that are the sole source of certain products; the loss or interruption of supply from our suppliers could have a disruptive effect on our business.

We purchase certain supplies from third-party suppliers and manufacturers. In some cases, due to the unique attributes of products that are incorporated into our tests, we maintain either a single-source supplier relationship or a very limited set of supplier relationships. Certain of our third-party suppliers possess exclusive intellectual property or otherwise may be the only party with the rights or expertise to provide us critical supplies. These third parties are independent entities subject to their own unique operational, regulatory compliance, and financial risks that are outside our control. These third parties may not be willing to enter or renew long-term supply arrangements with us or continue to supply us at all. Additionally, they may not perform their obligations in a timely and cost-effective manner and they may be unwilling to increase production capacity commensurate with demand for our tests or future products or services. Our relationships with suppliers may also be negatively affected by general supply chain material shortages worldwide, as suppliers struggle to keep pace with demand and manage their own supply chains.

We may become dependent on additional single- or limited-source suppliers, or become increasingly dependent on existing suppliers, as we expand and develop our product and service pipeline. For example, our oncomap and oncomap ExTra® tests are currently only validated to be performed on Illumina's sequencing platform and we are not aware of any other platform that we could use in the near future as a commercially viable alternative. Further, Illumina may be the only commercially viable supplier of certain equipment and reagents necessary for future tests we may develop, including MCED, MRD, and recurrence monitoring tests. We currently procure Illumina equipment and reagents on a purchase order basis, without any long-term supply agreement. In August 2021, Illumina completed its acquisition of GRAIL, which is commercializing a MCED test against which certain of our planned tests would compete. Illumina's ownership of GRAIL could incentivize Illumina to offer its sequencing products in a manner that advantages GRAIL over us and other competitors, including the potential that Illumina may be unwilling or unable to supply, or commit to supplying, us with sequencing equipment and reagents on commercially acceptable terms, or at all. Although Illumina has made an irrevocable standing offer to supply any customer with its sequencing products on certain terms, that offer may not provide pricing or other terms necessary for us or others to successfully compete against GRAIL, including outside of the U.S. Although we expect to continue our efforts to validate

alternative sequencing platforms on which we could run our oncomap or oncomap ExTra tests or other future tests in a commercially viable manner, we may expend considerable time and efforts, endure delays to our test development and commercialization timelines, and be ultimately unsuccessful in our efforts to validate alternatives. Even if we validate an alternative sequencing platform, we may become substantially dependent on the supplier of that platform.

Similarly, as an additional example, we rely on Hamilton Company to provide us laboratory equipment and related supplies (such as racking and pipette tips) necessary to perform certain critical DNA analysis steps in our clinical laboratory tests, including our Cologuard, Oncotype DX and COVID-19 tests. Although other companies may offer viable alternative platforms, we have invested significant capital, time and expertise to procure Hamilton machines and to optimize their use in our tests. Industry demand for Hamilton supplies has increased significantly since the onset of the COVID-19 pandemic, and although we have a long-term supply agreement with Hamilton, it is possible that Hamilton could become unable or unwilling to continue to provide us with certain equipment and supplies on commercially acceptable terms, if at all. Hamilton may require us to exclusively use Hamilton consumables and components in connection with certain Hamilton laboratory equipment. Therefore, if our access to certain Hamilton consumables and components became impacted, we may need to completely replace the Hamilton platform. Validating alternative vendors' offerings could be expensive, time-consuming, and unsuccessful. Further, because our Cologuard test is regulated by the FDA, we may also need FDA clearance or approval to replace certain Hamilton equipment and supplies with another vendor's offerings. FDA approval or clearance may entail extensive new clinical and material costs and delays and may be ultimately unsuccessful.

The loss of a critical supplier, the failure to perform by a critical supplier, the deterioration of our relationship with a critical supplier or any unilateral modification to the contractual terms under which we are supplied materials could have a disruptive effect on our business, and could adversely affect our results of operations for an extended period of time, particularly if we are required to validate an alternative supplier.

Failure in our information technology, storage systems, or our clinical laboratory equipment could significantly disrupt our operations and our research and development efforts.

Our ability to execute our business strategy depends, in part, on the continued and uninterrupted performance of our information technology ("IT") systems, which support our operations, including at our clinical laboratories, and our research and development efforts. We are dependent on our IT systems to receive and process test orders, securely store patient health records and deliver the results of our tests. The integrity and protection of our own data, and that of our customers and employees, is critical to our business. The regulatory environment governing information, security and privacy laws is increasingly demanding and continues to evolve. IT systems are vulnerable to damage from a variety of sources, including telecommunications or network failures, malicious human acts from criminal hackers, hacktivists, state-sponsored intrusions, industrial espionage and employee malfeasance, breaches due to employee error and natural disasters. Moreover, despite network security and back-up measures, some of our servers are potentially vulnerable to physical or electronic break-ins, computer viruses, and similar disruptive problems.

High-profile security breaches at other companies and in government agencies have increased in recent years, and security industry experts and government officials have warned about the risks of hackers and cyber-attacks targeting businesses such as ours. Cyber-attacks are becoming more sophisticated and frequent, and in some cases have caused significant harm. Computer hackers and others routinely attempt to breach the security of technology products, services and systems, and to fraudulently induce employees, customers, or others to disclose information or unwittingly provide access to systems or data. While we devote significant resources to security measures to protect our systems and data, these measures cannot provide absolute security.

We have experienced and expect to continue to experience attempted cyber-attacks of our IT systems or networks. To date, none of these attempted cyber-attacks has had a material effect on our operations or financial condition. However, any such breach or interruption could compromise our networks and the information stored therein could be accessed by unauthorized parties, publicly disclosed, lost or stolen. Despite the precautionary measures we have taken to prevent unanticipated problems that could affect our IT systems, unauthorized access, loss or disclosure could also disrupt our operations, including our ability to:

- process tests, provide test results, bill payers or patients;
- process claims and appeals;
- provide customer assistance services;
- conduct research and development activities;

- collect, process and prepare company financial information;
- provide information about our tests and other patient and healthcare provider education and outreach efforts through our website; and
- manage the administrative aspects of our business and damage to our reputation.

Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, such as the Health Insurance Portability and Accountability Act of 1996, similar U.S. state data protection regulations, including the California Consumer Privacy Act, the E.U. General Data Protection Regulation, or GDPR, and other regulations, the breach of which could result in significant penalties.

System upgrades and enhancements require significant expenditures and allocation of valuable employee resources. Differences in software and systems across our operations may create complexity and compatibility problems. As we complete acquisitions, it is necessary for us to integrate the acquired company's information technology systems into our existing systems. Delays in integration or disruptions to our business from implementation of new or upgraded systems could have a material adverse impact on our financial condition and operating results. There can be no assurance that our process of improving existing systems, developing new systems to support our expanding operations, integrating new systems, protecting confidential patient information, and improving service levels will not be delayed or that additional systems issues will not arise in the future. Although we carry insurance for this purpose, failure to adequately protect and maintain the integrity of our information systems and data, including as a result of a security breach, may result in significant losses that exceed our insurance coverage limits and have a material adverse effect on our financial position, results of operations and cash flows.

We rely on courier delivery services to transport Cologuard collection kits to patients and samples for all of our tests back to laboratory facilities for analysis. If these delivery services are disrupted or become significantly more expensive, customer satisfaction and our business could be negatively impacted.

In most cases, we ship Cologuard collection kits to patients, and patients ship samples to our Madison, Wisconsin laboratory facilities for analysis, by air and ground express courier delivery service. Additionally, medical providers typically ship samples for Oncotype testing to our laboratory facilities via air and ground express courier delivery service. Disruptions in delivery service, whether due to bad weather, natural disaster, labor disruptions, terrorist acts or threats, or for other reasons, can adversely affect customer satisfaction, specimen quality and our ability to provide our services on a timely basis. If the courier delivery services that transport Cologuard collection kits or other test samples institute significant price increases, our profitability would be negatively affected and we may need to identify alternative delivery methods, if possible, modify our service model, or attempt to raise our pricing, which may not be possible with regard to Medicare claims or commercially practicable with regard to commercial claims.

The success of our business is substantially dependent upon the efforts of our senior management team and our ability to attract and retain personnel.

Our success depends largely on the skills, experience, and performance of key members of our senior management team. Our executives are critical to directing and managing our growth and development in the future. Our success is substantially dependent upon our senior management's ability to lead our company, implement successful corporate strategies and initiatives, develop key relationships, including relationships with collaborators and business partners, and successfully commercialize products and services. If we were to lose any of our senior management team, we may experience difficulties in competing effectively, developing our technologies and implementing our business strategies.

Competition for desirable personnel is intense, and there can be no assurance that we will be able to attract and retain the necessary staff. Our research and development programs, commercial laboratory operations and information technology infrastructure depend on our ability to attract and retain highly skilled personnel. We may not be able to attract or retain qualified talent due to the competition for qualified personnel among life science and technology businesses. We also face competition from universities and public and private research institutions in recruiting and retaining highly qualified scientific personnel. In addition, our success depends on our ability to attract and retain salespeople with extensive experience in primary care, oncology, gastroenterology, women's health, and urology and close relationships with healthcare providers and other hospital personnel. All of our employees in the U.S. are at will, which means that either we or the employee may terminate their employment at any time. If we are not able to attract and retain the necessary personnel, our business and operating results could be harmed.

Our results of operations can be adversely affected by labor shortages, turnover, and labor cost increases.

Labor is a significant component of operating our business. A number of factors may adversely affect the labor force available to us or increase labor costs, including high employment levels, federal unemployment subsidies, including unemployment benefits offered in response to the COVID-19 pandemic, increased wages offered by other employers, vaccine mandates and other government regulations and our responses thereto. As more employers offer remote work, we may have more difficulty recruiting for jobs that require on-site attendance, such as certain clinical laboratory and sales roles. Although we have not experienced any material labor shortage to date, we have recently observed an overall tightening and increasingly competitive labor market. A sustained labor shortage or increased turnover rates within our employee base, caused by COVID-19 or as a result of general macroeconomic factors, could lead to increased costs, such as increased overtime or financial incentives to meet demand and increased wage rates to attract and retain employees, and could negatively affect our ability to efficiently operate our clinical laboratories and overall business. If we are unable to hire and retain employees capable of performing at a high level, or if mitigation measures we may take to respond to a decrease in labor availability have unintended negative effects, our business could be adversely affected.

Additionally, the operations of our vendors and partners could also suffer from labor shortages, turnover, and labor cost increases which could result in supply chain disruptions and increases in the costs of the products and services we purchase, each of which could adversely affect our operations.

Our business and reputation will suffer if we are unable to establish and comply with stringent quality standards to assure that the highest level of quality is observed in the performance of our tests.

Inherent risks are involved in providing and marketing cancer tests and related services. Patients and healthcare providers rely on us to provide accurate clinical and diagnostic information that may be used to make critical healthcare decisions. As such, users of our tests may have a greater sensitivity to errors than users of some other types of products and services.

We must maintain top service standards and FDA-mandated and other quality controls. Past or future performance or accuracy defects, incomplete or improper process controls, excessively slow turnaround times, unanticipated uses of our tests or mishandling of samples or test results (whether by us, patients, healthcare providers, courier delivery services, or others) can lead to adverse outcomes for patients and interruptions to our services. These events could lead to voluntary or legally mandated safety alerts relating to our tests or our laboratory facilities and could result in the removal of our products and services from the market or the suspension of our laboratories' operations. Insufficient quality controls and any resulting negative outcomes could result in significant costs and litigation, as well as negative publicity that could reduce demand for our tests and payers' willingness to cover our tests. Even if we maintain adequate controls and procedures, damaging and costly errors may occur.

Our inability to manage growth could harm our business.

In connection with the commercialization of our tests, we have added, and expect to continue to add personnel in the areas of sales and marketing, laboratory operations, billing and collections, quality assurance, and compliance. Our number of full-time employees has increased from 4,110, as of December 31, 2019, to 4,833, as of December 31, 2020 and to 6,278, as of December 31, 2021. Further, as we build our commercialization efforts and expand research and development activities for new products and services, the scope and complexity of our operations is increasing significantly. As a result of our growth, our operating expenses and capital requirements have also increased, and we expect that they will continue to increase significantly. Our ability to manage our growth effectively requires us to expend funds to improve our operational, financial and management controls, reporting systems and procedures. As we move forward in commercializing our tests, we will also need to effectively manage our growing manufacturing, laboratory operations, and sales and marketing needs. We are continuing to expand our current facilities and add new facilities to support anticipated demand for our tests and anticipated growth in our personnel. We face various risks in managing these expansion efforts, including financing, construction delays, budget management, quality control, design efficiency, and transition execution. If we are unable to manage our anticipated growth effectively, our business could be harmed.

We may engage in acquisitions that are not successful and which could disrupt our business, cause dilution to our stockholders and reduce our financial resources.

We undertake acquisition activities from time to time. For example, in November 2019 we completed the acquisition of Genomic Health, Inc., in March 2020 we completed the acquisitions of Paradigm Diagnostics, Inc. and Viomics, Inc., in October 2020 we completed the acquisitions of Base Genomics Limited ("Base Genomics"), in January 2021 we completed the acquisition of Thrive Earlier Detection Corporation, in April 2021 we completed the acquisition of Ashion Analytics, LLC, in June 2021 we completed the acquisition of PFS Genomics Inc., and in December 2021 we completed the acquisition of PreventionGenetics, LLC. Certain risks may exist as a result of these and other acquisition activities, including, among others, that:

- we may encounter potential unknown liabilities and unforeseen increased expenses, delays or unfavorable conditions in connection with the integration of the acquired businesses into our business;
- we may be unable to successfully integrate the acquired businesses into our business;
- we may lose key employees;
- we may encounter potential unknown liabilities and unforeseen risks associated with contracts containing consent and/or other provisions that may be triggered by the acquisitions;
- we may be unable to realize the anticipated benefits of the acquisitions or do so within the anticipated timeframe;
- our future results will suffer if we do not effectively manage our expanded operations; and
- the market price of our common stock may decline as a result of the acquisitions.

In the future, we may enter into transactions to acquire other businesses, products, services or technologies, which may ultimately be unsuccessful. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by investors, healthcare providers, patients and others. In addition to the risks outlined above, we may decide to incur debt in connection with an acquisition or issue our common stock or other securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

International expansion of our business exposes us to business, regulatory, political, operational, financial, liability, compliance and economic risks associated with doing business outside of the U.S.

Our business strategy incorporates international expansion, which includes growing our direct sales and healthcare provider outreach and education capabilities outside of the U.S. and developing our relationships with payers and distributors in foreign markets. Doing business internationally involves a number of risks, including:

- difficulties in complying with multiple, conflicting and changing laws and regulations such as tax laws, export and import restrictions, employment laws, privacy and data protection laws, regulatory requirements and other governmental approvals, permits and licenses;
- significant competition from local and regional product offerings;
- difficulties in complying with unclear product regulations in various jurisdictions, including the changing regulation in Europe with regard to medical device and in vitro diagnostic ("IVD") regulations;
- restrictions or prohibitions of transmitting personal data, including patient data, from foreign jurisdictions to our centralized laboratories in the U.S.;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payer reimbursement regimes, public payers or patient self-pay systems;
- logistics and regulations associated with shipping tissue samples, performing tests locally or complying with local regulations concerning the analysis of tissue, including infrastructure conditions and transportation delays;
- limits in our ability to access or penetrate international markets if we are not able to process tests locally;
- lack of intellectual property protection in certain markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our tests and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade and other business restrictions;

- regulatory and compliance risks that relate to maintaining accurate information and control over the activities of our salesforce and distributors that may fall within the purview of the U.S. FCPA, its books and records provisions or its anti-bribery provisions, or similar anti-bribery or anti-corruption laws or regulations, such as the U.K. Anti-bribery Act and the U.K. Criminal Finances Act;
- complexity of compliance with local standard contractual requirements to access public customers and payers.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our financial condition and results of operations.

The COVID-19 outbreak has and may further materially and adversely affect our business and financial results.

The COVID-19 pandemic, together with related precautionary measures, has materially disrupted our business since March 2020 and may continue to disrupt our business for an unknown period of time. COVID-19 has significantly impacted, and may continue to significantly impact, our work force, supply chain and operating results including our revenues, margins, and cash utilization, among other measures. The territories in which we market, sell, distribute and perform our tests are attempting to address the COVID-19 pandemic in varying ways, including stay-at-home orders, temporarily closing businesses, restricting gatherings, restricting travel, and mandating social distancing and face coverings. The level and nature of the disruption caused by COVID-19 is unpredictable, may be cyclical and long-lasting and may vary from location to location.

The COVID-19 pandemic has materially impacted our business, and may continue to impact our business for an unknown period of time. Such impacts may include the following:

- our sales team has been, and for an extended period of time may continue to be, limited in their in-person interactions with healthcare providers, and therefore, also limited in their ability to engage in various types of healthcare provider education activities;
- healthcare providers and patients have canceled or delayed scheduling standard wellness visits and other non-emergency appointments and procedures (including mammograms and prostate cancer screenings), contributing to a decline in orders for our products or services during certain periods;
- restrictions on travel, commerce, and shipping may prevent patients and pathologists from shipping samples to our clinical laboratories;
- pandemic-related supply chain disruptions (whether caused by restrictions, congestion, or slowdowns in shipping or logistics, increases in demand for certain goods used on our operations, or otherwise) may hinder, or even force us to suspend, operations at some or all of our clinical laboratories;
- illnesses, quarantines, financial hardships, restrictions on travel, commerce and shipping, or other consequences of the pandemic, may disrupt our supply chain or other business relationships, and we or other parties may assert rights under force majeure clauses to excuse performance;
- we have experienced periods of reduced volumes at our clinical laboratories and future reduction in volumes could result in the need to suspend operations at some or all of our clinical laboratories;
- our efforts to manage our operations through a volatile and cyclical pandemic, which have included cost cutting measures, may hinder our efforts to commercialize our products or delay the development of future products and services;
- we and our partners have postponed or canceled clinical studies, which may delay or prevent our launch of future products and services and increase the opportunity for competitors to develop products and services that compete with ours;
- our workforce may be infected by the virus or otherwise distracted, which could disrupt commercial or laboratory operations;
- a combination of factors, including infection from the virus, supply shortfalls or disruptions, and inability to obtain or maintain equipment, could increase our operating expenses and adversely affect our lab capacity and our ability to meet the demand for our testing services;
- we have adjusted, and expect to continue to adjust, our precautionary measures at our various locations based on our perception of local recovery levels and applicable governmental regulations, and our business could be negatively affected if these precautionary measures prove to be excessive, ineffective or inadequate; and
- we may inaccurately estimate the duration or severity of the COVID-19 pandemic, which could cause us to misalign our staffing, spending, activities, and precautionary measures with current market or future market conditions.

Despite our efforts, the ultimate impact of COVID-19 depends on factors beyond our knowledge or control, including the duration and severity of the outbreak, third-party actions taken to contain its spread and mitigate its public health effects, and short- and long-term changes in the behaviors of medical professionals and patients resulting from the pandemic.

We currently offer COVID-19 testing, but there can be no assurance that we will continue to successfully offer, perform, or generate revenues from the test.

In late March 2020, we began providing COVID-19 testing. In 2021, we saw an approximately 39% reduction in our COVID-19 testing revenues. The success of our test, our ability to continue to generate revenues from COVID-19 testing, and our ability to generate profits from COVID-19 testing will depend on a variety of factors, including:

- the level of demand for COVID-19 testing, the price we are able to charge for performing the test, and the length of time for which that demand persists;
- the availability of COVID-19 testing from other laboratories;
- the emergence of other forms of COVID-19 testing (including antigen and antibody screening tests) and other sample collection methods, which healthcare providers and patients may prefer to our test;
- the potential for supply disruptions and our reliance on certain single-source suppliers;
- the capacity of our laboratories to satisfy both COVID-19 testing and other testing demands;
- the extent to which we choose to allocate limited laboratory capacity, supplies, and other resources to areas of our business other than COVID-19 testing; and
- the complexity of billing for, and collecting payment for, our test.

COVID-19 testing may divert resources and distract management's attention from other projects that may be more profitable or strategic. If we are unable to successfully provide COVID-19 testing while continuing to operate our business, our results of operations, financial position, and reputation may suffer.

We may be a party to litigation in the normal course of business or otherwise, which could affect our business and financial position.

From time to time, we are a party to or otherwise involved in legal proceedings, claims and government investigations and other legal matters, both inside and outside the United States, arising in the ordinary course of our business or otherwise. We are currently involved in various legal proceedings and claims that have not yet been fully resolved, and additional claims may arise in the future. Additionally, the sale and use of our tests could lead to product or professional liability claims. Legal proceedings can be complex and take many months, or even years, to reach resolution, with the final outcome depending on a number of variables, some of which are not within our control. Litigation is subject to significant uncertainty and may be expensive, time-consuming, and disruptive to our operations. Although we will vigorously defend ourselves in such legal proceedings, their ultimate resolution and potential financial and other impacts on us are uncertain. For these and other reasons, we may choose to settle legal proceedings and claims, regardless of their actual merit. If a legal proceeding is resolved against us, it could result in significant compensatory damages, and in certain circumstances punitive or trebled damages, disgorgement of revenue or profits, remedial corporate measures or injunctive relief imposed on us. If our existing insurance does not cover the amount or types of damages awarded, or if other resolution or actions taken as a result of a legal proceeding were to restrain our ability to operate, our financial position, results of operations or cash flows could be materially adversely affected. Any claim brought against us, with or without merit, could increase our liability insurance rates or prevent us from securing insurance coverage in the future. In addition, legal proceedings, and any adverse resolution thereof, can result in adverse publicity and damage to our reputation, which could adversely impact our business.

The amounts we record for legal contingencies can result from a complex series of judgments about future events and uncertainties and can rely heavily on estimates and assumptions. While we have accrued for certain potential legal liabilities, there is no guarantee that additional costs will not be incurred beyond the amounts accrued. Additional information regarding certain legal matters in which we are involved can be found in Note 15 to our Condensed Consolidated Financial Statements in Part II, Item 8.

Risks Relating to Governmental Regulation and Reimbursement

We face uncertainty related to healthcare reform, pricing, coverage, and reimbursement.

Healthcare reform laws, including the Patient Protection, the ACA, and the Protecting Access to Medicare Act of 2014 ("PAMA"), are significantly affecting the U.S. healthcare and medical services industry. Existing legislation, and possible future legal and regulatory changes, including potential repeal or modification of the ACA, elimination of penalties regarding the individual mandate for coverage, or approval of health plans that allow lower levels of coverage for preventive services, could materially change the structure and finances of the health insurance system and the methodology for reimbursing medical services, drugs and devices, including our current and future products and services. The ACA has also been the subject of various legal challenges and if the plaintiffs in any case challenging the ACA are ultimately successful insurance coverage for our tests could be materially and adversely affected. Any change in reimbursement policy could result in a change in patient cost-sharing, which could adversely affect a provider's willingness to prescribe and patient's willingness and ability to use our tests and any other product or service we may develop. Healthcare reforms, which may intend to reduce healthcare costs, may have the effect of discouraging third-party payers from covering certain kinds of medical products and services, particularly newly developed technologies, like those we have developed in the past or we may develop in the future. We cannot predict whether future healthcare reform initiatives will be implemented at the federal or state level or the effect any such future legislation or regulation will have on us. The taxes imposed by new legislation, cost reduction measures and the expansion in the government's role in the U.S. healthcare industry may result in decreased profits to us, which may adversely affect our business, financial condition and results of operations.

PAMA presents significant uncertainty for future CMS reimbursement rates. Because Medicare currently covers a significant number of our patients, any reduction in the CMS reimbursement rate for our tests would negatively affect our revenues and our business prospects. Under PAMA, CMS reimbursement rates for clinical diagnostic laboratory tests are updated every three years or annually for clinical laboratory tests that are considered "advanced diagnostic laboratory tests." There can be no assurance under PAMA that adequate CMS reimbursement rates will continue to be assigned to our tests. Congress could modify or repeal PAMA in the future or CMS could modify regulations under PAMA, and any such action could have the effect of reducing the CMS reimbursement rate for our tests. Further, it is possible that Medicare or other federal payers that provide reimbursement for our tests may suspend, revoke or discontinue coverage at any time, may require co-payments from patients, or may reduce the reimbursement rates payable to us. Any such action could have a negative impact on our revenues.

Coverage of our Cologuard test and other screening products that we may develop may also depend, in whole or in part, on whether payers determine, or courts and/or regulatory authorities determine, coverage is required under applicable federal or state laws mandating coverage of certain cancer screening services. For example, while we believe the ACA Mandate requires most health insurers to cover our Cologuard test for most patients between the ages of 45 and 75 without patient cost-sharing, some health insurers have disagreed and determined not to cover our Cologuard test and others may take that position in the future. Further, if the ACA is repealed, replaced or overturned, or even if it is not, states may decide to modify their laws, which may include repeal of those coverage mandates that we believe currently apply to our Cologuard test.

Outside of the U.S., we largely depend on public or government-controlled or regulated payers for coverage of our Oncotype tests. In order to accommodate the unique characteristics of our Oncotype tests, public payers in certain non-U.S. markets have designed reimbursement frameworks specifically for our tests. These payers could decide to modify or discontinue these special frameworks, potentially leading to lower reimbursement prices or the impossibility of providing the test in the market. Existing reimbursement processes or changes to those processes could impose additional administrative burdens on us, such as complex public tendering procedures, or on ordering physicians, which could adversely affect the number of payers covering the test or the number of orders placed. Public payers could condition reimbursement of our tests upon performance of our tests locally or, even in laboratories owned or operated by the payers. Any such change would adversely affect our ability to continue to serve those patients through our centralized labs in the U.S.

If payers, including managed care organizations, do not approve and maintain reimbursement for our tests at adequate reimbursement rates, our commercial success could be compromised.

Our commercial success depends, in large part, on the availability of adequate reimbursement for our current tests, including our flagship Cologuard and Oncotype tests and our products in development, from government insurance plans, managed care organizations and private insurance plans. Although we received a positive coverage decision and what we believe is an adequate reimbursement rate from CMS for our Cologuard test, it is also critical that other third-party payers approve and maintain reimbursement for our Cologuard test at adequate reimbursement rates. We also have received positive coverage determinations for our Oncotype DX breast cancer test for N-, ER+ patients from most third-party payers, but have less favorable coverage for our other Oncotype tests. Healthcare providers may be reluctant to prescribe, and patients may be reluctant to complete, our tests if they are not confident that patients will be reimbursed for our tests.

Third-party payers, both in the United States and internationally, are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for healthcare products and services. As a result, there is uncertainty surrounding the future level of reimbursement, if any, for our current tests and any new tests we may develop. Reimbursement by a third-party payer may depend on a number of factors, including a payer's determination that tests using our technologies are: sufficiently sensitive and specific; not experimental or investigational; approved or recommended by the major guideline organizations; subject to applicable federal or state coverage mandates; reliable, safe and effective; medically necessary; appropriate for the specific patient; and cost-effective.

Moreover, coverage determinations and reimbursement rates are subject to change, and we cannot guarantee that even if we initially achieve adequate coverage and reimbursement rates for our tests, they will continue to apply in the future or remain adequate as we face increases in operating costs, such as labor and supply costs that are subject to inflation. As noted above, under PAMA, our Medicare reimbursement rates will be subject to adjustment based on our volume-weighted median commercial reimbursement rate. Any reduction in our Medicare reimbursement rates could significantly and adversely affect our business prospects, financial condition, and results of operations.

Even where a third-party payer agrees to cover one of our tests, other factors may have a significant impact on the actual reimbursement we receive from that payer. For example, if we do not have a contract with a given payer, we may be deemed an "out-of-network" provider by that payer, which could result in the payer allocating a portion of the cost of the test to the patient, notwithstanding any applicable coverage mandate. We may be unsuccessful in our efforts to enter into, or maintain, a network contract with a given payer, and we expect that our network status with a given payer may change from time to time for a variety of reasons, many of which may be outside our control. To the extent one of our tests is out of network for a given payer, healthcare providers may be less likely to prescribe that test for their patients and their patients may be less likely to comply with those prescriptions that are written. Also, some payers may require that they give prior authorization for a test before they are willing to pay for it or review claims post-service to ensure the service was medically appropriate for specific patients. Prior authorization and other medical management practices may require that we, patients, or healthcare providers provide the payer with extensive medical records and other information. Prior authorization and other medical management practices impose a significant additional cost on us, may be difficult to comply with given our position as a laboratory that generally does not have direct access to patient medical records, may make healthcare providers less likely to prescribe our tests for their patients, and may make patients less likely to comply with healthcare provider orders for our tests, all or any of which may have an adverse effect on our revenues.

Because of Medicare billing rules or changes in Medicare billing rules and processes, we may not receive reimbursement for all tests provided to Medicare patients or may experience delays in receiving payments.

Under Medicare billing rules, payment for our Oncotype tests performed on Medicare beneficiaries who were hospital patients at the time the tumor tissue samples were obtained and whose tests were ordered less than 14 days from discharge must be bundled into the payment that the hospital receives for the services provided. Effective January 1, 2018, CMS changed its rules to permit laboratories that perform molecular pathology tests on specimens collected during a hospital outpatient stay to bill Medicare directly for such tests if they were performed following a hospital outpatient's discharge from the hospital outpatient department. The rule remains unchanged with respect to payment for our Oncotype tests performed on Medicare beneficiaries who were hospital inpatients at the time the tumor tissue was collected and whose tests were ordered less than 14 days from discharge – payment for those tests must be bundled into the payment that the hospital receives for its services provided. In these circumstances, hospitals are required to furnish services such as our tests as "services furnished under arrangements between a provider and an outside vendor" and only the hospital may bill Medicare for such tests. Under these circumstances, where the date of service for Medicare billing purposes is the date the specimen was collected and such date is within 14 days of inpatient discharge, we are required to bill hospitals for such tests. We refer to this rule, as it has been in effect and most recently amended as of January 1, 2018, as the Medicare Date of Service billing regulation.

These billing rules may lead to confusion regarding whether Medicare provides adequate reimbursement for our tests, and could discourage providers from ordering our tests for Medicare patients or even non-Medicare patients. In addition, changes in Medicare billing rules and processes could result in delays in receiving payments or receiving payments that are less than the original invoice. When hospitals disclaim responsibility for or delay payment of our bills for tests affected by the Medicare Date of Service rule, and when our collection efforts are unsuccessful, we may be forced to accept payments from hospitals that are less than the original invoice or we may be unable to collect from hospitals at all. Our inability to successfully collect payment from a hospital financially responsible for a test affected by the Medicare Date of Service rule may lead us to reject orders from that hospital that implicate the Medicare Date of Service billing regulation until any outstanding bills are paid. Compared to our breast cancer tests, a greater proportion of eligible patients for our colon and prostate Oncotype tests are covered by Medicare. We cannot assure you that Medicare will continue the Medicare Date of Service billing regulation in its current form, that Medicare will not seek to include molecular pathology tests in hospital outpatient bundling rules in the future, or that other payers will not adopt similar billing rules. As described in Note 15 of the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report on Form 10-K, the United States DOJ is investigating Genomic Health's compliance with the Medicare Date of Service billing regulation. An adverse outcome could include our being required to pay treble damages, incur civil and criminal penalties, paying attorneys' fees, entering into a corporate integrity agreement, being excluded from participation in government healthcare programs, including Medicare and Medicaid, and other adverse actions that could materially and adversely affect our business, financial condition, and results of operations.

If we are unable to obtain or maintain adequate reimbursement for our Oncotype DX tests outside of the U.S., our ability to expand internationally will be compromised.

The majority of our international Oncotype DX breast, prostate, and colon cancer test revenues come from payer reimbursement, payments from our distributors, and patient self-pay. In many countries outside of the U.S., various coverage, pricing and reimbursement approvals are required for our tests to be available to patients in significant volume. We expect that it will take several years to establish broad coverage and reimbursement for our tests with payers in countries outside of the U.S., and our efforts may not be successful.

Even if public or private reimbursement is obtained, it may cover competing tests, or the reimbursement may be limited to a subset of the eligible patient population or conditioned upon local performance of the tests or other requirements we may have difficulty satisfying.

Reimbursement levels outside of the U.S. may vary considerably from the domestic reimbursement amounts we receive. In addition, because we generally rely on distributors to obtain reimbursement for our tests in certain countries outside of the U.S., to the extent we do not have direct reimbursement arrangements with payers, we may not be able to retain reimbursement coverage in those countries if our agreement with a distributor is terminated or expires, if a distributor fails to pay us or if other events prevent payment. We may also be negatively affected by the financial instability of, and austerity measures implemented by, several countries in the European Union and elsewhere.

If we fail to meet any applicable requirements of CLIA or similar state laws, that failure could adversely affect any future payer consideration of our technologies, prevent their approval entirely, and/or interrupt the commercial sale and/or marketing of any products and services and otherwise cause us to incur significant expense.

We and certain laboratories with whom we collaborate are subject to federal and state laws and regulations regarding the operation of clinical laboratories. Federal CLIA requirements and laws of certain states, including New York, impose certification requirements for clinical laboratories and establish standards for quality assurance and quality control, among other things. Some state laws restrict laboratory marketing activities, which may adversely affect our ability to market our laboratory services. Clinical laboratories are subject to inspection by regulators, and to sanctions for failing to comply with applicable requirements. Sanctions available under CLIA include prohibiting a laboratory from running tests, requiring a laboratory to implement a corrective plan, and imposing civil monetary penalties. If we or our third party partners fail to meet any applicable requirements of CLIA or state law, that failure could adversely affect any payer consideration of our current or future technologies, prevent their approval entirely, and/or interrupt the commercial sale and/or marketing of any products and services and otherwise cause us to incur significant expense.

Failure to maintain compliance with FDA requirements may prevent or delay the development, marketing or manufacturing of our Cologuard test, or future improvements to that test.

As a condition of the FDA approval of our Cologuard test, we were required to conduct a post-approval study. The post-approval study concluded in 2020 and final results were submitted to FDA in late 2020. There is a risk that the FDA may modify or withdraw the approval of our Cologuard test if the results of this post-approval study are not satisfactory. We anticipate feedback from FDA in 2022 on the acceptance of these data to close the post-approval order.

Our manufacturing and laboratory facilities are periodically subject to inspection by the FDA and other governmental agencies to ensure they meet production and quality requirements. Operations at these facilities could be interrupted or halted if the FDA or other governmental agency deems the findings of such inspections unsatisfactory.

Further, failure to comply with FDA or other regulatory requirements regarding the development, marketing, promotion, manufacturing and distribution of our tests could result in fines, unanticipated compliance expenditures, recall or seizures of our products, total or partial suspension of production or distribution, restrictions on labeling and promotion, termination of ongoing research, disqualification of data for submission to regulatory authorities, enforcement actions, injunctions and criminal prosecution.

If we do not meet applicable regulatory or quality standards, our products may be subject to recall, and, under certain circumstances, we may be required to notify applicable regulatory authorities about a recall. In 2017, we recalled one of the components of our Cologuard test kit and circumstances may arise that cause us to recall other products or components used in connection with our Cologuard test. Any such recalls could have an adverse effect on our ability to provide the Cologuard test, which in turn would adversely affect our financial condition.

Delays in obtaining regulatory clearances or approvals for new medical devices, or improvements to or expanded indications for our current offerings, could prevent, delay or adversely impact future product commercialization.

Although the FDA has historically exercised enforcement discretion with regard to certain types of tests — commonly referred to as lab developed tests or LDTs — that are developed by laboratories certified pursuant to federal Clinical Laboratory Improvement Amendments, we may develop new tests that are regulated by the FDA as medical devices. Unless otherwise exempted, medical devices must receive either FDA regulatory approval or clearance before being marketed in the U.S. The FDA determines whether a medical device will require either regulatory approval or clearance based on statutory criteria that include the risk associated with the device and whether the device is similar to an existing, legally marketed product. The process to obtain either regulatory approval or clearance will likely be costly, time-consuming, and uncertain. However, we believe the regulatory approval process is generally more challenging than the clearance process. Even if we design a product that we expect to be eligible for the regulatory clearance process, the FDA may require that the product undergo the regulatory approval process. There can be no assurance that the FDA will ever permit us to market any new product that we develop. Even if regulatory approval or clearance is granted, such approval may include significant limitations on indicated uses, which could materially and adversely affect the prospects of any new medical device.

FDA regulatory approval or clearance is not just required for new medical devices we develop, but would also be required for certain enhancements we may seek to make to our Cologuard test or future FDA-approved or -cleared tests. For example, FDA approval or clearance may be required to make changes to the processes, equipment, reagents, and other consumables used in connection with a test. The FDA's pathway to approve or clear changes to tests can be time-consuming and costly and the FDA could ultimately reject our proposed changes.

Delays in receipt of, or failure to obtain, clearances or approvals could materially delay or prevent us from commercializing our products or result in substantial additional costs that could decrease our profitability. In addition, even if we receive FDA clearance or approval for a new or enhanced product, the FDA may condition, withdraw, or materially modify its clearance or approval.

If the FDA were to change its position with respect to its regulation of the laboratory developed tests we offer or may seek to offer in the future, we could incur substantial costs and time delays associated with meeting requirements for pre-market clearance or approval or we could experience decreased demand for or reimbursement of our tests.

The FDA has regulatory responsibility over, among other areas, instruments, test kits, reagents, and other medical devices used by clinical laboratories to perform diagnostic testing. Clinical laboratories certified under the Clinical Laboratory Improvement Amendments of 1988, or CLIA, frequently develop internal LDTs to provide diagnostic results to customers. LDTs are subject to CMS oversight through its enforcement of CLIA. The FDA has also claimed regulatory authority over all LDTs, but indicates that it has exercised enforcement discretion with regard to most LDTs offered by CLIA-certified laboratories, and has not subjected these tests to the panoply of FDA rules and regulations governing medical devices. IVDs like our Cologuard test are regulated as medical devices by the FDA. We believe that our Oncotype tests are not diagnostic kits and also believe that they are LDTs that are subject to regulation under CLIA and applicable state laws. As a result, we believe our Oncotype products fall within the scope of FDA's exercise of enforcement discretion and should not be subject to FDA oversight or review under current FDA guidelines. Packaging requirements for receipt of tumor tissue for our Oncotype products may be subject to regulation under Department of Transportation, International Air Transport Association, and other state, regional, or local laws.

At various times since 2006, the FDA has issued documents outlining its intent to require varying levels of FDA oversight of many LDTs, including our tests. It is unclear whether the FDA will proceed with rulemaking to regulate LDTs in the future.

In addition, legislative proposals addressing oversight of LDTs have been introduced in previous Congresses, and we expect that new legislative proposals will be introduced from time to time in the future. It is possible that legislation will be enacted into law or guidance could be issued by the FDA which may result in increased regulatory burdens for us to continue to offer our Oncotype tests or to develop and introduce new LDTs.

If pre-market review is required for our current LDTs, our business could be negatively impacted in the U.S. until such review is completed and clearance or approval is obtained, and the FDA could require that we stop selling our tests pending pre-market clearance or approval.

If our Oncotype tests are allowed to remain on the market but there is uncertainty about the regulatory status of such tests, if they are labeled investigational by the FDA, or if labeling claims the FDA allows us to make are more limited than the claims we currently make, orders or reimbursement may decline. The regulatory approval process may involve, among other things, successfully completing additional clinical studies and submitting a pre-market clearance notice or filing a pre-market approval application with the FDA. Such pre-market clinical testing could delay the commencement or completion of other clinical testing, significantly increase our test development costs, delay commercialization of any future LDTs, and interrupt sales of our current LDTs. Many of the factors that may cause or lead to a delay in the commencement or completion of clinical studies may also ultimately lead to delay or denial of regulatory clearance or approval. If pre-market review is required by the FDA, there can be no assurance that our LDTs will be cleared or approved on a timely basis, if at all, nor can there be assurance that the labeling claims cleared or approved by the FDA will be consistent with our current claims or adequate to support continued adoption of and reimbursement for our LDTs. Ongoing compliance with FDA regulations with respect to our current LDTs would increase the cost of conducting our business, and subject us to inspection by and the regulatory requirements of the FDA, for example registration and listing and medical device reporting, and penalties in the event we fail to comply with these requirements. We may also decide voluntarily to pursue FDA pre-market review of our LDTs if we determine that doing so would be appropriate.

We cannot predict the ultimate timing or form of final FDA guidance, legislation or regulation of LDTs and the potential impact on our existing tests, our tests in development or the materials used to perform our tests. While we qualify all materials used in our LDTs according to CLIA regulations, we cannot be certain that the FDA will not enact rules or guidance documents that could impact our ability to purchase certain materials necessary for the performance of our LDTs, such as products labeled for research use only. Should any of the reagents obtained by us from suppliers and used in conducting our LDTs be affected by future regulatory actions, our business could be adversely affected by those actions, including increasing the cost of testing or delaying and limiting or prohibiting the purchase of reagents necessary to perform testing.

Changes in funding or disruptions at FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to perform normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and clear or approve new products or changes to existing products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, federal government shutdowns, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result.

Separately, in response to the COVID-19 pandemic, the FDA made its on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities.

If a prolonged government shutdown occurs, or if global health concerns continue to prevent or delay the FDA or other regulatory authorities from conducting, at all or in a timely manner, their regular inspections, reviews, or other regulatory activities (including pre-submission engagements), it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We are subject to numerous U.S. and foreign laws and governmental regulations, and any governmental enforcement action may materially affect our financial condition and business operations.

We are subject to regulation in the United States by both the federal government and the states in which we conduct our business, as well as in other jurisdictions outside of the United States, including:

- Federal, state, and local laws regarding the use, storage, handling and disposal of medical and hazardous waste, as well as regulations relating to the safety and health of laboratory employees;
- the Federal Anti-Kickback Statute and state anti-kickback prohibitions and EKRA;
- the Federal Physician Self-Referral Law, commonly known as the Stark Law, and the state equivalents;
- the Federal Health Insurance Portability and Accountability Act of 1996, as amended ("HIPAA") and the California Consumer Privacy Act of 2018;
- the Medicare civil money penalty and exclusion requirements;
- the Federal False Claims Act civil and criminal penalties and state equivalents; and
- the Foreign Corrupt Practices Act, the United Kingdom Anti-Bribery Act, the GDPR and other national or provincial laws protecting personal information, the E.U. Medical Device and In Vitro Diagnostic Device Regulations, and national laws restricting industry interaction with healthcare professionals, all of which may or will apply to our international activities.

The U.S. Attorney's Offices have increased their scrutiny over the healthcare industry in recent years. The U.S. Congress, DOJ, Office of Inspector General of the Department of Health and Human Services, and Department of Defense have all issued subpoenas and other requests for information to conduct investigations of and commenced civil and criminal litigation against healthcare companies related to financial arrangements with healthcare providers, regulatory compliance, product promotional practices, and documentation, coding and billing practices. In addition, the Federal False Claims Act and state equivalents have led to whistleblowers filing numerous qui tam civil lawsuits against healthcare companies, in part, because a whistleblower can receive a portion of any amount obtained by the government through such a lawsuit.

Governmental enforcement action or qui tam civil litigation against us may result in material costs and occupy significant management resources, even if we ultimately prevail. In addition, governmental enforcement action may result in substantial fines, penalties or administrative remedies, including exclusion from government reimbursement programs and entry into corporate integrity agreements with governmental agencies, which could entail significant obligations and costs. As described further in Note 15 of the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report on Form 10-K, we are currently responding to (1) a civil investigative demand initiated by the U.S. DOJ concerning Genomic Health's compliance with the Medicare Date of Service billing regulations and (2) qui tam civil investigation related to allegations that we offered or gave gift cards to patients in exchange for returning the Cologuard screening test, in violation of the Federal Anti-Kickback Statute and False Claims Act. Adverse outcomes from these investigations could include our being required to pay treble damages, incur civil and criminal penalties, paying attorney's fees, entering into a corporate integrity agreement, being excluded from participation in government healthcare programs, including Medicare and Medicaid, and other adverse actions that could materially and adversely affect our business, financial condition and results of operations.

We have adopted policies and procedures designed to comply with these laws. In the ordinary course of our business, we conduct internal reviews of our compliance with these laws. Our compliance is also subject to governmental review. The growth of our business and sales organization and our expansion outside of the United States may increase the potential of violating these laws or our internal policies and procedures. The risk of our being found in violation of these or other laws and regulations is further increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action brought against us for violation of these or other laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of these laws and regulations, we may be subject to any applicable penalty associated with the violation, including civil and criminal penalties, damages and fines, we could be required to refund payments received by us, and we could lose the ability to bill for our tests and we could be required to curtail or cease our operations. Any of the foregoing consequences could seriously harm our business and our financial results.

Our business is subject to various complex laws and regulations applicable to clinical diagnostics. We could be subject to significant fines and penalties if we or our partners fail to comply with these laws and regulations.

As a provider of clinical diagnostic products and services, we and our partners are subject to extensive and frequently changing federal, state, local and foreign laws and regulations governing various aspects of our business. In particular, the clinical laboratory and healthcare industry is subject to significant governmental certification and licensing regulations, as well as federal, state and foreign laws regarding:

- test ordering and billing practices;
- marketing, sales and pricing practices;
- health information privacy and security, including HIPAA and comparable state and foreign laws;
- insurance, including foreign public reimbursement;
- anti-markup legislation; and
- consumer protection.

We are also required to comply with FDA regulations, including with respect to our labeling and promotion activities. In addition, advertising of our tests is subject to regulation by the Federal Trade Commission, or FTC, and advertising of laboratory services is regulated by certain state laws. Violation of any FDA requirement could result in enforcement actions, such as seizures, injunctions, civil penalties and criminal prosecutions, and violation of any FTC or state law requirement could result in injunctions and other associated remedies, all of which could have a material adverse effect on our business. Most states also have similar regulatory and enforcement authority for devices. Additionally, most foreign countries have authorities comparable to the FDA and processes for obtaining marketing approvals. In particular, the entry into application of the E.U.'s In Vitro Diagnostic Device Regulation will impose new requirements and create new compliance risks. Obtaining and maintaining these approvals, and complying with all laws and regulations, may subject us to similar risks and delays as those we could experience under FDA, FTC and state regulation. We incur various costs in complying and overseeing compliance with these laws and regulations. The growth of our business and sales organization, the acquisition of additional businesses or products and services and our expansion outside of the U.S. may increase the potential of violating these laws, regulations or our internal policies and procedures.

Healthcare policy has been a subject of extensive discussion in the executive and legislative branches of the federal and many state governments and healthcare laws and regulations are subject to change. Development of the existing commercialization strategy for our tests and planned development of products in our pipeline has been based on existing healthcare policies. We cannot predict what additional changes, if any, will be proposed or adopted or the effect that such proposals or adoption may have on our business, financial condition and results of operations.

If we or our partners, including our German laboratory partner, fail to comply with these laws and regulations, we could incur significant fines and penalties and our reputation and prospects could suffer. Additionally, any such partners could be forced to cease offering our products and services in certain jurisdictions, which could materially disrupt our business.

Due to billing complexities in the diagnostic and laboratory service industry, we may not be able to collect payment for the tests we perform, and delays in submitting claims could have an adverse effect on our revenue.

Billing for diagnostic and laboratory services is a complex process. Laboratories bill many different payers including patients, private insurance companies, Medicare, Medicaid, and employer groups, all of which have different billing requirements. We are continuing to work with third-party payers to cover and reimburse our tests. If we are unsuccessful, we may not receive payment for the tests we perform for patients on a timely basis, if at all, and we may not be able to provide services for patients with certain healthcare plans. In the past, failures to submit claims to insurers timely have required us to record downward adjustments to our revenue. Despite efforts to improve our billing systems and prevent recurrences of these failures, future failures to timely submit claims could result in further downward adjustments to revenue.

We may have to litigate to enforce coverage obligations under Medicare laws and laws that mandate coverage for certain screening or diagnostic tests or to enforce contractual coverage obligations. Such litigation may be costly, may divert management attention from other responsibilities, may cause payers, including those not directly involved in the litigation, to resist contracting with us, and may ultimately prove unsuccessful for a variety of reasons. We may face lawsuits by government or commercial payers if they believe they have overpaid us for our test services or as a result of other circumstances. We may face write-offs of doubtful accounts, disputes with payers and patients, and long collection cycles. We may face patient dissatisfaction, complaints or lawsuits, including to the extent our tests are not fully covered by insurers and patients become responsible for all or part of the price of the test. As a result, patient demand for our tests could be adversely affected. To the extent patients express dissatisfaction with our billing practices to their healthcare providers, those healthcare providers may be less likely to prescribe our tests for other patients, and our business would be adversely affected.

Even if payers do agree to cover our tests, our billing and collections process may be complicated by the following and other factors, which may be beyond our control:

- disputes among payers as to which payer is responsible for payment;
- disparity in coverage among various payers or among various healthcare plans offered by a single payer;
- payer medical management requirements, including prior authorization requirements;
- differing information and billing requirements among payers;
- failure by patients or healthcare providers to provide complete and correct billing information; and
- limitations and requirement for patient billing, including those related to deductibles, co-payments, and co-insurance originating from contracts with commercial payers.

Sometimes, when we have a contract with a commercial payer to cover our tests, we are not permitted to bill patients insured by that payer for amounts beyond deductibles, co-payments, and co-insurance as prescribed in the coverage agreement between the payer and the patients. Therefore, when such contracted payers do not pay us our full, contracted rate for a test, for example, for failure to satisfy prior-authorization or other payer medical management requirements, we may not be permitted to collect the balance from the patient and our business is adversely impacted.

The uncertainty of receiving payment for our tests and complex laboratory billing processes could negatively affect our business and our operating results.

Some of our activities may subject us to risks under federal and state laws prohibiting 'kickbacks' and false or fraudulent claims.

In addition to FDA marketing and promotion restrictions, several other types of state and federal healthcare fraud and abuse laws have been applied in recent years to restrict certain marketing practices in the healthcare product and service industry and to regulate billing practices and financial relationships with healthcare providers, hospitals and other healthcare providers. These laws include a federal law commonly known as the Medicare/Medicaid anti-kickback law, and several similar state laws, which prohibit payments intended to induce healthcare providers or others either to refer patients or to acquire or arrange for or recommend the acquisition of healthcare products or services. While the federal law applies only to referrals, products or services for which payment may be made by a federal healthcare program, state laws often apply regardless of whether federal funds may be involved. These laws constrain the sales, marketing and other promotional activities of manufacturers of medical devices and providers of laboratory services by limiting the kinds of financial arrangements, including sales programs, that may be used with hospitals, healthcare providers, laboratories and other potential purchasers or prescribers of medical devices and laboratory services. Other federal and state laws generally prohibit individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent, or are for items or services that were not provided as claimed.

In 2018, Congress passed EKRA as part of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act. Similar to the Medicare/Medicaid anti-kickback law, EKRA imposes criminal penalties for knowing or willful payment or offer, or solicitation or receipt, of any remuneration, whether directly or indirectly, overtly or covertly, in cash or in kind, in exchange for the referral or inducement of laboratory testing (among other healthcare services) unless a specific exception applies. However, unlike the Medicare/Medicaid anti-kickback law, EKRA is not limited to services covered by federal or state healthcare programs but applies more broadly to services covered by "healthcare benefit programs," including commercial insurers. As currently drafted, EKRA potentially expands the universe of arrangements that could be subject to government enforcement under federal fraud and abuse laws. In addition, while the Medicare/Medicaid anti-kickback law includes certain exceptions that are widely relied upon in the healthcare industry, not all of those same exceptions apply under EKRA. Because EKRA is a relatively new law, there is no agency guidance or court precedent to indicate how and to what extent it will be applied and enforced. We cannot assure you that our relationships with healthcare providers, sales representatives, hospitals, customers, or any other party will not be subject to scrutiny or will survive regulatory challenge under EKRA.

Additionally, to avoid liability under federal false claims laws, we must carefully and accurately code claims for reimbursement, proactively monitor the accuracy and appropriateness of Medicare claims and payments received, diligently investigate any credible information indicating that we may have received an overpayment, and promptly return any overpayments. Medicare payments are subject to audit, including through the Comprehensive Error Rate Testing ("CERT") program, and payments may be recouped by CMS if it is determined that they were improperly made. Currently, a significant percentage of our revenues are generated by payments from Medicare. The federal anti-kickback statute and certain false claims laws prescribe civil and criminal penalties (including fines) for noncompliance that can be substantial. While we continually strive to comply with these complex requirements, interpretations of the applicability of these laws to marketing and billing practices are constantly evolving and even an unsuccessful challenge could cause adverse publicity and be costly to respond to, and thus could harm our business and prospects. Our failure to comply with applicable laws could result in various adverse consequences that could have a material adverse effect upon our business, including the exclusion of our products and services from government programs and the imposition of civil or criminal sanctions.

Some of our activities may subject us to risks under foreign laws prohibiting 'kickbacks' as well as the Foreign Corrupt Practices Act.

Many countries in which we offer our tests have regulations prohibiting providers, as well as medical and in vitro diagnostic device manufacturers, from offering or providing a benefit to a healthcare professional in order to induce business. In situations involving healthcare providers employed by public or state-funded institutions or national healthcare services, violation of local anti-corruption or anti-gift laws may also constitute a violation of the U.S. FCPA.

The FCPA prohibits any U.S. individual, business entity or employee of a U.S. business entity from offering or providing, directly or through a third party, including the distributors we rely on in certain markets, anything of value to a foreign government official with corrupt intent to influence an award or continuation of business or to gain an unfair advantage, whether or not such conduct violates local laws. In addition, it is illegal for a company that reports to the SEC to have false or inaccurate books or records or to fail to maintain a system of internal accounting controls. We are also required to maintain accurate information and control over sales and distributors' activities that may fall within the purview of the FCPA, its books and records provisions and its anti-bribery provisions.

Other countries, including the U.K. and other OECD Anti-Bribery Convention members, have similar extraterritorial anti-corruption laws.

Any violation of these laws, or allegations of such violations, could disrupt our operations, involve significant management distraction, cause us to incur significant costs and expenses, including legal fees, and result in a material adverse effect on our business. We could also suffer severe penalties, including criminal and civil penalties, disgorgement and other remedial measures.

Compliance with privacy laws and regulations may increase our costs.

The HIPAA privacy, security and breach notification regulations, including the expanded requirements under HITECH, establish comprehensive federal standards with respect to the uses and disclosures of protected health information ("PHI") by health plans, healthcare providers and healthcare clearinghouses, in addition to setting standards to protect the confidentiality, integrity and security of PHI. The regulations establish a complex regulatory framework on a variety of subjects, including:

- the circumstances under which uses and disclosures of PHI are permitted or required without a specific authorization by the patient, including but not limited to treatment purposes, activities to obtain payments for our services, and our healthcare operations activities;
- a patient's rights to access, amend and receive an accounting of certain disclosures of PHI;
- requirements to notify individuals if there is a breach of their PHI;
- the contents of notices of privacy practices for PHI;
- administrative, technical and physical safeguards required of entities that use or receive PHI; and
- the protection of computing systems maintaining electronic PHI.

We have implemented practices intended to meet the requirements of the HIPAA privacy, security and breach notification regulations, as required by law. We are required to comply with federal privacy, security and breach notification regulations as well as varying state privacy, security and breach notification laws and regulations, which may be more stringent than federal HIPAA requirements. In addition, for healthcare data transfers from other countries relating to citizens of those countries, we must comply with the laws of those countries. The federal privacy regulations restrict our ability to use or disclose patient identifiable data, without patient authorization, for purposes other than payment, treatment, healthcare operations and certain other specified disclosures such as public health and governmental oversight of the healthcare industry.

HIPAA provides for significant fines and other penalties for wrongful use or disclosure of PHI, including potential civil and criminal fines and penalties. Computer networks are always vulnerable to breach and unauthorized persons may in the future be able to exploit weaknesses in the security systems of our computer networks and gain access to PHI. Additionally, we share PHI with third parties who are legally obligated to safeguard and maintain the confidentiality of PHI. Unauthorized persons may be able to gain access to PHI stored in such third parties' computer networks. Any wrongful use or disclosure of PHI by us or such third parties, including disclosure due to data theft or unauthorized access to our or our third parties' computer networks, could subject us to fines or penalties that could adversely affect our business and results of operations. Although the HIPAA statute and regulations do not expressly provide for a private right of damages, we could also incur damages under state laws to private parties for the wrongful use or disclosure of confidential health information or other private personal information.

Our employees, independent contractors, consultants, commercial partners, and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct, or other illegal activity by our employees, independent contractors, consultants, commercial partners, and vendors. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the rules and regulations of the CMS, FDA, and other comparable foreign regulatory authorities; provide true, complete and accurate information to such regulatory authorities; comply with manufacturing and clinical laboratory standards; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. In particular, research, sales, marketing, education, and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing, and other abusive practices, as well as off-label product promotion. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs, and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of participant recruitment for clinical studies, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. Even if it is later determined after an action is instituted against us that we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions, and have to divert significant management resources from other matters.

We expect to rely on third parties to conduct any future studies of our technologies that may be required by the FDA or other U.S. or foreign regulatory bodies, and those third parties may not perform satisfactorily.

We expect to rely on third parties such as contract research organizations, medical institutions and clinical investigators to conduct studies, including the post-approval studies required by the FDA for our Cologuard test. Our reliance on these third parties for clinical development activities will reduce our control over these activities. These third parties may not complete activities on schedule or conduct studies in accordance with regulatory requirements or our study design. Our reliance on third parties that we do not control will not relieve us of our requirement to prepare, and ensure our compliance with, various procedures required under good clinical practices, even though third-party contract research organizations may prepare and comply with their own, comparable procedures. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third parties need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our studies may be extended, delayed, suspended or terminated, and we may not be able to obtain a required regulatory approval.

We are subject to increasingly complex taxation rules and practices, which may affect how we conduct our business and our results of operations.

As our business grows, we are required to comply with increasingly complex taxation rules and practices. We are subject to tax in multiple U.S. tax jurisdictions and in foreign tax jurisdictions as we continue to expand internationally. The development of our tax strategies requires additional expertise and may impact how we conduct our business. Our future effective tax rates could be unfavorably affected by changes in or interpretations of tax rules and regulations in the jurisdictions in which we do business or by changes in the valuation of our deferred tax assets and liabilities. Furthermore, we provide for certain tax liabilities that involve significant judgment. We are subject to the examination of our tax returns by federal, state and foreign tax authorities, which could focus on our intercompany transfer pricing methodology as well as other matters. If our tax strategies are ineffective or we are not in compliance with domestic and international tax laws, our financial position, operating results and cash flows could be adversely affected.

Our business is subject to complex and evolving laws, as well as customer and patient expectations, regarding data privacy, protection and security.

The interpretation and application of consumer, health related and data protection laws in the U.S., Europe and elsewhere are often uncertain, contradictory and in flux. In order to mitigate concerns about overseas data transfers and to comply with provisions of the GDPR and its predecessor regulations, we self-certified with the Department of Commerce for compliance with the U.S.-E.U. Privacy Shield. However, the Court of Justice of the European Union invalidated the U.S.-E.U. Privacy Shield program in its July 2020 Schrems II decision. Although we are taking other measures to ensure compliance with the GDPR, the changing legal landscape could cause us to incur substantial costs or change our operations and compliance procedures, all of which may adversely affect our business.

If we fail to comply with the GDPR, recently enacted state privacy laws, and other applicable data privacy, protection and security laws, or if we fail to satisfy customer or patient concerns or customer contractual requirements regarding data handling, we could be subject to class action litigation, government injunctions, or other enforcement actions including a prohibition on processing patient data at our centralized laboratories in the U.S. or sites outside the U.S., as well as private litigation, civil, administrative, or criminal penalties, reduced orders, loss of national markets, and adverse publicity.

We are subject to evolving corporate governance and public disclosure expectations and regulations that impact compliance costs and risks of noncompliance.

We are subject to changing rules and regulations promulgated by a number of governmental and self-regulatory organizations, including the SEC and Nasdaq, as well as evolving investor expectations around corporate governance and environmental and social practices and disclosures. These rules and regulations continue to evolve in scope and complexity, and many new requirements have been created in response to laws enacted by the U.S. and foreign governments, making compliance more difficult and uncertain. The increase in costs to comply with such evolving expectations, rules and regulations, as well as any risk of noncompliance, could adversely impact us.

Risks Relating to Product Development, Commercialization, and Sales of our Products

We have finite resources, which may restrict our success in commercializing our products, and we may be unsuccessful in entering into or maintaining third-party arrangements to support our internal efforts.

To grow our business as planned, we must expand our sales, marketing and customer support capabilities, which will involve developing and administering our commercial infrastructure and/or collaborative commercial arrangements and partnerships. We must also maintain satisfactory arrangements for the manufacture and distribution of our tests and operate CLIA-certified lab facilities to process our tests and provide patient results.

Since 2019, when we had a single commercialized product, our Cologuard test, we have significantly expanded our operations and product offerings both organically and through acquisitions, and we have limited experience managing a sales force, customer support operation and operating manufacturing and clinical laboratory operations for multiple products in multiple locations with divergent regulatory requirements. We may encounter difficulties retaining and managing the specialized workforce these activities require. We may seek to partner with others to assist us with any or all of these functions. For example, we rely on a third-party partner to operate our German laboratory that is expected to perform a portion of our international tests. However, we may be unable to find appropriate third parties with whom to enter into these arrangements or maintain successful relationships with third parties once established.

If we are unable to deploy and maintain effective sales, marketing and medical affairs capabilities, we will have difficulty achieving market awareness and selling our products and services.

To achieve commercial success for our Cologuard and Oncotype tests and our future products and services, we must continue to develop and grow our sales, marketing and medical affairs organizations to effectively explain to healthcare providers the reliability, effectiveness and benefits of our current and future products and services as compared to alternatives. Our sales efforts have grown in size and complexity, and we may not be able to successfully manage our dispersed or inside sales forces or our sales force may not be effective. Because of the competition for their services, we may be unable to hire, partner with or retain additional qualified sales representatives or marketing or medical affairs personnel, either as our employees or independent contractors or through independent sales or other third-party organizations. Market competition for commercial, marketing and medical affairs talent is significant, and we may not be able to hire or retain such talent on commercially reasonable terms, if at all.

Establishing and maintaining sales, marketing, and medical affairs capabilities will be expensive and time-consuming. Our expenses associated with maintaining our sales force may be disproportional compared to the revenues we may be able to generate on sales of the Cologuard and Oncotype tests or any future products or services.

The success of our Cologuard test, our Oncotype tests, and any other screening or diagnostic product or service we may offer or develop will depend on the degree of market acceptance by healthcare providers, patients, healthcare payers, and others in the medical community.

Our products and services may not gain market acceptance by healthcare providers, healthcare payers, and others in the medical community. The degree of market acceptance of our Cologuard test, our Oncotype tests, and other products and services that we may offer will depend on a number of factors, including:

- demonstrated performance and utility;
- price;
- the availability and attractiveness of alternative tests;
- the willingness of healthcare providers to prescribe our products and services;
- the ease of use of our ordering process for healthcare providers; and
- adequate third-party coverage or reimbursement.

Our assumptions regarding the market opportunity for our products or services may not prove true. For example, we estimate the potential market opportunity for our Cologuard test assuming, among other things, the size of the screening population, the adoption rate in the screening population and a three-year screening interval. Although ACS guidelines and others recommend a three-year screening interval for our Cologuard test and CMS has determined that Medicare will cover the test at this interval, the label for our Cologuard test does not specify a three-year interval and healthcare providers, healthcare payers, the FDA, and other regulators and opinion leaders could recommend a different interval. Further, patients may not adhere to any recommended testing interval.

Recommendations, guidelines, and quality metrics issued by various organizations may significantly affect payers' willingness to cover and healthcare providers' willingness to prescribe our products.

Securing influential recommendations, inclusion in healthcare guidelines, and inclusion in quality measures are keys to our healthcare provider and payer engagement strategies. These guidelines, recommendations, and quality metrics may shape payers' coverage decisions and healthcare providers' cancer screening procedures.

The USPSTF, a panel of primary care providers and epidemiologists and other national experts funded by the U.S. Department of Health and Human Services' Agency for Healthcare Research and Quality, makes influential recommendations on clinical preventive services. USPSTF updates its screening recommendations periodically, approximately every five to eight years. The USPSTF's most recent recommendation statement for colorectal cancer screening gave an "A" grade to colorectal cancer screening starting at age 50 and continuing until age 75 and gave a "B" grade to colorectal cancer screening for ages 45 to 49. Any update to the USPSTF recommendations that may have the effect of reducing screening, that does not include FIT-DNA in a favorable manner, or that adds new technologies could have a material adverse effect on our business.

Maintaining a high USPSTF recommendation for our Cologuard test may have certain potentially significant implications. For example, the ACA mandates that certain non-grandfathered health insurers cover evidence-based items or services that have in effect a rating of "A" or "B" in the current recommendations of USPSTF without imposing any patient cost-sharing (the "ACA Mandate"). Similarly, federal regulations require that Medicare Advantage plans cover "A" or "B" graded preventive services without patient cost-sharing. Following the updated 2016 USPSTF recommendation statement, the Centers for Medicare & Medicaid Services ("CMS") issued an updated Evidence of Coverage notice for Medicare Advantage plans that affirms such plans must include coverage of our Cologuard test every three years without patient cost-sharing. While we believe the ACA Mandate requires certain health insurers to cover our Cologuard test for individuals between the ages of 45 and 75 without patient cost-sharing, some health insurers have disagreed. Enforcement of the ACA Mandate is difficult and depends on state, federal, or other third-party enforcement actions that we do not control. Further, a court or regulatory agency may agree with arguments that have been made, or that may in the future be made, by insurers and determine that the ACA Mandate does not require that they cover our Cologuard test or may otherwise interpret the ACA Mandate in a manner unfavorable to us. Also, Congress may modify or repeal all or part of the ACA, and any such modification or repeal may repeal or limit the ACA Mandate for preventive services. Additionally, the ACA has also been the subject of various legal challenges and, if the plaintiffs are successful in any such challenges, insurance coverage for our Cologuard test could be materially and adversely affected. If the ACA Mandate for preventive services is repealed, overturned or modified, if the ACA Mandate is determined not to require coverage of our Cologuard test, if the ACA Mandate is otherwise interpreted in a manner unfavorable to us, or if we are unable to influence or secure effective enforcement of the ACA Mandate, even if it is held to require coverage of our Cologuard test, our business prospects may be adversely affected.

The healthcare industry in the United States has experienced a trend toward cost containment and value-based purchasing of healthcare services. Some government and private payers are adopting pay-for-performance programs that differentiate payments for healthcare services based on the achievement of documented quality metrics, cost efficiencies, or patient outcomes. Payers may look to quality measures such as the NCQA, HEDIS, and the CMS Medicare Advantage Star Ratings to assess quality of care. These measures are intended to provide incentives to service providers to deliver the same or better results while consuming fewer resources. Our Cologuard test has been included in NCQA's HEDIS measures since 2017 and in CMS's Medicare Advantage Star Ratings since 2018. If for some reason our Cologuard test was removed from or not included in HEDIS, the Star Ratings, or other quality metrics, payers may be less inclined to reimburse our Cologuard test at adequate levels, if at all, which could adversely impact our business. Additionally, if our Cologuard test was removed from or not included in HEDIS, the Star Ratings, or other quality metrics, healthcare providers may not earn quality credit for prescribing our Cologuard test and therefore may be less inclined to do so. If our Cologuard test fails to maintain its current position within any updated USPSTF colorectal cancer screening recommendations, our Cologuard test may, as a result, become excluded from the HEDIS measures and the Star Ratings.

We expect to make significant investments to research and develop new cancer tests, which may not be successful.

We are seeking to increase our Cologuard test's specificity by substituting new biomarkers and to develop a pipeline for future products and services, including multi-cancer early detection, minimal residual disease, recurrence monitoring, and hereditary cancer tests. We expect to incur significant expenses on these development efforts, but they may not be successful.

Developing new or improved cancer tests is a speculative and risky endeavor. Candidate products and services that may initially show promise may fail to achieve the desired results in larger clinical studies or may not achieve acceptable levels of clinical accuracy. Results from early studies or trials are not necessarily predictive of future clinical study or trial results, and interim results of a trial are not necessarily indicative of final results. From time to time, we may publicly disclose then-available data from clinical studies before the studies are complete, and the results and related findings and conclusions may be subject to change following the final analysis of the data related to the particular study or trial. As a result, such data should be viewed with caution until the final data are available. Additionally, such data from clinical studies are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment and/or follow-up continues and more patient data become available. Significant adverse differences between initial or interim data and final data could significantly harm our reputation and business prospects.

Any cancer screening test we develop will need to demonstrate in clinical studies a high level of accuracy. Because cancer screening tests seek to identify relatively rare occurrences, if in a clinical study a candidate product or service fails to identify even a small number of cancer cases, the sensitivity rate may be materially and adversely affected and we may have to abandon the candidate product or service. Any cancer diagnostic test we develop will need to address an unmet medical need with accurate performance and utility.

We may need to explore a number of different biomarker combinations, alter our candidate products or platform technologies, and repeat clinical studies before we identify a potentially successful candidate. We may need to acquire, whether through purchase, license or otherwise, technologies owned by third parties, and we may not be able to acquire such technologies on commercially reasonable terms or at all. Product development is expensive, may take years to complete, and can have uncertain outcomes. Failure can occur at any stage of development. If, after development, a candidate product or service appears successful, we may, depending on the nature of the product or service, still need to obtain FDA and other regulatory clearances or approvals before we can market it. The FDA's clearance or approval pathways are likely to involve significant time, as well as additional research, development, and clinical study expenditures. There can be no guarantee that the FDA would clear or approve any future product or service we may develop.

Even if the FDA clears or approves a new product or service we develop, we would need to commit substantial resources to commercialize, sell and market it before it could be profitable, and the product or service may never be commercially viable. In developing a test, we must make numerous assumptions regarding the commercial viability of a test, including with respect to healthcare providers' and patients' interest in a test, payers' willingness to pay for a test, our costs to perform a test, and availability and attractiveness of competing offerings. Frequently, we must make those assumptions many years before a test is ready for clinical use.

If we determine that any of our current or future development programs is unlikely to succeed, we may abandon it without any return on our investment into the program. We may need to raise significant additional capital to bring any new products or services to market, which may not be available on acceptable terms, if at all.

Our dependence on distributors for sales outside of the U.S. could limit or prevent us from selling our tests in foreign markets and impact our revenue.

As of December 31, 2021, we have entered into exclusive distribution agreements for the sale of our Oncotype tests with distributors covering dozens of countries. We may enter into other similar arrangements to distribute our tests in other countries in the future. We intend to continue to grow our business internationally, and to do so we may need to attract additional distributors to expand the territories in which we sell our tests. Despite contractual obligations, distributors may not commit the necessary resources to market and sell our tests to the level of our expectations. If current or future distributors do not perform adequately, or we are unable to enter into or maintain arrangements with distributors to market our tests in particular geographic areas, we may not realize long-term international revenue growth. Additionally, local laws may make it very difficult or costly for us to terminate or replace distributors, and local public procurement law may complicate providing our centralized laboratory services through a distributor. Furthermore, our revenue from distributors could be negatively impacted as a result of changes in business cycles, business or economic conditions, coverage determinations, reimbursement rates, changes in foreign currency exchange rates that make our tests more expensive in our distributors' local currencies, or other factors that could affect their ability to pay us for tests on a timely basis or at all.

Our research and development efforts will be hindered if we are not able to obtain samples, contract with third parties for access to samples, or complete timely enrollment in future clinical studies.

Access to human sample types, such as blood, tissue, stool, or urine is necessary for our research and product development. Acquiring samples from individuals with clinical diagnoses or associated clinical outcomes through purchase or clinical studies is necessary. Lack of available samples can delay development timelines and increase costs of development. Generally, the agreements under which we gain access to human samples are non-exclusive. Other companies may compete with us for access. Additionally, the process of negotiating access to samples can be lengthy and it may involve numerous parties and approval levels to resolve complex issues such as usage rights, institutional review board approval, privacy rights, publication rights, intellectual property ownership, and research parameters. If we are not able to negotiate access to clinical samples with research institutions, hospitals, clinical partners, pharmaceutical companies, or companies developing therapeutics on a timely basis, or at all, or if other laboratories or our competitors secure access to these samples before us, our ability to research, develop and commercialize future products will be limited or delayed. Finally, we may not be able to conduct or complete clinical studies on a timely basis if we are not able to enroll sufficient numbers of patients in such studies, and our failure to do so could have an adverse effect on our research and development and product commercialization efforts.

Risks Relating to our Intellectual Property

We rely on strategic collaborative and licensing arrangements with third parties to develop critical intellectual property. We may not be able to successfully establish and maintain such intellectual property.

The development and commercialization of our products and services rely, directly or indirectly, upon strategic collaborations and licensing agreements with third parties. We have collaborative and licensing arrangements with Mayo Foundation for Medical Education and Research, under which Mayo provides us with certain exclusive and non-exclusive intellectual property rights and ongoing product development and research and development assistance. In addition, we have licensing agreements with Hologic, Johns Hopkins University, Ludwig Institute for Cancer Research, Translational Genomics Research Institute, and others. Such arrangements provide us with intellectual property and other business rights crucial to our product development and commercialization. We have incorporated licensed technology into our Cologuard test and expect to incorporate licensed technology into our pipeline products. Our dependence on licensing, collaboration, and other similar agreements with third parties may subject us to a number of risks. There can be no assurance that any current contractual arrangements between us and third parties or between our strategic partners and other third parties will be continued on materially similar terms and will not be breached or terminated early. Any failure to obtain or retain the rights to necessary technologies on acceptable commercial terms could require us to re-configure our products and services, which could negatively impact their commercial sale or increase the associated costs, either of which could materially harm our business and adversely affect our future revenues and ability to achieve sustained profitability.

We expect to continue and expand our reliance on collaborative and licensing arrangements. Establishing new strategic collaborations and licensing arrangements is difficult and time-consuming. Discussions with potential collaborators or licensors may not lead to the establishment of collaborations on favorable terms, if at all. To the extent we agree to work exclusively with one collaborator in a given area, our opportunities to collaborate with other entities could be limited. Potential collaborators or licensors may reject collaborations with us based upon their assessment of our financial, regulatory, or intellectual property

position or other factors. Even if we successfully establish new collaborations, these relationships may never result in the successful commercialization of any product or service. In addition, the success of the projects that require collaboration with third parties will be dependent on the continued success of such collaborators. There is no guarantee that our collaborators will continue to be successful and, as a result, we may expend considerable time and resources developing products or services that will not ultimately be commercialized.

We may be subject to substantial costs and liability or be prevented from using technologies incorporated in our screening or diagnostic tests as a result of litigation or other proceedings relating to patent or other intellectual property rights.

Third parties may assert infringement or other intellectual property claims against our licensors, our licensees, our suppliers, our strategic partners, or us. We pursue a patent strategy that we believe provides us with a competitive advantage in the non-invasive early detection of cancer and pre-cancer, as well as in the guidance of cancer treatment decisions, and is designed to maximize our patent protection against third parties. We have filed patent applications that we believe cover the methods we have designed and use in our Cologuard test to detect colorectal cancer and pre-cancer, our Oncotype tests to provide prognosis and guide treatment decisions, and for pipeline cancer tests still in development. In order to protect or enforce our patent and other intellectual property rights, we may have to initiate actions against third parties. Any actions regarding patents could be costly and time consuming and divert the attention of our management and key personnel from our business. Additionally, such actions could result in challenges to the validity, enforceability, or applicability of our patents. Because the U.S. Patent & Trademark Office maintains patent applications in secrecy until a patent application publishes or the patent is issued, we have no way of knowing if others may have filed patent applications covering technologies used by our partners or us. Additionally, there may be third-party patents, patent applications, and other intellectual property relevant to our technologies that may block or compete with our technologies. From time to time we have received correspondence from third parties alleging to hold intellectual property rights that could block our development or commercialization of products. While none of these inquiries to date have had any material effect on us, we may receive inquiries in the future that could have a material effect on our business. Even if third-party claims are without merit, defending a lawsuit may result in substantial expense to us and may divert the attention of management and key personnel. In addition, we cannot provide assurance that we would prevail in any such suits to the extent necessary to conduct our business according to our strategic plan or that the damages or other remedies, if any, awarded against us would not be substantial. Claims of intellectual property infringement may require that we, or our strategic partners, enter into royalty or license agreements with third parties that may only be available on unacceptable terms, if at all. These claims may also result in injunctions against the further development and commercial sale of services or products containing our technologies, which would have a material adverse effect on our business, financial condition, and results of operations.

Also, patents and patent applications owned by us may become the subject of interference proceedings in the U.S. Patent and Trademark Office ("USPTO") to determine priority of invention, which could result in substantial cost to us as well as a possible adverse decision as to the priority of invention of the patent or patent application involved. An adverse decision in an interference proceeding may result in the loss of rights under a patent or patent application subject to such a proceeding.

If we are unable to protect or enforce our intellectual property effectively, we may be unable to prevent third parties from using our intellectual property, which would impair any competitive advantage we may otherwise have.

We rely on patent protection as well as a combination of trademark, copyright, and trade secret protection and other contractual restrictions to protect our proprietary technologies and other intellectual property rights, all of which provide limited protection and may not adequately protect our rights or permit us to gain or keep any competitive advantage. If we fail to protect our intellectual property, third parties may be able to compete more effectively against us and we may incur substantial litigation costs in our attempts to recover or restrict use of our intellectual property, which may not be entirely successful, if at all. Additionally, certain of our patents began to expire in 2018. This loss of intellectual property protection may permit third parties to use certain intellectual property assets previously exclusively reserved for our use.

We cannot assure you that any of our currently pending or future patent applications will result in issued patents, and we cannot predict how long it will take for any such patents to be issued. Further, we cannot assure you that other parties will not challenge any patents issued to us or that courts or regulatory agencies will hold our patents to be valid or enforceable. We have been in the past, and may be in the future, the subject of opposition proceedings relating to our patents. We cannot guarantee that we will be successful in defending challenges made against our patents and patent applications. Any successful third-party challenge to our patents could result in co-ownership of such patents with the third party or the unenforceability or invalidity of such patents. Furthermore, in the life sciences field, courts frequently render opinions that may affect the patentability of certain inventions or discoveries, including opinions that may affect the patentability of isolated DNA and/or methods for analyzing or comparing DNA. Such decisions may adversely impact our ability to obtain new patents and facilitate third-party challenges to our existing patents.

Even where we have valid patents, third parties may be able to successfully design their products and services around those patents, such that their products and services do not infringe our patents. We may face competition internationally in jurisdictions where we do not have intellectual property protection. Our business may be adversely affected to the extent third parties are able to develop or commercialize competing products and services that do not infringe our patents. We may also be adversely affected to the extent third parties develop or commercialize competing products or services in countries where we did not apply for patents, where our patents have not issued, or where our intellectual property rights are not recognized.

We depend on trademarks to establish a market identity for our company and our products and services. To maintain the value of our trademarks, we may have to file lawsuits against third parties to prevent them from using trademarks confusingly similar to or dilutive of our registered or unregistered trademarks. We also may not obtain registrations for our pending or future trademark applications, and might have to defend our registered trademarks and pending applications from challenges by third parties. Enforcing or defending our registered and unregistered trademarks might result in significant litigation costs and, if we are unsuccessful, might result in damages, including the inability to continue using certain trademarks.

If patent regulations or standards are modified, such changes could have a negative impact on our business.

From time to time, the U.S. Supreme Court, other federal courts, the U.S. Congress, or the USPTO may change the standards of patentability and validity of patents within the cancer screening and diagnostics space, and any such changes could have a negative impact on our business.

There have been several cases involving “gene patents” and diagnostic claims that have been considered by the U.S. Supreme Court that have affected the legal concept of subject matter eligibility by seemingly narrowing the scope of the statute defining patentable inventions.

Additionally, in December 2014 and again in 2019, the USPTO published revised guidelines for patent examiners to apply when examining process claims that narrow the scope of patentable subject matter. While these guidelines may be subject to review and modification by the USPTO over time, we cannot assure you that our patent portfolio will not be negatively impacted by the decisions mentioned above, rulings in other cases, or changes in guidance or procedures issued by the USPTO.

Additional substantive changes to patent law, whether new or associated with the America Invents Act — which substantially revised the U.S. patent system — may affect our ability to obtain, enforce or defend our patents. Accordingly, it is not clear what, if any, impact these substantive changes will ultimately have on the cost of prosecuting our patent applications, our ability to obtain patents based on our discoveries, and our ability to enforce or defend our issued patents, all of which could have a material adverse effect on our business.

Risks Relating to our Securities

We are required to assess our internal control over financial reporting on an annual basis and any future adverse results from such assessments could result in a loss of investor confidence and have an adverse effect on our stock price.

Pursuant to the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated by the SEC, we are required to furnish in our Form 10-K a report by our management regarding the effectiveness of our internal control over financial reporting. The report includes, among other things, an assessment of the effectiveness of our internal control over financial reporting as of the end of our fiscal year, including a statement as to whether our internal control over financial reporting is effective. This assessment must include disclosure of any material weaknesses in our internal control over financial reporting identified by management. While we believe our internal control over financial reporting is currently effective, the effectiveness of our internal controls in future periods is subject to the risk that our controls may become inadequate because of changes in conditions. Establishing, testing, and maintaining an effective system of internal control over financial reporting requires significant resources and time commitments on the part of our management and our finance staff, may require additional staffing and infrastructure investments, and would increase our costs of doing business. If we are unable to assert that our internal control over financial reporting is effective in any future period (or if our auditors are unable to express an opinion on the effectiveness of our internal controls or conclude that our internal controls are ineffective), we could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on our stock price.

We face risks associated with currency exchange rate fluctuations, which could adversely affect our operating results.

As a result of our international operations, we receive a portion of our revenues and pay a portion of our expenses in currencies other than the U.S. dollar, such as the Euro, the Swiss franc, the British pound and the Canadian dollar. In addition, many of our distribution agreements contain clauses requiring regular U.S. dollar price re-adjustments to account for fluctuations in the exchange rate between the U.S. dollar and the local currency. As a result, we are at risk from exchange rate fluctuations between such foreign currencies and the U.S. dollar, which could adversely affect our results of operations. Additionally, the volume of our international orders may be negatively impacted by a strong U.S. dollar. For the year ended December 31, 2021, approximately 6.2% of our revenues came from foreign denominated currencies. If the U.S. dollar strengthens against foreign currencies, the translation of these foreign currency denominated transactions will result in decreased revenues and operating expenses. We may not be able to offset adverse foreign currency impact with increased revenues. We enter into forward contracts to mitigate the impact of adverse movements in foreign exchange rates related to the re-measurement of monetary assets and liabilities and hedge our foreign currency exchange rate exposure. Even with this strategy in place to mitigate balance sheet foreign currency risk, we will not eliminate our exposure to foreign exchange rate fluctuations on our financial results.

Delaware law, our charter and bylaw documents, and certain provisions of our convertible notes could impede or discourage a takeover or change of control that stockholders may consider favorable.

As a Delaware corporation, we are subject to certain anti-takeover provisions. Under Delaware law, a corporation may not engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other things, the board of directors has approved the transaction. Accordingly, our board of directors could rely on Delaware law to prevent or delay an acquisition of our company. In addition, certain provisions of our certificate of incorporation and bylaws may have the effect of delaying or preventing a change of control or changes in our management. These provisions include the following:

- Our board of directors is divided into three classes serving staggered three-year terms.
- Only our board of directors can fill vacancies on the board.
- Our stockholders may not act by written consent.
- There are various limitations on persons authorized to call a special meeting of stockholders and advance notice requirements for stockholders to make nominations of candidates for election as directors or to bring matters before an annual meeting of stockholders.
- Our board of directors may issue, without stockholder approval, shares of undesignated preferred stock.

These types of provisions could make it more difficult for a third party to acquire control of us, even if the acquisition would be beneficial to our stockholders.

Certain provisions of our outstanding convertible notes we issued in 2018, 2019, and 2020 could make it more difficult or more expensive for a third party to acquire us. Upon the occurrence of certain transactions constituting a "fundamental change," as such term is defined in the indenture for the notes, holders of the convertible notes will have the right, at their option, to require us to repurchase all of their convertible notes or any portion of the principal amount of such convertible notes in integral multiples of $1,000. We may also be required to increase the conversion rate in the event of a "make-whole fundamental change," as such term is defined in the indenture for the notes. In addition, the indenture and the convertible notes will prohibit us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the convertible notes and the indenture. These and other provisions in the indenture could deter or prevent a third party from acquiring us.

Our bylaws provide, subject to certain exceptions, that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for certain stockholder litigation matters, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees, or stockholders.

Our bylaws provide, subject to limited exceptions, that the Court of Chancery of the State of Delaware will, to the fullest extent permitted by law, be the sole and exclusive forum for any claims, including any derivative actions or proceedings brought on our behalf, (1) that are based upon a violation of a duty by a current or former director or officer or stockholder in such capacity or (2) that may be brought in the Court of Chancery pursuant to the Delaware General Corporation Law. This provision would not apply to suits brought to enforce a duty or liability created by the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended. Any person or entity purchasing or otherwise acquiring any interest in shares of our common stock shall be deemed to have notice of and to have consented to the provisions of our bylaws described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provision that is contained in our bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and results of operations.

Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.

As of December 31, 2021, we had federal, state, and foreign net operating loss carryforwards ("NOLs") of approximately $2.15 billion, $1.04 billion, and $15.9 million, respectively. In general, under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs to offset future taxable income. An ownership change is generally defined as a greater than 50% change in equity ownership by value over a specified time period (generally three years). Given the Code's broad definition, an ownership change could be the unintended consequence of otherwise normal market trading in our stock that is outside our control. An ownership change under Section 382 of the Code could also be triggered by certain strategic transactions. Additionally, tax law limitations may result in our NOLs expiring before we have the ability to use them. Pursuant to the Tax Cuts and Jobs Act (H.R. 1) of 2017, federal NOLs arising in tax years beginning after December 31, 2017 have an indefinite carryover period and may only be used to offset 80% of current year taxable income. For these reasons, even if we attain profitability, our ability to utilize our NOLs may be limited, potentially significantly so.

Our stock price has fluctuated widely and is likely to continue to be volatile.

The market price for our common stock varied between a high of $159.54 and a low of $71.81 in the twelve-month period ended December 31, 2021. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including those listed in this "Item 1A. Risk Factors" section and other, unknown factors. Among numerous other factors, our stock price also may be affected by:

- comments by securities analysts regarding our business or prospects;
- our quarterly operating performance;
- our issuance of common stock or other securities;
- our inability to accurately forecast future performance;
- our inability to meet analysts' expectations;
- our entering into merger, acquisition, or other similar transactions;
- general fluctuations in the stock market or in the stock prices of companies in the life sciences or healthcare diagnostics industries; and
- general conditions and publicity regarding the life sciences or healthcare diagnostics industries.

Consequently, the current market price of our common stock may not be indicative of future market prices, and we may be unable to sustain or increase the value of an investment in our common stock. Further, sharp drops in the market price of our common stock, such as we experienced at certain times in our history, may expose us to securities class-action litigation. Such litigation could result in substantial expenses and diversion of management's attention and corporate resources, which would seriously harm our business, financial condition, and results of operations.

We have never paid cash dividends and do not intend to do so.

We have never declared or paid cash dividends on our common stock. We currently plan to use any cash proceeds from our operations to finance the growth of our business rather than to pay cash dividends. Payments of any cash dividends in the future will depend on our financial condition, results of operations and capital requirements, as well as other factors deemed relevant by our board of directors.

Our balance sheet includes significant amounts of goodwill and intangible assets. The impairment of a significant portion of these assets would negatively affect our results of operations.

Our balance sheet includes goodwill and intangible assets that represent 66% of our total assets at December 31, 2021. These assets consist primarily of goodwill and identified intangible assets associated with our acquisitions. On at least an annual basis, we assess whether there have been impairments in the carrying value of goodwill. In addition, we review intangible assets for impairment whenever events or changes in circumstances indicate the carrying amount of the asset may not be recoverable. If the carrying value of the asset is determined to be impaired, then it is written down to fair value by a charge to operating earnings. An impairment of a significant portion of goodwill or intangible assets could have a material negative effect on our results of operations.

Our management has broad discretion over the use of our available cash and marketable securities and might not spend available cash and marketable securities in ways that increase the value of your investment.

From time to time we may carry high levels of cash and marketable securities. As of December 31, 2021, we had $1.03 billion in combined cash and marketable securities. Our management currently expects to deploy our cash and marketable securities primarily to expand our Cologuard and Oncotype operations and commercialization activities, to fund our product development efforts, and for general corporate purposes, including working capital and possible acquisitions. However, our management has broad discretion to pursue other objectives, we may raise additional capital, and we may use our current and future resources for other purposes. Our management might not effectively deploy our cash and marketable securities which could have an adverse effect on our business.

Our indebtedness could adversely affect our business, financial condition, and results of operations and our ability to meet our payment obligations under such indebtedness.

Pursuant to the convertible note offerings we completed in 2018, 2019, and 2020, we incurred $2.21 billion of indebtedness. This level of debt could have significant consequences on our future operations, including:

- increasing our vulnerability to adverse economic and industry conditions;
- making it more difficult for us to meet our payment and other obligations;
- making it more difficult to obtain any necessary future financing for working capital, capital expenditures, debt service requirements, or other purposes;
- requiring the dedication of a substantial portion of any cash flow from operations to service our indebtedness, thereby reducing the amount of cash flow available for other purposes, including capital expenditures;
- placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital than we have; and
- limiting our flexibility in planning for, or reacting to, changes in our business and the markets in which we compete.

Any of the above-listed factors could have an adverse effect on our business, financial condition, and results of operations and our ability to meet our payment obligations under the convertible notes.

Our ability to meet our payment and other obligations under the convertible notes depends on our ability to generate significant cash flow in the future. This, to some extent, is subject to general economic, financial, competitive, legislative, and regulatory factors as well as other factors that are beyond our control. We cannot assure you that our business will generate cash flow from operations, or that future borrowings will be available to us, in an amount sufficient to enable us to meet our payment obligations under the convertible notes and to fund other liquidity needs. If we are not able to generate sufficient cash flow to service our debt obligations, we may need to refinance or restructure our debt, including the convertible notes, sell assets, reduce or delay capital investments, or seek to raise additional capital. If we are unable to implement one or more of these alternatives, we may not be able to meet our payment obligations under the convertible notes, and such a default could cause us to be in default on any other currently existing or future outstanding indebtedness.

Servicing our debt will require a significant amount of cash, and we may not have sufficient cash flow from our business to pay amounts due under our indebtedness, including the convertible notes.

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, including the $2.21 billion aggregate principal amount of our 1.0%, 0.375%, and 0.375% convertible senior notes due 2025, 2027, and 2028, respectively, depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service our debt, including the convertible notes, and make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt, or obtaining additional equity capital or share-settling the convertible notes which could be 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 on our debt obligations.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

As of December 31, 2021, we occupied approximately 1,316,000 square feet of space at our significant facilities in the Madison, Wisconsin area and 254,000 square feet in our facilities in Redwood City, California. See Note 15 in the Notes to Consolidated Financial Statements included in Part II, Item 8, "Consolidated Financial Statements and Supplementary Data" for further discussion surrounding our leased facilities and Note 9 in the Notes to our Consolidated Financial Statements for further discussion surrounding mortgages on our owned properties.

As of December 31, 2021, our material facilities are as follows:

Location	Primary Function	Total Square Feet (approx.)	Leased or Owned
Madison, Wisconsin	Research and development, corporate, operations and clinical laboratory	1,316,000	Leased/Owned
Redwood City, California	Research and development, corporate, operations and clinical laboratory	254,000	Leased

Item 3. Legal Proceedings

From time to time we are a party to various legal proceedings arising in the ordinary course of our business. Legal proceedings, including litigation, government investigations and enforcement actions could result in material costs, occupy significant management resources and entail civil and criminal penalties. The information called for by this item is incorporated by reference to the information in Note 15 of the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report on Form 10-K.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is currently listed on the NASDAQ Capital Market under the symbol "EXAS."

As of February 21, 2022, there were 174,116,598 shares of our common stock outstanding held by approximately 201 holders of record.

We have never paid any cash dividends on our common stock and do not plan to pay any cash dividends in the foreseeable future.

See Note 14 in the Notes to Consolidated Financial Statements for further information on our stock-based compensation plans.

Unregistered Sales of Equity Securities

On December 31, 2021, we completed the acquisition of PreventionGenetics LLC. As part of the purchase price, we issued to certain of the selling equity holders an aggregate of 1,070,410 shares of common stock as merger consideration for their ownership in PreventionGenetics LLC.

On December 31, 2021, we issued 2,533 shares of restricted stock to Mayo Foundation for Medical Education and Research as part of the existing services and license agreement.

We believe that the offers and sales of the securities referenced above were exempt from registration under the Securities Act of 1933 (the "Securities Act") by virtue of Section 4(a)(2) of the Securities Act and/or Regulation D promulgated thereunder as transactions not involving any public offering. Use of this exemption is based on the following facts:

- Neither we nor any person acting on our behalf solicited any offer to buy or sell securities by any form of general solicitation or advertising.
- At the time of the acquisitions, the recipients of the securities were accredited investors, as defined in Rule 501(a) of the Securities Act.
- The recipients of the securities have had access to information regarding the Company and are knowledgeable about us and our business affairs.

Item 6. Reserved

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

Objective

The purpose of this Management's Discussion and Analysis is to better allow our investors to understand and view our company from management's perspective. We are providing an overview of our business and strategy including a discussion of our financial condition and results of operations. The following discussion of our financial condition and results of operations should be read in conjunction with the consolidated financial statements and the related notes thereto included elsewhere in this Annual Report on Form 10-K. We have omitted discussion of 2019 results where it would be redundant to the discussion previously included in Management's Discussion and Analysis of Financial Condition and Results of Operations on Form 10-K for the year ended December 31, 2020, which has been filed with the SEC.

Overview

Exact Sciences Corporation is a leading, global, advanced cancer diagnostics company. We have developed some of the most impactful tests in cancer diagnostics, and we are currently working on the development of additional tests, with the goal of bringing new innovative cancer tests to patients throughout the world.

Acquisitions

On December 31, 2021, we completed the acquisition of PreventionGenetics. PreventionGenetics is a CLIA-certified and CAP-accredited clinical DNA testing laboratory, providing more than 5,000 predefined genetic tests for nearly all clinically relevant genes, additional custom panels, and comprehensive germline whole exome and whole genome sequencing tests. We expect this acquisition to complement our advanced cancer diagnostics portfolio and support our entrance into hereditary cancer testing.

On June 23, 2021, we completed the acquisition of PFS Genomics. PFS is a healthcare company focused on personalizing treatment for breast cancer patients to improve outcomes and reduce unnecessary treatment. We expect this acquisition to expand our ability to help guide early stage breast cancer treatment through individualized radiotherapy treatment decisions.

On April 14, 2021, we completed the acquisition of all of the outstanding equity interests of Ashion from PMed Management, LLC, which is a subsidiary of TGen. Ashion is a CLIA-certified and CAP-accredited sequencing lab based in Phoenix, Arizona and developed oncomap ExTra, one of the most comprehensive genomic cancer tests available, and provides access to whole exome, matched germline, and transcriptome sequencing capabilities.

On January 11, 2021, we acquired a worldwide exclusive license to the proprietary TARDIS technology from TGen, an affiliate of City of Hope. We intend to use the TARDIS technology to develop a test to detect small amounts of tumor DNA that may remain in patients' blood after they have undergone initial treatment, known as MRD.

On January 5, 2021, we completed the acquisition of Thrive. Thrive is a healthcare company dedicated to developing a blood-based, MCED test. We intend to combine Thrive's expertise with our scientific capabilities, clinical organization, and commercial infrastructure to bring an accurate blood-based, multi-cancer early detection test to patients faster.

2022 Priorities

Our top priorities for 2022 are to (1) impact more lives, (2) advance new tests, and (3) take care of the people we serve.

Impact More Lives

We are committed to delivering critical answers to patients by getting more people tested with our laboratory testing services.

Advance New Tests

In 2022, we are focused on advancing new tests to provide answers to patients, beginning with assessing risk for cancer through screening and throughout the cancer journey, by changing the way cancer is detected and treated. We plan to continue investing in ongoing and additional clinical trials to support our product development efforts in enhancing existing products and bringing new products to patients and providers. We are focused on three important programs within this priority: (1) advancing our colon cancer screening programs, (2) multi-cancer early detection, and (2) minimal residual disease and recurrence testing.

Take Care of the People we Serve

We want to take even better care of everyone we serve. We plan to improve customer relations by delivering simple and smooth workflows, providing communication that is clear and easy to understand, and providing results that are fast and accurate. Our goal is to become a caring partner to answer questions and help people navigate what is a difficult time in their life.

Business Environment and Current Trends

COVID-19 Impact

The spread of COVID-19 has affected many segments of the global economy, including the cancer screening and diagnostics industry. The pandemic and related precautionary measures have materially disrupted our business since March 2020 and may continue to disrupt our business for an unknown period of time. COVID-19 has significantly impacted, and may continue to impact, our workforce, supply chain and operating results including our testing volumes, revenues, margins, and cash utilization among other measures. The level and nature of the disruption caused by COVID-19 is unpredictable, may be cyclical and long-lasting, and may vary from location to location. As a result of the pandemic, we continue to provide COVID-19 testing, the revenue from which has partially offset the pandemic's impact on our Screening and Precision Oncology testing revenue.

Our Screening and Precision Oncology businesses have been negatively impacted by the pandemic but have in large part recovered. While Cologuard test orders have increased from the early pandemic lows, the growth has been slower than expected due to continuing restrictions on patients' and our sales representatives' access to healthcare provider offices and additional outbreaks of COVID-19 and its variants during 2021, which further diminished access to healthcare provider offices. Our Cologuard test is promotionally responsive, and preventive health and wellness visits continue to be deprioritized due to the risk of COVID-19. The COVID-19 pandemic has also reduced well-patient access to healthcare providers, which has contributed to, and may continue to contribute to, delays to clinical studies that are critical to the launch of future products and services. Even after the pandemic subsides, some healthcare providers and health systems may limit the extent and type of sales representatives' access to their facilities and personnel. We have seen the impact of the COVID-19 variants to a lesser degree in our Precision Oncology business than we have with our Cologuard test. This is partly due to the fact that patients are already diagnosed with cancer and there is greater urgency to access healthcare providers and our Oncotype tests. In addition, it is reported that 40% of breast cancer diagnoses occur as a result of an at-home examination or symptoms recognized by the patient (i.e. a lump or swelling). Therefore, demand for our Oncotype DX Breast Recurrence Score test is less dependent on screening mammograms than our Cologuard test is on patients attending regular wellness visits, where our Cologuard test is most often prescribed today. We could see a delayed impact in our Precision Oncology business from the COVID-19 variants if patients deprioritize preventive services, including mammograms and prostate cancer screening.

Pandemic-related cost inflation and supply chain disruptions, whether caused by restrictions or slowdowns in shipping or logistics, increases demand for certain goods used in our operations, or otherwise, could impact our operations. See our Risk Factor, *The COVID-19 outbreak has and may further materially and adversely affect our business and financial results*, in Item 1A, for additional detail on the potential impacts to our business. In addition, personnel related costs have continued to rise as a result of the aforementioned inflation, which has and may continue to impact our operations.

We have adjusted and expect to continue to adjust our COVID-19 precautionary measures at our various locations based on local recovery levels and applicable governmental regulations. In 2021, we announced that anyone working onsite at an Exact Sciences U.S. facility and anyone going into a healthcare setting to perform their job in the U.S. must be fully vaccinated. We provided information to help educate and encourage our employees to receive the COVID-19 vaccination. We have also authorized more employees to work onsite and expect more teams to return onsite throughout 2022. Our business could be negatively affected if we take excessive, ineffective, or inadequate precautions.

Pfizer

In September 2021, we completed an expedited hiring process and onboarded approximately 400 former Pfizer sales representatives to increase adoption of our Cologuard test and our pipeline of innovative screening tests. Prior to late August 2021, when Pfizer announced a decrease in the number of sales positions supporting its Internal Medicine therapeutic area, these employees had been promoting our Cologuard test under our Promotion Agreement with Pfizer.

In November 2021, we entered into an amended and restated promotion agreement with Pfizer pursuant to which Pfizer ceased promoting our Cologuard test on November 30, 2021. The amendment requires us to pay Pfizer a total of $35.9 million in three installments throughout 2022 and eliminated our obligation to pay Pfizer royalties or other fees except for certain media fees, advertising fees, and any detail fees owed to Pfizer for promoting our Cologuard test prior to November 30, 2021. Pfizer will continue to purchase certain advertising for our Cologuard test on our behalf through the third quarter of 2022, which we will reimburse Pfizer for, and will provide support in transitioning responsibilities for purchasing such advertising.

We continue to plan for future growth through investing in our existing operations and through the acquisitions further discussed in our consolidated financial statements included in this Annual Report on Form 10-K.

Results of Operations

Revenue. Our revenue is primarily generated by our laboratory testing services from our Cologuard, Oncotype, and COVID-19 tests.

Amounts in millions	2021	2020	Change
Screening	$ 1,062.3	$ 815.1	$ 247.2
Precision Oncology	561.7	440.5	121.2
COVID-19 Testing	143.1	235.8	(92.7)
Total	$ 1,767.1	$ 1,491.4	$ 275.7

The increase in Screening revenue, which primarily includes laboratory service revenue from our Cologuard test, was primarily due to an increase in the number of completed Cologuard tests, partially offset by a decrease in transaction price as discussed below. Relative recovery from the COVID-19 pandemic and increases in electronic ordering rates, screening of patients in the 45 to 49 age group, and screening of patients that previously completed a Cologuard test contributed to the increase in completed Cologuard tests for the year ended December 31, 2021. The increase in Precision Oncology revenue, which primarily includes laboratory service revenue from our global Oncotype products, was primarily due to an increase in the number of completed Oncotype tests, which was driven by an increase in Oncotype DX breast test orders, both domestically and internationally, and to revenue generated from new products as a result of our acquisition of Ashion during the year.

During the year ended December 31, 2021, we recorded a downward adjustment to revenue of $11.8 million on completed tests from the prior year after identifying a lower realized reimbursement rate on a portion of our laboratory testing services. This change in transaction price is primarily driven by certain prior claims not being submitted to insurance timely. We are working to address these issues, and are more broadly working on improvements to our billing systems to prevent recurrence. Pursuant to our contracts with payers and standards within the industry, claims submitted outside of specified timeframes may not be reimbursed. Successful reimbursement for our laboratory testing services will continue to depend on our ability to execute our order to cash operations efficiently. At each reporting period-end, we monitor our estimates of transaction price to ensure reflection of conditions that exist at each reporting date, and while we strive to restrict volatility in our realized reimbursement rates, changes in transaction price can occur. During the year ended December 31, 2021, we identified new constraints on variable consideration that had not previously existed resulting in an adjustment to revenue.

We expect revenues to continue to increase in 2022, both from our Screening and Precision Oncology laboratory testing services. We would expect revenue from our COVID-19 testing to decline as the pandemic abates and alternative testing options become more widely available. Our revenues are affected by the test volume of our products, patient adherence rates, payer mix, the levels of reimbursement, our order to cash operations, and payment patterns of payers and patients.

Cost of sales (exclusive of amortization of acquired intangible assets). Cost of sales includes costs related to inventory production and usage, shipment of collection kits and tissue samples, royalties, and the cost of services to process tests and provide results to healthcare providers. The increase in cost of sales is primarily due to an increase in production costs, which is a direct result of an increase in completed Cologuard and Oncotype tests. The increase was partially offset by a reduction in the number of COVID-19 tests completed year over year. We expect that cost of sales (exclusive of amortization of acquired intangible assets) will continue to increase in future years as a result of an increase in production costs in line with an increase in completed Cologuard and Oncotype tests, along with a corresponding increase in personnel and support services associated with this growth.

Amounts in millions	2021	2020	Change
Production costs	$ 252.8	$ 186.3	$ 66.5
Personnel expenses	126.8	103.3	23.5
Facility and support services	61.1	51.4	9.7
Stock-based compensation	16.8	12.9	3.9
Other cost of sales expenses	1.3	0.4	0.9
Total cost of sales expense	$ 458.8	$ 354.3	$ 104.5

Research and development expenses. The decrease in research and development expenses was primarily due to relatively smaller intellectual property acquisitions in 2021 as compared to 2020. In 2020 we acquired Base Genomics, which resulted in an expense of $412.6 million, whereas in 2021 we spent a total of $85.3 million to acquire PFS Genomics and an exclusive license to TARDIS. The acquisitions were accounted for as asset acquisitions and are further described in Note 19 of our consolidated financial statements included in this Annual Report on Form 10-K. When excluding the impact of these asset acquisitions, research and development expenses increased by $158.8 million. The increase in research and development expenses is primarily a result of the acquisition of Thrive in January 2021, which resulted in increased direct research and development expenses, as well as an increase in personnel and stock-based compensation expenses due to the increase in headcount. We also saw an increase in clinical trial related expenses, which were driven by the BLUE-C study, as enrollment increased in 2021 following a slowdown in 2020 due to the COVID-19 pandemic and cost cutting measures that were put in place. We expect that research and development expenses will continue to increase in future years as we continue to invest in our pipeline products and the improvement of our current products, which are further discussed above in this Annual Report on Form 10-K.

Amounts in millions	2021	2020	Change
Intellectual property acquisition	$ 85.3	$ 412.6	$ (327.3)
Personnel expenses	98.8	60.5	38.3
Direct research and development expenses	111.5	42.9	68.6
Stock-based compensation	49.7	20.0	29.7
Facility and support services	25.4	12.7	12.7
Professional fees	9.0	3.1	5.9
Other research and development expenses	5.9	2.3	3.6
Total research and development expenses	$ 385.6	$ 554.1	$ (168.5)

Sales and marketing expenses. The increase in sales and marketing expenses was primarily due to an increase in direct marketing spend to support the future growth of our products and increased personnel expenses and stock-based compensation as a result of an increase in headcount, including the approximately 400 former Pfizer sales representatives that were onboarded in the third quarter of 2021. In addition, professional fees increased during the year ended December 31, 2021 primarily due to an increase in costs related to our Promotion Agreement with Pfizer during the second and third quarters of 2021 as compared to 2020, which were reduced due to cost saving measures as a result of the COVID-19 pandemic. The increase in professional fees also includes the $35.9 million fee incurred in the fourth quarter of 2021 as a result of the amendment of the Promotion Agreement with Pfizer as further discussed above. We expect that sales and marketing expenses will continue to increase in future years to support the expected future growth of our Cologuard, Oncotype, and pipeline products.

Amounts in millions	2021	2020	Change
Personnel expenses	$ 387.7	$ 280.3	$ 107.4
Direct marketing costs	193.9	133.8	60.1
Professional and legal fees	150.2	77.7	72.5
Facility and support services	67.8	45.5	22.3
Stock-based compensation	55.7	44.0	11.7
Other sales and marketing expenses	6.6	8.6	(2.0)
Total sales and marketing expenses	$ 861.9	$ 589.9	$ 272.0

General and administrative expenses. The increase in general and administrative expenses was in part due to $140.6 million in acquisition and integration related costs incurred during the year ended December 31, 2021 as part of our acquisitions completed during the year, which primarily consists of integration related stock-based compensation and professional and legal fees incurred. Personnel expenses and stock-based compensation also increased due to an increase in headcount to prepare for future growth in our operations and from our recent acquisitions. Due to the COVID-19 pandemic and the protective measures that were put in place, we experienced lower spend in our personnel and professional fees during the first half of 2020. As our business began to recover in the third quarter of 2020, personnel expenses and stock-based compensation increased due to additional headcount. These factors account for a portion of the increase that we see for the year ended December 31, 2021 when compared to the prior year. We expect significant leverage in general and administrative expenses going forward, but expenses will continue to increase in future years due to an increase in headcount that will be necessary to support the growth in our existing and pipeline products.

Amounts in millions	2021	2020	Change
Personnel expenses	$ 316.1	$ 222.0	$ 94.1
Professional and legal fees	125.7	86.4	39.3
Stock-based compensation	217.0	76.0	141.0
Facility and support services	86.1	58.3	27.8
Other general and administrative	56.4	38.7	17.7
Total general and administrative expenses	$ 801.3	$ 481.4	$ 319.9

Amortization of acquired intangible assets. Amortization of acquired intangible assets increased to $95.0 million for the year ended December 31, 2021 compared to $93.4 million for the year ended December 31, 2020. This increase in amortization of acquired intangible assets was primarily due to the amortization of intangible assets acquired as part of our acquisition of Ashion.

Intangible asset impairment charge. Intangible asset impairment charge was $20.2 million for the year ended December 31, 2021 compared to $209.7 million for the year ended December 31, 2020. The impairment recorded during the year ended December 31, 2021 relates to the impairment of the supply agreement intangible asset acquired as part of the combination with Genomic Health. The impairment recorded during the year ended December 31, 2020 primarily relates to the impairment of the in-process research and development intangible asset acquired as part of the combination with Genomic Health.

Other operating income. Other operating income decreased to zero for the year ended December 31, 2021 compared to $23.7 million for the year ended December 31, 2020. The income generated during the year ended December 31, 2020 represents the funding received under the Coronavirus Aid, Relief, and Economic Security Act (“CARES Act”) Provider Relief Fund, which was accepted from the Department of Health & Human Services in May 2020.

Investment income, net. Investment income, net increased to $31.8 million for the year ended December 31, 2021 compared to $6.6 million for the year ended December 31, 2020. The increase in investment income, net was due to the realized gain of $30.5 million that was recorded on our preferred stock investment in Thrive at closing in January 2021, which represented the adjustment to our historical investment to its fair value prior to our acquisition of Thrive. Our acquisition of Thrive is further described in Note 19 of our consolidated financial statements included in this Annual Report on Form 10-K.

Interest expense. Interest expense decreased to $18.6 million for the year ended December 31, 2021 compared to $67.9 million for the year ended December 31, 2020. Interest expense recorded from our outstanding convertible notes totaled $16.1 million and $65.9 million for the years ended December 31, 2021 and 2020, respectively. Of the interest expense recorded on outstanding convertible notes for the year ended December 31, 2020, $50.8 million is due to the loss on settlement of convertible notes. The convertible notes are further described in Note 10 of our consolidated financial statements included in this Annual Report on Form 10-K.

Income tax benefit. Income tax benefit increased to $246.9 million for the year ended December 31, 2021 compared to $5.5 million for the year ended December 31, 2020. The increase in income tax benefit is primarily due to an income tax benefit of $239.2 million recorded as a result of the change in the deferred tax asset valuation allowance resulting from the acquisition of Thrive.

Liquidity and Capital Resources

Overview

We have incurred losses and negative cash flows from operations since our inception, and have historically financed our operations primarily through public offerings of our common stock and convertible debt and through revenue generated by the sale of our laboratory testing services. We expect our operating expenditures to continue to increase to support future growth of our laboratory testing services, as well as an increase in research and development and clinical trial costs to support the advancement of our pipeline products and bringing new tests to market. We expect that cash and cash equivalents and marketable securities on hand at December 31, 2021, along with cash flows generated through our operations, will be sufficient to fund our current operations for at least the next twelve months based on current operating plans. We have access to additional financing resources, if needed, and we may raise additional capital to expand our business, to pursue strategic investments, to take advantage of financing opportunities or for other reasons. If we are unable to obtain sufficient additional funds to enable us to fund our planned operations, our results of operations and financial condition could be materially adversely affected, and we may be required to delay the implementation of our plans or otherwise scale back our operations. There can be no certainty that we will ever be successful in generating sufficient cash flow from operations to achieve and maintain profitability and meet all of our obligations as they come due.

Cash, Cash Equivalents and Marketable Securities

As of December 31, 2021, we had approximately $315.5 million in unrestricted cash and cash equivalents and approximately $715.0 million in marketable securities.

The majority of our investments in marketable securities consist of fixed income investments, and all are deemed available-for-sale. The objectives of this portfolio are to provide liquidity and safety of principal while striving to achieve the highest rate of return. Our investment policy limits investments to certain types of instruments issued by institutions with investment grade credit ratings and places restrictions on maturities and concentration by type and issuer.

Cash Flows

Amounts In millions	2021	2020
Net cash provided by (used in) operating activities	$ (102.2)	$ 136.5
Net cash used in investing activities	(1,082.1)	(702.0)
Net cash provided by financing activities	8.5	1,879.6

Operating activities

The increase in cash used in operating activities for the year ended December 31, 2021 was primarily due to an increase in cash payments made related to expenses necessary to process our tests and an increase in operating expenses to prepare for future growth of our operations as further discussed above. The increase in cash used in operating activities was partially offset by an increase in revenue, which was driven by an increase in completed Cologuard and Oncotype tests.

Investing activities

Net cash used in investing activities was $1.08 billion for the year ended December 31, 2021. We purchased $1.16 billion in marketable securities, while $794.3 million of our marketable securities were sold or matured during the year. Excluding the impact of purchases, sales, and maturities of marketable securities, net cash used in investing activities consisted primarily of our acquisition of Thrive of $343.2 million, our acquisition of PreventionGenetics of $84.2 million, our acquisition of Ashion of $72.3 million, our asset acquisition of PFS Genomics of $33.1 million, and our TARDIS license asset acquisition of $25.0 million, purchases of property and equipment of $135.8 million, and investments in privately held companies of $18.0 million. Net cash used in investing activities was $702.0 million for the year ended December 31, 2020. We purchased $1.09 billion in marketable securities, while $886.7 million of our marketable securities were sold or matured during the year. We used net cash of $411.4 million in the acquisition of Base Genomics and $6.7 million in other business combinations. We also invested $65.1 million in property and equipment and $15.9 million in investments in privately held companies.

Financing activities

Net cash provided by financing activities was $8.5 million for the year ended December 31, 2021. Net cash provided by financing activities consisted of proceeds of $14.4 million from the exercise of stock options and $23.1 million from our employee stock purchase plan, which was partially offset by cash outflows of $23.7 million for payments on our construction loan and $5.3 million for other financing activities. Net cash provided by financing activities was $1.88 billion for the year ended December 31, 2020. We received proceeds of $1.13 billion from the issuance of convertible notes with a maturity date of March 1, 2028 (the “2028 Notes”), and we used $150.1 million of cash to settle a portion of the convertible notes with a maturity date of January 1, 2025 (the “2025 Notes”). We also received proceeds of $861.7 million from the sale of common stock, net of issuance costs. Additionally, we received proceeds of $27.1 million from the exercise of stock options, and $18.4 million from our employee stock purchase plan.

Material Cash Requirements

Convertible Notes

As of December 31, 2021, we had outstanding aggregate principal of $2.21 billion on our convertible notes with maturity dates of January 15, 2025 (the “2025 Notes”), March 15, 2027 (the “2027 Notes”), and March 1, 2028 Notes (the "2028 Notes" and collectively, the “Notes”). The 2025 Notes have a maturity date of January 15, 2025 and an outstanding principal balance of $315.0 million. The 2027 Notes have a maturity date of March 15, 2027 and an outstanding principal balance of $747.5 million. The 2028 Notes have a maturity date of March 1, 2028 and an outstanding principal balance of $1.15 billion. The 2025 Notes, 2027 Notes, and 2028 Notes accrue interest at a fixed rate of 1.0%, 0.375%, and 0.375% per year, respectively, which is payable in cash semi-annually in arrears each year until the maturity date. See Note 10 in the Notes to Consolidated Financial Statements for further information. Until the six-months immediately preceding the maturity date of the applicable series of Notes, each series of Notes is convertible only upon the occurrence of certain events and during certain periods. The Notes will be convertible into cash, shares of our common stock (plus, if applicable, cash in lieu of any fractional share), or a combination of cash and shares of our common stock, at our election. It is our intent and policy to settle all conversions through a combination settlement, consisting primarily of shares of our common stock.

Lease Commitments

We act as lessee in our lease agreements, which include operating leases for corporate offices, laboratory space, warehouse space, vehicles, and certain laboratory and office equipment, and finance leases for certain equipment and vehicles. As of December 31, 2021, we had minimum operating and finance lease payments of $262.0 million and $20.2 million, respectively. Of the outstanding operating lease obligations, $30.7 million matures in 2022, and the remaining $231.3 million will mature in periods subsequent to 2022. Of the outstanding finance lease obligations, $7.0 million matures in 2022, and the remaining $13.1 million will mature in periods subsequent to 2022. See Note 15 in the Notes to Consolidated Financial Statements for further information.

Contingent Consideration

Certain of our business combinations and asset acquisitions involve potential payment of future consideration that is contingent upon the achievement of certain regulatory and product revenue milestones. A liability is recorded for the estimated fair value of the contingent consideration on the acquisition date for business combinations. A liability is recorded for the estimated fair value of the contingent consideration when the achievement of a milestone becomes probable for asset acquisitions.

As a result of the acquisition of Thrive in January 2021, an additional $450.0 million would be payable in cash to Thrive's former shareholders upon the achievement of two discrete events, FDA approval and CMS coverage, for $150.0 million, and $300.0 million, respectively, in relation to the development and commercialization of a blood-based, multi-cancer early detection test. The projected fiscal year of payment range is from 2024 to 2027. See Note 19 in the Notes to Consolidated Financial Statements for further information.

As a result of the acquisition of Ashion in April 2021, an additional $20.0 million would be payable in cash to Ashion's former shareholders upon the commercial launch, on or before the tenth anniversary of the acquisition of Ashion, of a test for MRD detection and/or treatment. An additional $30.0 million would be payable in cash to Ashion's former shareholders upon reaching cumulative revenues of $500.0 million, on or before the fifth anniversary of the acquisition of Ashion from MRD products. See Note 19 in the Notes to Consolidated Financial Statements for further information.

As a result of the acquisition of the proprietary TARDIS technology from TGen in January 2021, an additional $45.0 million would be payable in cash to TGen upon the achievement of cumulative product revenue milestones related to MRD detection and/or treatment. Milestone payments of $10.0 million and $35.0 million would be payable upon achieving $100.0 million and $250.0 million, respectively, in cumulative revenue on or before December 31, 2030. See Note 19 in the Notes to Consolidated Financial Statements for further information.

License Agreements

We license certain technologies that are, or may be, incorporated into our technology under several license agreements, as well as the rights to commercialize certain diagnostic tests through collaboration agreements. Generally, the license agreements require us to pay single-digit royalties and sales-based milestone payments based on net revenues received using the technologies and may require minimum royalty amounts or maintenance fees.

The timing and amounts of any such royalty or milestone payments is unknown due to the uncertain nature of the product development and associated net revenues using these technologies. Refer to Note 11 and Note 19 in the Notes to Consolidated Financial Statements for further information.

Capital Expenditures

We expect to continue to invest in capital expenditures to support the growth of our existing products and our research and development activities. Our current projects include the build out of additional lab and warehouse space at our existing facilities in Madison, WI and the construction of a research and development facility in Madison, WI. These projects are expected to be completed in 2022 and 2023. We also have assets under construction related to leasehold improvements, laboratory equipment, and software projects. We expect to incur approximately $200.0 million in capital expenditures in 2022.

Sources of Cash

In November 2021, we entered into a Revolving Loan Agreement with a revolving line of credit of up to $150.0 million. We believe that our anticipated income from operations, cash and marketable securities on hand, and borrowing capacity under our line of credit will be adequate to meet these short-term and long-term commitments. However, we may need to raise additional capital to fully fund our current strategic plan and and meet our commitments. We continuously evaluate our liquidity and capital resources, including access to external capital, in light of current economic and market conditions and our operational performance.

As of December 31, 2021, we had no off-balance sheet arrangements.

Net Operating Loss Carryforwards

As of December 31, 2021, we had federal, state, and foreign NOL carryforwards of approximately $2.15 billion, $1.04 billion, and $15.9 million, respectively. We also had federal and state research tax credit carryforwards of approximately $63.0 million and $39.8 million, respectively. The net operating loss and tax credit carryforwards will expire at various dates through 2040, if not utilized. The Internal Revenue Code and applicable state laws impose substantial restrictions on a corporation's utilization of net operating loss and tax credit carryforwards if an ownership change is deemed to have occurred. Additionally, tax law limitations may result in our NOLs expiring before we have the ability to use them. The Tax Cuts and Jobs Act (H.R. 1) of 2017 limits the deduction for NOLs to 80% of current year taxable income and provides for an indefinite carryover period for federal NOLs. Both provisions are applicable for losses arising in tax years beginning after December 31, 2017. As of December 31, 2021, we had $1.32 billion of NOLs incurred after December 31, 2017. For these reasons, even if we attain profitability our ability to utilize our NOLs may be limited, potentially significantly so.

A valuation allowance is provided for deferred tax assets if it is more likely than not these items will either expire before we are able to realize their benefit, or that future deductibility is uncertain. In general, companies that have a history of operating losses are faced with a difficult burden of proof on their ability to generate sufficient future income in order to realize the benefit of the deferred tax assets. We have recorded a valuation against our deferred tax assets based on our history of losses and current uncertainty as to timing of future taxable income. Given the future limitations on and expiration of certain Federal and State deferred tax assets, the recording of a valuation allowance resulted in a deferred tax liability of approximately $28.8 million remaining at the end of 2021, which is included in other long-term liabilities on our consolidated balance sheet.

Critical Accounting Policies and Estimates

Management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. ("GAAP"). The preparation of these financial statements requires us to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. On an ongoing basis, we evaluate our estimates and judgments. We base our estimates on historical experience and on various other factors that are believed to be appropriate under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 1 in the Notes to Consolidated Financial Statements, we believe that the following judgments are most critical to aid in fully understanding and evaluating our reported financial results.

Revenue Recognition. We recognize revenues when we release a result to the ordering healthcare provider, in an amount that reflects the consideration we expect to collect in exchange for those services. The amount of revenue we recognize is based on the established billing rates less contractual and other adjustments, which yields the unconstrained amount that we expect to ultimately collect.

We determine the amount we expect to ultimately collect using historical collections, established reimbursement rates, and other adjustments. Any changes in these inputs would ultimately impact the amount of revenue recognized during the period. The expected amount is typically lower than, if applicable, the agreed-upon reimbursement amount due to several factors, such as the amount of any patient co-payments, out-of-network payers, the existence of secondary payers, and claim denials. The consideration derived from our contracts is fixed when we contract with a direct bill payer. Our ability to collect is not contingent on the customer's ability to collect through their downstream billing efforts.

In the case of some of our agreements, the right to bill and collect exists prior to the receipt of a specimen and release of a test result to the ordering healthcare provider, which results in deferred revenue. The deferred revenue balance is generally relieved upon the release of the applicable patient's test result to the ordering healthcare provider or as of the date the customer has surpassed the window of time in which they are able to exercise their rights for testing services. We believe these points in time represent our fulfillment of our obligations to the customer.

The quality of our billing operations, most notably those activities that relate to obtaining the correct information in order to bill effectively for services provided, directly impacts the collectability of our receivables and revenue estimates. As such, we continually assess the state of our order to cash operations in order to identify areas of risk and opportunity that allow us to appropriately estimate receivables and revenue. Upon ultimate collection, the aggregate amount received from payers and patients where reimbursement was estimated is compared to previous collection estimates and, if necessary, the transaction price is adjusted. Finally, should we later determine the judgments underlying estimated collections change, our financial results could be negatively impacted in future quarters.

Tax Positions. We record a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized.

We compute our provision for income taxes based on the statutory tax rates and tax planning opportunities available to us in the various jurisdictions that we operate. Judgment is required in evaluating our tax positions and determining our annual tax provision.

We have incurred significant losses since our inception and due to the uncertainty of the amount and timing of future taxable income, it may be necessary to record an allowance to reduce the tax assets we have recognized.

Management has determined that a valuation allowance of $262.2 million and $293.4 million at December 31, 2021 and 2020, respectively is necessary to reduce the tax assets to the amount that is more likely than not to be realized. Due to the existence of the valuation allowance, future changes in our unrecognized tax benefits will not impact our effective tax rate.

Business Combinations and Asset Acquisitions. We account for acquired businesses using the acquisition method of accounting, which requires that the assets acquired and liabilities assumed be recorded at the date of acquisition at their respective fair values. Goodwill is the residual after allocating the purchase price to net assets acquired, unless the transaction is an asset acquisition in which the excess is allocated to acquired assets on a relative fair value basis. Determining the fair value of identifiable assets and liabilities, particularly intangible assets, requires management to make significant judgements and estimates.

As a result of the acquisitions of Ashion and PreventionGenetics, we identified developed technology intangibles which we determined to have a fair value of $39.0 million and $64.0 million, respectively. Key assumptions used to value developed technology include projected revenue growth, projected gross margin and operating expenses, discount rates, terminal growth rate, and other factors. We believe that the estimates applied are based on reasonable assumptions, but the estimates are inherently uncertain. As a result, the actual results may differ from the assumptions and judgments used to determine fair value of the assets acquired, which could result in material impairment charges in the future. Determining the useful life of the developed technology also requires judgment and actual useful life may differ.

As a result of the acquisition of Thrive, we recorded an in-process research and development (“IPR&D”) asset of $1.25 billion. There are major risks and uncertainties associated with IPR&D due to the regulatory approvals needed, which rely on the success of clinical trials that demonstrate product effectiveness. Key assumptions used to calculate the fair value of the IPR&D asset included inputs such as projected revenues, gross margin, required rate of return, tax rate, probability of commercial success, and obsolescence factor. We believe that the estimates applied are based on reasonable assumptions, but the estimates are inherently uncertain. As a result, the eventual realized value of the IPR&D project may vary from its fair value at the date of acquisition, and material IPR&D impairment charges may occur in future periods.

Business Combinations may include contingent consideration to be paid based on the occurrence of future events, such as the achievement of certain development, regulatory and sales milestones. Contingent consideration is a financial liability recorded at fair value at the acquisition date. The estimate of fair value contains uncertainties as it involves judgement about the likelihood and timing of achieving milestones as well as the present-value factor. We recorded contingent consideration liabilities of $352.0 million and $19.0 million as a result of the Thrive and Ashion acquisitions, respectively.

Remeasurement of Contingent Consideration. We remeasure the fair value of outstanding contingent consideration liabilities at each reporting period. The estimate of fair value contains uncertainties as it involves judgement about the likelihood and timing of achieving milestones as well as the present-value factor. A change in the probability of success assumption could have a material impact on the estimated fair value.

Impairment of Indefinite-Lived Assets. We test indefinite-lived assets for impairment on an annual basis during the fourth quarter, or more frequently if events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Based on the qualitative assessment, if it is determined that the fair value of indefinite-lived intangible assets is more likely than not to be less than its carrying amount, the fair value will be calculated and compared with its carrying amount and an impairment charge will be recognized for the amount that the carrying value exceeds the fair value. Determining whether impairment indicators exist and estimating the fair value of our indefinite-lived intangible assets if necessary for impairment testing requires significant judgment. We performed our annual goodwill assessment using a qualitative assessment and concluded there were no impairments. Qualitative factors considered in this assessment included industry and market conditions, overall financial performance, and other relevant events and factors. We also performed our annual IPR&D assessment using a qualitative assessment and concluded there were no impairments for the year ended December 31, 2021. Qualitative factors considered in this assessment included industry and market conditions, financial and strategic factors, the status of product development, and the consideration of legal, competitive, regulatory, and technical risks. We recorded an impairment charge of $200.0 million during the year ended December 31, 2020 related to the IPR&D acquired as part of the combination with Genomic Health due to the abandonment of further development of the IPR&D.

Impairment of Long-Lived Assets. We evaluate the fair value of long-lived assets, which include property, plant and equipment, finite-lived intangible assets, and investments in privately held companies, for impairment whenever events or changes in circumstances indicate that the carrying amounts of the assets may not be fully recoverable. The review of qualitative factors requires significant judgement. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the fair value of the assets. We recorded an impairment charge of $20.2 million during the year ended December 31, 2021 related to the supply agreement intangible asset acquired as part of the combination with Genomic Health. We utilized the income approach to measure the fair value of the supply agreement which required management to make estimates including revenue projections, estimated cash flows and discount rate. We recorded an impairment charge of $9.7 million during the year ended December 31, 2020 related to the patent intangible asset acquired as part of an asset purchase agreement with Armune Biosciences, Inc. due to the abandonment of the research and development activities using the acquired assets. We believe that the estimates applied are based on reasonable assumptions, but the estimates are inherently uncertain. As a result, the eventual realized value of the impaired asset may vary from its fair value.

Recent Accounting Pronouncements

See Note 1 in the Notes to Consolidated Financial Statements for the discussion of Recent Accounting Pronouncements.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Interest Rate Risk

Our exposure to market risk is principally confined to our cash, cash equivalents and marketable securities. We invest our cash, cash equivalents, and marketable securities in securities of the U.S. governments and its agencies and in investment-grade, highly liquid investments consisting of commercial paper, bank certificates of deposit, and corporate bonds, which as of December 31, 2021 and December 31, 2020 were classified as available-for-sale. We place our cash, cash equivalents, restricted cash, and marketable securities with high-quality financial institutions, limit the amount of credit exposure to any one institution, and have established investment guidelines relative to diversification and maturities designed to maintain safety and liquidity.

Based on a hypothetical ten percent adverse movement in interest rates, the potential losses in future earnings, fair value of risk-sensitive financial instruments, and cash flows are immaterial, although the actual effects may differ materially from the hypothetical analysis. While we believe our cash, cash equivalents, restricted cash, and marketable securities do not contain excessive risk, we cannot provide absolute assurance that, in the future, our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash, cash equivalents, restricted cash, and marketable securities at one or more financial institutions that are in excess of federally insured limits. Given the potential instability of financial institutions, we cannot provide assurance that we will not experience losses on these deposits. We do not utilize interest rate hedging agreements or other interest rate derivative instruments.

A hypothetical ten percent change in interest rates would not have a material adverse impact on our future operating results or cash flows. All of our significant interest-bearing liabilities bear interest at fixed rates and therefore are not subject to fluctuations in market interest rates; however, because these interest rates are fixed, we may be paying a higher interest rate, relative to market, in the future if circumstances change.

Foreign Currency Risk

The functional currency for most of our international subsidiaries is the U.S. dollar, and as a result we are not subject to material gains and losses from foreign currency translation of the subsidiary financial statements. Substantially all of our revenues are recognized in U.S. dollars, although a small portion is denominated in foreign currency as we continue to expand into markets outside of the U.S. Certain expenses related to our international activities are payable in foreign currencies. As a result, factors such as changes in foreign currency exchange rates or weak economic conditions in foreign markets will affect our financial results.

We enter into forward contracts to mitigate the impact of adverse movements in foreign exchange rates related to the re-measurement of monetary assets and liabilities and hedge our foreign currency exchange rate exposure. As of December 31, 2021, we had open foreign currency forward contracts with notional amounts of $46.7 million. Although the impact of currency fluctuations on our financial results has been immaterial in the past, there can be no guarantee that the impact of currency fluctuations related to our international activities will not be material in the future.

Item 8. Consolidated Financial Statements and Supplementary Data

EXACT SCIENCES CORPORATION
Index to Financial Statements

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Exact Sciences Corporation

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Exact Sciences Corporation and its subsidiaries (the "Company") as of December 31, 2021 and 2020, and the related consolidated statements of operations, of comprehensive loss, of stockholders' equity and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control - Integrated Framework (2013) issued by the COSO.

Change in Accounting Principle

As discussed in Note 1 to the consolidated financial statements, the Company changed the manner in which it accounts for convertible debt in 2021.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

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

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

Critical Audit Matters

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

Valuation of Net Accounts Receivable - Variable Consideration

As described in Note 1 to the consolidated financial statements, the Company's revenue is primarily generated by its laboratory testing services utilizing its Cologuard and Oncotype DX tests. The Company's customer is primarily the patient. Management estimates the amount of variable consideration using the expected value method, which represents the sum of probability-weighted amounts in a range of possible consideration amounts. When estimating the amount of variable consideration, management considers several factors, such as historical collections experience, patient insurance eligibility and payer reimbursement contracts. The Company's net accounts receivable as of December 31, 2021 was $216.6 million.

The principal considerations for our determination that performing procedures relating to the valuation of net accounts receivable - variable consideration is a critical audit matter are the significant judgment by management when developing the estimate of the amount of variable consideration, due to the estimation uncertainty involved in developing the estimate. This in turn led to significant auditor judgment, subjectivity and effort in performing procedures and evaluating audit evidence obtained related to management's estimate of the amount of variable consideration.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to management's estimate of the amount of variable consideration, including controls over management's methodology and data used in the estimate. These procedures also included, among others, testing management's process for developing the estimated amount of variable consideration. Testing management's process included evaluating the appropriateness of the method and testing completeness and accuracy of the underlying historical collection data used in the method; testing, on a sample basis, the accuracy of revenue transactions and cash collections from the historical billing and collection data used in management's method; and performing a retrospective comparison of actual cash collected subsequent to year-end to evaluate the reasonableness of the prior year estimate of the amount of variable consideration.

Acquisition of Thrive - Valuation of Acquired In-Process Research and Development (IPR&D)

As described in Note 19 to the consolidated financial statements, in 2021 the Company completed the acquisition of all of the outstanding capital stock of Thrive for consideration of approximately $2.19 billion, which resulted in a $1.25 billion fair value of IPR&D recorded. Thrive is a healthcare company dedicated to incorporating earlier cancer detection into routine medical care with an early-stage multi-cancer early detection test. The IPR&D asset was valued using the multiple-period excess earnings method approach, which involves significant unobservable inputs (Level 3 inputs). These inputs include projected revenues, gross margin, required rate of return, tax rate, probability of commercial success, and obsolescence factor.

The principal considerations for our determination that performing procedures relating to the valuation of acquired IPR&D in connection with the acquisition of Thrive is a critical audit matter are the significant judgment by management when developing the fair value of the acquired IPR&D asset. This in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating management's multi-period excess earnings method approach and significant assumptions related to projected revenues, gross margin, required rate of return, tax rate, probability of commercial success, and obsolescence factor. In addition, the audit effort involved the use of professionals with specialized skill and knowledge.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to management's valuation of the acquired IPR&D and controls over the development of significant assumptions related to projected revenues, gross margin, required rate of return, tax rate, probability of commercial success, and obsolescence factor. These procedures also included, among others, reading the purchase agreement and testing management's process for estimating the fair value of the IPR&D asset. Testing management's process included evaluating the appropriateness of the multi-period excess earnings method approach, testing the completeness and accuracy of data provided by management, and evaluating the reasonableness of management's significant assumptions related to projected revenues, gross margin, required rate of return, tax rate, probability of commercial success, and obsolescence factor., considering (i) internal and external market and industry data, and (ii) whether these assumptions were consistent with evidence obtained in other areas of the audit. Professionals with specialized skill and knowledge were used to assist in the evaluation of the Company's use of multi-period excess earnings method approach and the required rate of return and obsolescence factor assumptions.

/s/ PricewaterhouseCoopers LLP
Chicago, Illinois
February 22, 2022

We have served as the Company's auditor since 2020.

Report of Independent Registered Public Accounting Firm

Shareholders and Board of Directors
Exact Sciences Corporation
Madison, Wisconsin

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows of Exact Sciences Corporation (the "Company") for the year ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the results of its operations and its cash flows for the year ended December 31, 2019**,** in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Method Related to Leases

As discussed in Notes 1 and 15 to the consolidated financial statements, the Company has changed its method of accounting for leases in 2019 due to the adoption of Topic 842 — Leases.

Change in Accounting Method Related to Convertible Notes

As discussed in Notes 1 and 10 to the consolidated financial statements, the Company has changed its method of accounting for convertible notes in 2021 due to the adoption of ASU 2020-06.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audit. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audit included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audit provides a reasonable basis for our opinion.

/s/ BDO USA, LLP

We have served as the Company's auditor from 2012 to 2020.

Madison, Wisconsin
February 21, 2020, except for the adoption of ASU 2020-06 as discussed in Notes 1 and 10, which is as of February 22, 2022

EXACT SCIENCES CORPORATION
Consolidated Balance Sheets
(Amounts in thousands, except share data)

	December 31, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 315,471	$ 1,491,288
Marketable securities	715,005	348,699
Accounts receivable, net	216,645	233,185
Inventory	104,994	92,265
Prepaid expenses and other current assets	74,122	33,157
Total current assets	1,426,237	2,198,594
Long-term assets:		
Property, plant and equipment, net	580,248	451,986
Operating lease right-of-use assets	174,225	125,947
Goodwill	2,335,172	1,237,672
Intangible assets, net	2,094,411	847,123
Other long-term assets, net	74,591	63,770
Total assets	$ 6,684,884	$ 4,925,092
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 67,829	$ 35,709
Accrued liabilities	398,556	233,604
Operating lease liabilities, current portion	19,710	11,483
Convertible notes, net, current portion	—	312,715
Debt, current portion	—	1,319
Other current liabilities	30,973	38,265
Total current liabilities	517,068	633,095
Long-term liabilities:		
Convertible notes, net, less current portion	2,180,232	1,861,685
Long-term debt, less current portion	—	22,342
Other long-term liabilities	417,782	51,342
Operating lease liabilities, less current portion	182,166	121,075
Total liabilities	3,297,248	2,689,539
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.01 par value Authorized—5,000,000 shares issued and outstanding—no shares at December 31, 2021 and December 31, 2020	—	—
Common stock, $0.01 par value Authorized—400,000,000 shares issued and outstanding—173,674,067 and 159,423,410 shares at December 31, 2021 and December 31, 2020	1,738	1,595
Additional paid-in capital	6,028,861	4,279,327
Accumulated other comprehensive income (loss)	(1,443)	526
Accumulated deficit	(2,641,520)	(2,045,895)
Total stockholders' equity	3,387,636	2,235,553
Total liabilities and stockholders' equity	$ 6,684,884	$ 4,925,092

The accompanying notes are an integral part of these consolidated financial statements.

EXACT SCIENCES CORPORATION
Consolidated Statements of Operations
(Amounts in thousands, except per share data)

	Year Ended December 31,		
	2021	2020	2019
Revenue	$ 1,767,087	$ 1,491,391	$ 876,293
Operating expenses:			
Cost of sales (exclusive of amortization of acquired intangible assets)	458,757	354,324	216,717
Research and development	385,646	554,052	139,694
Sales and marketing	861,889	589,919	385,176
General and administrative	801,262	481,393	352,453
Amortization of acquired intangible assets	95,001	93,398	16,035
Intangible asset impairment charge	20,210	209,666	—
Total operating expenses	2,622,765	2,282,752	1,110,075
Other operating income	—	23,665	—
Loss from operations	(855,678)	(767,696)	(233,782)
Other income (expense)			
Investment income, net	31,778	6,574	26,530
Interest expense	(18,606)	(67,941)	(199,192)
Total other income (expense)	13,172	(61,367)	(172,662)
Net loss before tax	(842,506)	(829,063)	(406,444)
Income tax benefit	246,881	5,458	193,354
Net loss	$ (595,625)	$ (823,605)	$ (213,090)
Net loss per share—basic and diluted	$ (3.48)	$ (5.45)	$ (1.62)
Weighted average common shares outstanding—basic and diluted	171,348	151,137	131,257

The accompanying notes are an integral part of these consolidated financial statements.

EXACT SCIENCES CORPORATION
Consolidated Statements of Comprehensive Loss
(Amounts in thousands)

	Year Ended December 31,		
	2021	2020	2019
Net loss	$ (595,625)	$ (823,605)	$ (213,090)
Other comprehensive loss:			
Unrealized gain (loss) on available-for-sale investments	(2,162)	771	1,322
Foreign currency adjustment	23	25	—
Comprehensive loss, before tax	(597,764)	(822,809)	(211,768)
Income tax expense related to items of other comprehensive loss	170	(170)	—
Comprehensive loss, net of tax	$ (597,594)	$ (822,979)	$ (211,768)

The accompanying notes are an integral part of these consolidated financial statements.

EXACT SCIENCES CORPORATION
Consolidated Statements of Stockholders' Equity
(Amounts in thousands, except share data)

	Common Stock		Additional Paid In Capital	Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Number of Shares	$0.01 Par Value				
Balance, January 1, 2019	123,192,540	$ 1,232	$ 1,456,648	$ (1,422)	$ (1,009,200)	$ 447,258
Shares issued to settle convertible notes	2,159,716	22	182,413	—	—	182,435
Exercise of common stock options	641,925	6	8,781	—	—	8,787
Issuance of common stock to fund the Company's 2018 401(k) match	86,532	1	7,408	—	—	7,409
Compensation expense related to issuance of stock options and restricted stock awards	4,322,366	43	108,440	—	—	108,483
Purchase of employee stock purchase plan shares	176,458	2	8,394	—	—	8,396
Issuance of common stock for business combinations	17,046,159	171	1,406,909	—	—	1,407,080
Stock issuance costs	—	—	(441)	—	—	(441)
Net loss	—	—	—	—	(213,090)	(213,090)
Accumulated other comprehensive income	—	—	—	1,322	—	1,322
Balance, December 31, 2019	147,625,696	$ 1,477	$ 3,178,552	$ (100)	$ (1,222,290)	$ 1,957,639
Exercise of common stock options	702,907	7	27,070	—	—	27,077
Issuance of common stock to fund the Company's 2019 401(k) match	136,559	1	12,006	—	—	12,007
Compensation expense related to issuance of stock options and restricted stock awards	1,665,408	17	152,889	—	—	152,906
Purchase of employee stock purchase plan shares	301,064	3	18,352	—	—	18,355
Issuance of common stock for business combinations	386,293	4	28,843	—	—	28,847
Issuance of common stock for registered direct offering	8,605,483	86	861,615	—	—	861,701
Stock issuance costs	—	—	—	—	—	—
Net loss	—	—	—	—	(823,605)	(823,605)
Accumulated other comprehensive income	—	—	—	626	—	626
Balance, December 31, 2020	159,423,410	$ 1,595	$ 4,279,327	$ 526	$ (2,045,895)	$ 2,235,553
Conversion of convertible notes, net of tax	580	—	43	—	—	43
Exercise of common stock options	1,295,104	13	14,424	—	—	14,437
Issuance of common stock to fund the Company's 2020 401(k) match	162,606	2	22,932	—	—	22,934
Compensation expense related to issuance of stock options and restricted stock awards	1,879,169	19	334,004	—	—	334,023
Purchase of employee stock purchase plan shares	331,769	3	23,067	—	—	23,070
Issuance of common stock for business combinations and asset	10,581,429	106	1,355,064	—	—	1,355,170
Net loss	—	—	—	—	(595,625)	(595,625)
Accumulated other comprehensive loss	—	—	—	(1,969)	—	(1,969)
Balance, December 31, 2021	173,674,067	$ 1,738	$ 6,028,861	$ (1,443)	$ (2,641,520)	$ 3,387,636

The accompanying notes are an integral part of these consolidated financial statements.

EXACT SCIENCES CORPORATION
Consolidated Statements of Cash Flows
(Amounts in thousands, except share data)

	Year Ended December 31,		
	2021	2020	2019
Cash flows from operating activities:			
Net loss	$ (595,625)	$ (823,605)	$ (213,090)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Depreciation and amortization	85,345	69,964	34,212
Loss on disposal of property, plant and equipment	1,055	2,470	1,394
Unrealized (gain) loss on equity investments	1,492	(1,179)	207
Deferred tax benefit	(253,169)	(6,748)	(193,605)
Stock-based compensation	253,063	152,906	108,483
Post-combination expense for acceleration of unvested equity	80,960	—	—
Realized gain on preferred stock investment	(30,500)	—	—
Loss on settlement of convertible notes	—	50,819	187,698
Amortization of deferred financing costs, convertible note debt discount and issuance costs, and other liabilities	6,683	1,546	(1,758)
Accretion (Amortization) of discount (premium) on short-term investments	4,618	1,549	(3,102)
Amortization of acquired intangible assets	95,001	93,398	16,035
Asset acquisition IPR&D expense	85,337	412,568	—
Intangible asset impairment charge	20,210	209,666	—
Remeasurement of contingent consideration	6,360	(323)	—
Non-cash lease expense	25,825	15,720	5,427
Changes in assets and liabilities, net of effects of acquisition:			
Accounts receivable, net	25,150	(100,526)	(27,633)
Inventory, net	(9,221)	(30,310)	(19,041)
Operating lease liabilities	(16,685)	(8,784)	(4,114)
Accounts payable and accrued liabilities	169,800	55,165	3,469
Other assets and liabilities	(57,935)	42,186	(6,237)
Net cash provided by (used in) operating activities	(102,236)	136,482	(111,655)
Cash flows from investing activities:			
Purchases of marketable securities	(1,164,050)	(1,089,953)	(634,117)
Maturities of marketable securities	794,322	886,675	1,657,204
Purchases of property, plant and equipment	(135,766)	(65,078)	(172,654)
Investment in privately held companies	(18,044)	(15,947)	—
Business combination, net of cash acquired	(499,730)	(6,658)	(973,861)
Asset acquisitions, net of cash acquired	(58,073)	(411,421)	—
Other investing activities	(744)	345	(1,000)
Net cash used in investing activities	(1,082,085)	(702,037)	(124,428)
Cash flows from financing activities:			
Proceeds from issuance of convertible notes, net	—	1,125,547	729,477
Proceeds from exercise of common stock options	14,437	27,077	8,787
Proceeds from sale of common stock, net of issuance costs	—	861,701	—
Proceeds in connection with the Company's employee stock purchase plan	23,070	18,355	8,396
Payments on settlement of convertible notes	—	(150,054)	(493,356)
Payments on construction loan	(23,749)	(1,250)	—
Other financing activities	(5,286)	(1,755)	(123)
Net cash provided by financing activities	8,472	1,879,621	253,181
Effects of exchange rate changes on cash and cash equivalents	23	—	—
Net increase (decrease) in cash, cash equivalents and restricted cash	(1,175,826)	1,314,066	17,098
Cash, cash equivalents and restricted cash at the beginning of period	1,491,594	177,528	160,430
Cash, cash equivalents and restricted cash at the end of period	$ 315,768	$ 1,491,594	$ 177,528

EXACT SCIENCES CORPORATION
Consolidated Statements of Cash Flows
(Amounts in thousands, except share data)

	Year Ended December 31,		
	2021	2020	2019
Supplemental disclosure of non-cash investing and financing activities:			
Property, plant and equipment acquired but not paid	$ 33,177	$ 2,685	$ 10,265
Unrealized (loss) gain on available-for-sale investments	$ (2,162)	$ 771	$ 1,322
Issuance of 162,606, 136,559, and 86,532 shares of common stock to fund the Company's 401(k) matching contribution for 2020, 2019, and 2018, respectively	$ 22,934	$ 12,007	$ 7,409
Issuance of 2,159,716 shares of common stock upon settlement of convertible notes	$ —	$ —	$ (182,435)
Issuance of 10,581,429, 386,293, and 17,046,159 shares of common stock in 2021, 2020, and 2019, respectively, for business combination	$ (1,355,170)	$ (28,847)	$ (1,407,080)
Business acquisition contingent consideration liability	$ 350,348	$ —	$ —
Supplemental disclosure of cash flow information:			
Interest paid	$ 10,735	$ 9,384	$ 5,128

The accompanying notes are an integral part of these consolidated financial statements.

(1) SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Business

Exact Sciences Corporation (together with its subsidiaries, "Exact," or the "Company") was incorporated in February 1995. Exact is a leading global cancer diagnostics company. It has developed some of the most impactful tests in cancer screening and diagnostics, including Cologuard® and Oncotype DX®. Exact is currently working on the development of additional tests, with the goal of bringing new innovative cancer tests to patients throughout the world.

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Exact Sciences Corporation and those of its wholly-owned subsidiaries and variable interest entities. All intercompany transactions and balances have been eliminated upon consolidation.

Use of Estimates

The preparation of the consolidated financial statements in conformity with accounting principles generally accepted in the United States ("GAAP") requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Critical accounting policies are those that affect the Company's financial statements materially and involve difficult, subjective or complex judgments by management, and actual results could differ from those estimates. These estimates include revenue recognition, valuation of intangible assets and goodwill, and accounting for income taxes among others.

The spread of the coronavirus ("COVID-19") has affected many segments of the global economy, including the cancer screening and diagnostics industry. The Company assessed certain accounting matters that generally require consideration of forecasted financial information in context with the information reasonably available to the Company and the unknown future impacts of COVID-19 as of December 31, 2021 and through the date of the filing of this Annual Report on Form 10-K. The accounting matters assessed included, but were not limited to, the Company's allowance for doubtful accounts and credit losses, marketable and non-marketable investments, software, and the carrying value of the goodwill and other long-lived assets. The Company's future assessment of the magnitude and duration of COVID-19, as well as other factors, could result in additional material impacts to the Company's consolidated financial statements in future reporting periods.

The pandemic and related precautionary measures began to materially disrupt the Company's operations in March 2020 and may continue to disrupt the business for an unknown period of time. As a result, the pandemic had a significant impact on the Company's revenues and operating results.

The ultimate impact of COVID-19 depends on factors beyond the Company's knowledge or control, including the duration and severity of the outbreak, as well as third-party actions taken to contain its spread and mitigate its public health effects. As a result, the Company is unable to estimate the extent to which COVID-19 will negatively impact its financial results or liquidity.

Cash and Cash Equivalents

The Company considers cash on hand, demand deposits in a bank, money market funds, and all highly liquid investments with an original maturity of 90 days or less to be cash and cash equivalents.

Marketable Securities

Management determines the appropriate classification of debt securities at the time of purchase and re-evaluates such designation as of each balance sheet date. Debt securities carried at amortized cost are classified as held-to-maturity when the Company has the positive intent and ability to hold the securities to maturity. Debt securities not classified as held-to-maturity are classified as available-for-sale. Available-for-sale securities are carried at fair value. The unrealized gains and losses, net of tax, on the Company's debt securities are reported in other comprehensive income. Marketable equity securities are measured at fair value and the unrealized gains and losses, net of tax, are recognized in other income (expense) in the consolidated

statements of operations. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity computed under the effective interest rate method. Such amortization is included in investment income, net. Realized gains and losses and declines in value as a result of credit losses on available-for-sale securities are included in the consolidated statements of operations as investment income, net. The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in the consolidated statements of operations as investment income, net.

The Company's investment policy limits investments to certain types of instruments issued by institutions with investment grade credit ratings and places restrictions on maturities and concentration by type and issuer. Investments in which the Company has the ability and intent, if necessary, to liquidate in order to support its current operations (including those with a contractual term greater than one year from the date of purchase) are classified as current.

The Company periodically evaluates its available-for-sale debt securities in unrealized loss positions to determine whether any impairment is a result of a credit loss or other factors. This evaluation includes, but is not limited to, significant quantitative and qualitative assessments and estimates regarding credit ratings, significance of a security's loss position, adverse conditions specifically related to the security, and the payment structure of the security.

Allowance for Doubtful Accounts

The Company estimates an allowance for doubtful accounts against accounts receivable using historical collection trends, aging of accounts, current and future implications surrounding the ability to collect such as economic conditions, and regulatory changes. The allowance for doubtful accounts is evaluated on a regular basis and adjusted when trends, significant events, or other substantive evidence indicate that expected collections will be less than applicable accrual rates. At December 31, 2021 and 2020, the allowance for doubtful accounts recorded was not material to the Company's consolidated balance sheets. For the years ended December 31, 2021, 2020 and 2019, there was an immaterial amount of bad debt expense written off against the allowance and charged to operating expense.

Inventory

Inventory is stated at the lower of cost or net realizable value. The Company determines the cost of inventory using the first-in, first out method ("FIFO"). The Company estimates the recoverability of inventory by reference to internal estimates of future demands and product life cycles, including expiration. The Company periodically analyzes its inventory levels to identify inventory that may expire prior to expected sale, no longer meet quality specifications, or has a cost basis in excess of its estimated realizable value and records a charge to cost of sales for such inventory as appropriate.

Direct and indirect manufacturing costs incurred during process validation with probable future economic benefit are capitalized. Validation costs incurred for other research and development activities, which are not permitted to be sold, have been expensed to research and development in the Company's consolidated statements of operations.

Property, Plant and Equipment

Property, plant and equipment are stated at cost and depreciated using the straight-line method over the assets' estimated useful lives. Land is stated at cost and does not depreciate. Additions and improvements are capitalized, including direct and indirect costs incurred to validate equipment and bring to working conditions. Revalidation costs, including maintenance and repairs are expensed when incurred.

Software Development Costs

Costs related to internal use software, including hosted arrangements, are incurred in three stages: the preliminary project stage, the application development stage, and the post-implementation stage. Costs incurred during the preliminary project and post-implementation stages are expensed as incurred. Costs incurred during the application development stage that meet the criteria for capitalization are capitalized and amortized, when the software is ready for its intended use, using the straight-line basis over the estimated useful life of the software, or the duration of the hosting agreement.

Investments in Privately Held Companies

The Company determines whether its investments in privately held companies are debt or equity based on their characteristics, in accordance with the applicable accounting guidance for such investments. The Company also evaluates the investee to determine if the entity is a variable interest entity ("VIE") and, if so, whether the Company is the primary beneficiary of the VIE, in order to determine whether consolidation of the VIE is required. If consolidation is not required and the Company does not have voting control of the entity, the investment is evaluated to determine if the equity method of accounting should be applied. The equity method applies to investments in common stock or in substance common stock where the Company exercises significant influence over the investee.

Investments in privately held companies determined to be equity securities are accounted for as non-marketable securities. The Company adjusts the carrying value of its non-marketable equity securities for changes from observable transactions for identical or similar investments of the same issuer, less impairment. All gains and losses on non-marketable equity securities, realized and unrealized, are recognized in investment income, net in the consolidated statements of operations.

Investments in privately held companies determined to be debt securities are accounted for as available-for-sale or held-to-maturity securities, in accordance with the applicable accounting guidance for such investments.

Derivative Financial Instruments

The Company hedges a portion of its foreign currency exposures related to outstanding monetary assets and liabilities using foreign currency forward contracts. The foreign currency forward contracts are included in prepaid expenses and other current assets or in accrued liabilities in the consolidated balance sheets, depending on the contracts' net position. These contracts are not designated as hedges, and as a result, changes in their fair value are recorded in other income (expense) in the consolidated statements of operations.

Business Combinations and Asset Acquisitions

Business Combinations are accounted for under the acquisition method in accordance with Accounting Standards Codification ("ASC") 805, Business Combinations. The acquisition method requires identifiable assets acquired and liabilities assumed and any non-controlling interest in the business acquired be recognized and measured at fair value on the acquisition date, which is the date that the acquirer obtains control of the acquired business. The amount by which the fair value of consideration transferred as the purchase price exceeds the net fair value of assets acquired and liabilities assumed is recorded as goodwill. Acquisitions that do not meet the definition of a business combination under ASC 805 are accounted for as asset acquisitions. Asset acquisitions are accounted for by allocating the cost of the acquisition to the individual assets acquired and liabilities assumed on a relative fair value basis. Goodwill is not recognized in an asset acquisition with any consideration in excess of net assets acquired allocated to acquired assets on a relative fair value basis. Transaction costs are expensed in a business combination and are considered a component of the cost of the acquisition in an asset acquisition.

Intangible Assets

Purchased intangible assets are recorded at fair value. The Company uses a discounted cash flow model to value intangible assets. The discounted cash flow model requires assumptions about the timing and amount of future net cash flows, risk, the cost of capital, terminal values and market participants.

Patent costs are capitalized as incurred, only if the Company determines that there is some probable future economic benefit derived from the transaction. A capitalized patent is amortized over its estimated useful life, beginning when such patent is approved. Capitalized patent costs are expensed upon disapproval, upon a decision by the Company to no longer pursue the patent or when the related intellectual property is either sold or deemed to be no longer of value to the Company. The Company determined that all patent costs incurred during the years ended December 31, 2021, 2020 and 2019 should be expensed and not capitalized as the future economic benefit derived from the patent costs incurred cannot be determined.

Acquired In-process Research and Development ("IPR&D")

Acquired IPR&D represents the fair value assigned to research and development assets that have not reached technological feasibility. The value assigned to acquired IPR&D is determined by estimating the costs to develop the acquired technology into commercially viable products, estimating the resulting revenues from the projects and discounting the net cash flows to present value. The revenues and cost projections used to value acquired IPR&D are, as applicable, reduced based on the probability of success. IPR&D projects acquired in a business combination that are not complete are capitalized and accounted for as indefinite-lived intangible assets until completion or abandonment of the related research and development ("R&D") efforts. Upon successful completion of the project, the capitalized amount is amortized over its estimated useful life. If a project is abandoned, all remaining capitalized amounts are written off immediately. There are often major risks and uncertainties associated with IPR&D projects as the Company is required to obtain regulatory approvals in order to be able to market the resulting products. Such approvals require completing clinical trials that demonstrate the products effectiveness. Consequently, the eventual realized value of the IPR&D project may vary from its fair value at the date of acquisition, and IPR&D impairment charges may occur in future periods.

Capitalized IPR&D projects are tested for impairment annually and whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. The Company considers various factors for potential impairment, including the current legal and regulatory environment, current and future strategic initiatives and the competitive landscape. Adverse clinical trial results, significant delays in obtaining marketing approval, the inability to bring a product to market and the introduction or advancement of competitors' products could result in partial or full impairment of the related intangible assets.

Contingent Consideration

Certain of the Company's business combinations involve potential payment of future consideration that is contingent upon the achievement of certain regulatory and product development milestones being achieved. The Company records contingent consideration at fair value at the date of acquisition based on the consideration expected to be transferred, estimated as the probability-weighted future cash flows, discounted back to present value. The fair value of contingent consideration is measured using projected probabilities of success, projected payment dates, present value-factors, and projected revenues (for revenue-based considerations). Changes in probabilities of success, present-value factors, and projected payment dates may result in adjustments to the fair value measurements. Contingent consideration is remeasured each reporting period using Level 3 inputs, and the change in fair value, including accretion for the passage of time, is recognized as income or expense within general and administrative expenses on the Company's consolidated statements of operations. Contingent consideration payments made soon after the acquisition date are classified as investing activities in the consolidated statements of cash flows. Contingent consideration payments not made soon after the acquisition date that are related to the acquisition date fair value are reported as financing activities in the consolidated statements of cash flows, and amounts paid in excess of the original acquisition date fair value are reported as operating activities in the consolidated statements of cash flows.

Goodwill

The Company evaluates goodwill for possible impairment in accordance with ASC 350 on an annual basis during the fourth quarter, or more frequently if events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Qualitative factors considered in this assessment include industry and market conditions, overall financial performance, and other relevant events and factors affecting the Company's business. Based on the qualitative assessment, if it is determined that the fair value of goodwill is more likely than not to be less than its carrying amount, the fair value of a reporting unit will be calculated and compared with its carrying amount and an impairment charge will be recognized for the amount that the carrying value exceeds the fair value.

Impairment of Long-Lived Assets

The Company evaluates the fair value of long-lived assets, which include property, plant and equipment, finite-lived intangible assets, and investments in privately held companies, for impairment whenever events or changes in circumstances indicate that the carrying amounts of the assets may not be fully recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the fair value of the assets. Assets to be disposed of are reported at the lower of the carrying amount or fair value less costs to sell.

Accounting for Government Assistance

There is no GAAP that specifically addresses the accounting by business entities for government assistance and tax credits. Absent authoritative accounting standards, interpretative guidance issued and commonly applied by financial statement preparers allows for the selection of accounting policies amongst acceptable alternatives. Based on the facts and circumstances of the government assistance and tax credits received by the Company as discussed below, the Company determined it most appropriate to account for the these transactions by analogy to International Accounting Standards 20 ("IAS 20"), *Accounting for Government Grants and Disclosure of Government Assistance.* IAS 20 permits for the recognition in earnings either separately under a general heading such as other income, or as a reduction of the related expenses.

In April 2020, the Company received $23.7 million from the United States Department of Health and Human Services ("HHS") as a distribution from the Public Health and Social Services Emergency Fund provided for in the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act"). The fund payments are grants, not loans, and HHS will not require repayment provided the funds are utilized to offset expenses incurred to address COVID-19 or to replace lost revenues. The Company accepted the terms and conditions of the grant in May 2020 and recognized the entire $23.7 million during the year ended December 31, 2020, due to lost revenue attributable to COVID-19. The Company has elected to recognize government grant income separately to present a clearer distinction in its consolidated financial statements between its operating income and the amount of income resulting from the CARES Act grant received. The Company believes this presentation method promotes greater comparability amongst all periods presented. Accordingly, the $23.7 million grant recognized during the year ended December 31, 2020 was reflected in other operating income in the consolidated statement of operations and as an operating activity in the consolidated statement of cash flows.

In December 2021 the Company entered into an amended agreement with the Wisconsin Economic Development Corporation ("WEDC") to earn refundable tax credits on the condition of certain capital investment and job creation requirements. The Company has elected to recognize the tax credits as a reduction of the related expenses, as they are earned through the performance of the Company's ongoing operating activities.

Net Loss Per Share

Basic net loss per common share was determined by dividing net loss applicable to common stockholders by the weighted average common shares outstanding during the period. Basic and diluted net loss per share is the same because all outstanding common stock equivalents have been excluded, as they are anti-dilutive as a result of the Company's losses.

The following potentially issuable common shares were not included in the computation of diluted net loss per share because they would have an anti-dilutive effect due to net losses for each period:

	December 31,		
(In thousands)	2021	2020	2019
Shares issuable in connection with acquisitions	45	157	—
Shares issuable upon exercise of stock options	2,284	2,231	2,700
Shares issuable upon the release of restricted stock awards	4,321	3,968	3,801
Shares issuable upon the release of performance share units	878	619	583
Shares issuable upon conversion of convertible notes	20,309	20,309	12,196
	27,837	27,284	19,280

Accounting for Stock-Based Compensation

The Company requires all share-based payments to employees, including grants of employee stock options, restricted stock, restricted stock units, shares purchased under an employee stock purchase plan (if certain parameters are not met), and performance share units to be recognized in the financial statements based on their grant date fair values. Forfeitures of any share-based awards are recognized as they occur.

The fair values and recognition of the Company's share-based payment awards are determined as follows:

The fair value of each service-based option award is estimated on the date of grant using the Black-Scholes option-pricing model. The Black-Scholes pricing model utilizes the following assumptions:

Expected Term—Expected life of an option award is the average length of time over which the Company expects employees will exercise their options, which is based on historical experience with similar grants.

Expected Volatility—Expected volatility is based on the Company's historical stock volatility data over the expected term of the awards.

Risk-Free Interest Rate—The Company bases the risk-free interest rate on the implied yield currently available on U.S. Treasury zero-coupon issues with an equivalent expected term.

The estimated fair value of these awards is recognized to expense using the straight-line method over the expected term.

The fair value of service-based awards for each restricted stock unit award is determined on the date of grant using the closing stock price on that day. The estimated fair value of these awards is recognized to expense using the straight-line method over the vesting period.

The fair value of performance-based equity awards is determined on the date of grant using the closing stock price on that day. The expense recognized each period is also dependent on the probability of what performance conditions will be met which is determined by management's evaluation of internal and external factors. Determining the appropriate amount to expense based on the anticipated achievement of the stated goals requires judgment, including forecasting future financial results. The estimate of the timing of the expense recognition is revised periodically based on the probability of achieving the goals and adjustments are made as appropriate. The cumulative impact of any revision is reflected in the period of the change. If the financial performance targets and operational milestones are not achieved, the award would not vest resulting in no stock-based compensation being recognized and any previously recognized stock-based compensation expense being reversed.

Research and Development Costs

Research and development costs are expensed as incurred. These expenses include the costs of the Company's proprietary research and development efforts, as well as costs of IPR&D projects acquired as part of an asset acquisition that have no alternative future use. Upfront and milestone payments due to third parties in connection with research and development collaborations prior to regulatory approval are expensed as incurred. Milestone payments due to third parties upon, or subsequent to, regulatory approval are capitalized and amortized into research and development costs over the shorter of the remaining license or product patent life, when there are no corresponding revenues related to the license or product. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received, rather than when the payment is made.

The Company incurred research and development expenses of $385.6 million, $554.1 million, and $139.7 million during the years ended December 31, 2021, 2020, and 2019, respectively, including IPR&D of $85.3 million and $412.6 million that was acquired in asset acquisitions that had no alternative future use during the years ended December 31, 2021 and 2020, respectively. The value of the acquired IPR&D that was expensed was determined by identifying those acquired specific IPR&D projects that would be continued and which (a) were incomplete and (b) had no alternative future use. Acquired IPR&D assets that are acquired in an asset acquisition and which have no alternative future use are classified as an investing cash outflow in the consolidated statements of cash flows.

Advertising Costs

The Company expenses the costs of media advertising at the time the advertising takes place. The Company expensed approximately $144.0 million, $97.6 million, and $90.5 million of media advertising during the years ended December 31, 2021, 2020, and 2019, respectively, which is recorded in sales and marketing expenses on the Company's consolidated statements of operations.

Fair Value Measurements

The Financial Accounting Standards Board ("FASB") has issued authoritative guidance that requires fair value to be based on the assumptions market participants would use when pricing an asset or liability and establishes a fair value hierarchy that prioritizes the information used to develop those assumptions. Under that standard, fair value measurements are separately disclosed by level within the fair value hierarchy. The fair value hierarchy establishes and prioritizes the inputs used to measure fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs. Observable inputs are inputs that reflect the assumptions that market participants would use in pricing the asset or liability developed based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the assumptions market participants would use in pricing the asset or liability developed based on the best information available in the circumstances.

Leases

The Company acts as lessee in its lease agreements, which include operating leases for corporate offices, laboratory space, warehouse space, vehicles and certain laboratory and office equipment, and finance leases for certain equipment and vehicles.

The Company determines whether an arrangement is, or contains, a lease at inception. At the beginning of fiscal year 2019, the company adopted ASC 842. The Company records the present value of lease payments as right-of-use ("ROU") assets and lease liabilities on the consolidated balance sheets. ROU assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent an obligation to make lease payments based on the present value of lease payments over the lease term. Classification of lease liabilities as either current or non-current is based on the expected timing of payments due under the Company's obligations.

As most of the Company's leases do not provide an implicit interest rate, the Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments. The incremental borrowing rate is the rate of interest that a lessee would have to pay to borrow on a collateralized basis over a similar term and at an amount equal to the lease payments in a similar economic environment. The Company calculates its incremental borrowing rates for specific lease terms, used to discount future lease payments, as a function of the US. Treasury rate and an indicative Moody's rating for operating leases or finance leases.

The ROU asset also consists of any lease incentives received. The lease terms used to calculate the ROU asset and related lease liability include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. "Reasonably certain" is assessed internally based on economic, industry, company, strategic and contractual factors. The leases have remaining lease terms of 1 year to 15 years, some of which include options to extend the lease for up to 10 years, and some of which include options to terminate the lease within 1 year. Operating lease expense and amortization of finance lease ROU assets are recognized on a straight-line basis over the lease term as an operating expense. Finance lease interest expense is recorded as interest expense on the Company's consolidated statements of operations.

The Company accounts for leases acquired in business combinations by measuring the lease liability at the present value of the remaining lease payments as if the acquired lease were a new lease for the Company. This measurement includes recognition of a lease intangible for any below-market terms present in the leases acquired. The below-market lease intangible is included in the ROU asset on the consolidated balance sheets and are amortized over the remaining lease term. The Company has not acquired any leases with above-market terms.

The Company has taken advantage of certain practical expedients offered to registrants at adoption of ASC 842. The Company does not apply the recognition requirements of ASC 842 to short-term leases. Instead, those lease payments are recognized in profit or loss on a straight-line basis over the lease term. Further, as a practical expedient, all lease contracts are accounted for as one single lease component, as opposed to separating lease and non-lease components to allocate the consideration within a single lease contract.

Revenue Recognition

Revenues are recognized when the satisfaction of the performance obligation occurs, in an amount that reflects the consideration the Company expects to collect in exchange for those services. The Company's revenue is primarily generated by its laboratory testing services utilizing its Cologuard, Oncotype DX, and COVID-19 tests. The services are completed upon release of a patient's test result to the ordering healthcare provider. To determine revenue recognition for the arrangements that

the Company determines are within the scope of ASC 606, Revenue from Contracts with Customers, the Company performs the following five steps: (1) identify the contract(s) with a customer, (2) identify the performance obligations in the contract, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations in the contract and (5) recognize revenue when (or as) the entity satisfies a performance obligation.

The key aspects considered by the Company include the following:

Contracts—The Company's customer is primarily the patient, but the Company does not enter into a formal reimbursement contract with a patient. The Company establishes a contract with a patient in accordance with other customary business practices, which is the point in time an order is received from a provider and a patient specimen has been returned to the laboratory for testing. Payment terms are a function of a patient's existing insurance benefits, including the impact of coverage decisions with Center for Medicare & Medicaid Services ("CMS") and applicable reimbursement contracts established between the Company and payers. However, when a patient is considered self-pay, the Company requires payment from the patient prior to the commencement of the Company's performance obligations. The Company's consideration can be deemed variable or fixed depending on the structure of specific payer contracts, and the Company considers collection of such consideration to be probable to the extent that it is unconstrained.

Under the Company's Laboratory Service Agreements ("LSA") and Laboratory Reference Agreements ("LRA") the Company contracts with a direct bill payer who is the customer for an agreed upon amount of laboratory testing services for a specified amount of time at a fixed reimbursement rate, and certain of the Company's agreements obligate the customer to pay for testing services prior to result.

Performance obligations—A performance obligation is a promise in a contract to transfer a distinct good or service (or a bundle of goods or services) to the customer. The Company's contracts have a single performance obligation, which is satisfied upon rendering of services, which culminates in the release of a patient's test result to the ordering healthcare provider. Or, in the context of some of the Company's agreements, the satisfaction of the performance obligation occurs when a specimen sample is not returned to the laboratory for processing before the end of the allotted testing window. The Company elects the practical expedient related to the disclosure of unsatisfied performance obligations, as the duration of time between providing testing supplies, the receipt of a sample, and the release of a test result to the ordering healthcare provider is far less than one year.

Transaction price—The transaction price is the amount of consideration that the Company expects to collect in exchange for transferring promised goods or services to a customer, excluding amounts collected on behalf of third parties (for example, some sales taxes). The consideration expected to be collected from a contract with a customer may include fixed amounts, variable amounts, or both.

Fixed consideration is derived from the Company's LSA, LRA, and direct bill payer contracts that exist between the Company and the direct bill payers. The contracted reimbursement rate is deemed to be fixed as the Company expects to fully collect all amounts billed under these relationships. Variable consideration is primarily derived from payer and patient billing and can result due to several factors such as the amount of contractual adjustments, any patient co-payments, deductibles or patient adherence incentives, the existence of secondary payers, and claim denials.

The Company estimates the amount of variable consideration using the expected value method, which represents the sum of probability-weighted amounts in a range of possible consideration amounts. When estimating the amount of variable consideration, the Company considers several factors, such as historical collections experience, patient insurance eligibility and payer reimbursement contracts.

The Company limits the amount of variable consideration included in the transaction price to the unconstrained portion of such consideration. In other words, the Company recognizes revenue up to the amount of variable consideration that is not subject to a significant reversal until additional information is obtained or the uncertainty associated with the additional payments or refunds is subsequently resolved. Differences between original estimates and subsequent revisions, including final settlements, represent changes in the estimate of variable consideration and are included in the period in which such revisions are made.

The Company monitors its estimates of transaction price to depict conditions that exist at each reporting date. If the Company subsequently determines that it will collect more or less consideration than it originally estimated for a contract with a patient, it will account for the change as an increase or decrease in the estimate of the transaction price (i.e., an upward or downward revenue adjustment) in the period identified.

When the Company does not have significant historical experience or that experience has limited predictive value, the constraint over estimates of variable consideration may result in no revenue being recognized upon completion of the performance obligations associated with the Company's tests, with recognition, generally occurring at the date of cash receipt.

Allocate transaction price—The transaction price is allocated entirely to the performance obligation contained within the contract with a customer.

Point in time recognition—The Company's single performance obligation is satisfied at a point in time. That point in time is defined as the date the Company releases a result to the ordering healthcare provider, or, in the context of some of the Company's agreements, that point in time could be the date the allotted testing window ends if a specimen sample is not returned to the laboratory for processing. The point in time in which revenue is recognized by the Company signifies fulfillment of the performance obligation to the patient or direct bill payer.

Contract Balances—The timing of revenue recognition, billings and cash collections results in billed accounts receivable and deferred revenue on the consolidated balance sheets. Generally, billing occurs subsequent to the release of a patient's test result to the ordering healthcare provider, resulting in an account receivable. However, the Company sometimes receives advance payment from a patient or a direct bill payer before a test result is completed, resulting in deferred revenue. The deferred revenue recorded is recognized as revenue at the point in time results are released to the patient's healthcare provider. Or, in the context of some of the Company's agreements, the satisfaction of the performance obligation occurs when a specimen sample is not returned to the laboratory for processing before the end of the allotted testing window.

Practical Expedients—The Company does not adjust the transaction price for the effects of a significant financing component, as at contract inception, the Company expects the collection cycle to be one year or less.

The Company expenses sales commissions when incurred because the amortization period would have been one year or less. These costs are recorded within sales and marketing expenses in the Company's consolidated statements of operations.

The Company incurs certain other costs that are incurred regardless of whether a contract is obtained. Such costs are primarily related to legal services and patient communications (e.g. adherence reminder letters). These costs are expensed as incurred and recorded within general and administrative expenses in the Company's consolidated statements of operations.

Foreign Currency Transactions

The functional currency for most of the Company's international subsidiaries is the U.S. dollar. In these instances where the functional currency differs from the local currency, monetary assets and liabilities are remeasured at the current period-end exchange rate, while non-monetary assets and liabilities are remeasured at the historical rate. The gains and losses as a result of exchange rate adjustments of these subsidiaries are recognized in the consolidated statements of operations. Net foreign currency transaction gains or losses were not material to the consolidated statements of operations for the periods presented.

For the Company's international subsidiaries where the functional currency is other than the U.S. dollar, assets and liabilities are translated into the U.S. dollar at the current period-end exchange rate. Revenue and expense items are translated at the average exchange rates for the period. The cumulative adjustments resulting from the translation of the financial statements into the U.S. dollar are included in the Company's consolidated balance sheet as a component of accumulated other comprehensive income (loss).

Concentration of Credit Risk

Financial instruments that subject the Company to credit risk consist of cash, cash equivalents and marketable securities. As of December 31, 2021, the Company had cash and cash equivalents deposited in financial institutions in which the balances exceed the federal government agency insured limit of $250,000 by approximately $234.9 million. The Company has not experienced any losses in such accounts and management believes it is not exposed to any significant credit risk.

Through December 31, 2021, the Company's revenues have been primarily derived from the sale of Cologuard, Oncotype DX, and COVID-19 tests. The following is a breakdown of revenue and accounts receivable from major payers:

	% Revenue for the years ended December 31,			% Accounts Receivable at December 31,		
Major Payer	**2021**	**2020**	**2019**	**2021**	**2020**	**2019**
Centers for Medicare and Medicaid Services	20%	21%	29%	11%	14%	19%
UnitedHealthcare	11%	10%	13%	8%	7%	7%
State of Wisconsin	8%	12%	—%	9%	22%	—%

Tax Positions

A valuation allowance to reduce the deferred tax assets is reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. The Company has incurred significant losses since its inception and due to the uncertainty of the amount and timing of future taxable income, the Company has determined that a $262.2 million and $293.4 million valuation allowance at December 31, 2021 and 2020 is necessary to reduce the tax assets to the amount that is more likely than not to be realized. The change in valuation allowance as of December 31, 2021 and 2020 was a decrease of $31.2 million and an increase of $98.0 million, respectively. An income tax benefit of $246.9 million was recorded primarily as a result of the change in the deferred tax asset valuation allowance resulting from the acquisition of Thrive Earlier Detection Corporation ("Thrive"). Due to the existence of the valuation allowance, future changes in the Company's unrecognized tax benefits will not impact the Company's effective tax rate.

Recent Accounting Pronouncements

Recently Adopted Accounting Pronouncements

In August 2020, The FASB issued Accounting Standards Update ("ASU") No. 2020-06, *Debt – Debt with Conversion and Other Options (subtopic 470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40)*. This update simplifies the accounting for convertible debt instruments by removing the beneficial conversion and cash conversion separation models for convertible instruments. Under the update, the embedded conversion features are no longer separated from the host contract for convertible instruments with conversion features that are not required to be accounted for as derivatives or that do not result in substantial premiums accounted for as paid-in capital. The update also amends the accounting for certain contracts in an entity's own equity that are currently accounted for as derivatives because of specific settlement provisions. In addition, ASU 2020-06 requires the application of the if-converted method for calculating diluted earnings per share and the treasury stock method will no longer be available. This standard may be adopted through either a modified retrospective method of transition or a full retrospective method of transition. The amendments in this update are effective for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020.

The Company adopted the standard on January 1, 2021 through application of the full retrospective method of transition. This method of adoption was applied to enhance comparability between the periods presented in the Company's financial statements. The Company applied the standard to convertible notes outstanding as of the date of the first offering of the Company's outstanding convertible notes as discussed in Note 10.

The Company's convertible debt instruments are now accounted for as a single liability measured at its amortized cost. The notes are no longer bifurcated between debt and equity, rather accounted for entirely as debt at face value net of any discount or premium and issuance costs. Interest expense is comprised of (1) cash interest payments, (2) amortization of any debt discounts or premiums based on the original offering, and (3) amortization of any debt issuance costs. Gain or loss on extinguishment of convertible notes is calculated as the difference between the (i) fair value of the consideration transferred and (ii) the sum of the carrying value of the debt at the time of repurchase.

As of January 1, 2019, the cumulative effect of adoption resulted in an increase in the net carrying amount of convertible notes, net, of $233.7 million, a decrease in additional-paid-in-capital of $260.2 million, a decrease in accumulated deficit of $26.6 million, and an increase to net deferred tax assets of $55.7 million offset by a corresponding increase of $55.7 million in the valuation allowance. For the year ended December 31, 2019, interest expense in the consolidated statement of operations increased by $137.7 million as a result of a decrease in amortization of debt discounts, premiums, and issuance costs of $39.5

million, which was offset by an increase in loss on extinguishment of $177.1 million in connection with the extinguishment of $493.4 million face value of the 2025 Notes. Income tax benefit increased by $8.5 million and net loss per share, basic and diluted, increased by $0.98 per share. For the year ended December 31, 2020, interest expense in the condensed consolidated statement of operations decreased by $28.1 million as a result of a decrease in amortization of debt discounts, premiums, and issuance costs of $70.9 million, which was offset by an increase in loss on extinguishment of $42.8 million in connection with the extinguishment of $100.0 million face value of the 2025 Notes. Income tax benefit decreased by $3.1 million and net loss per share, basic and diluted, decreased by $0.17 per share.

In November 2021, the FASB issued ASU No. 2021-10, *Government Assistance (Topic 832)*. This update requires certain annual disclosures about transactions with a government that are accounted for by applying a grant or contribution model by analogy. The amendments in this update are effective for fiscal years beginning after December 15, 2021. Early application of the amendments is permitted. The Company early adopted these disclosure requirements and applied them to its disclosure of the WEDC tax credits earned during fiscal year 2021 and the funding received as part of the CARES Act in 2020.

Recently Issued Accounting Pronouncements Not Yet Adopted

In October 2021, The FASB issued ASU No. 2021-08, *Business Combinations (Topic 805)*. This update requires that an entity (acquirer) recognize and measure contract assets and contract liabilities acquired in a business combination in accordance with ASC 606. This differs from the current requirement to measure contract assets and contract liabilities acquired in a business combination at fair value. The amendments in this update should be applied prospectively, and are effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted, Including adoption in an interim period. This ASU will only impact the Company if it acquires another entity through a business combination.

Guarantees and Indemnifications

The Company, as permitted under Delaware law and in accordance with its bylaws, indemnifies its officers and directors for certain events or occurrences, subject to certain limits, while the officer or director is or was serving at the Company's request in such capacity. The term of the indemnification period is for the officer's or director's lifetime. The maximum amount of potential future indemnification is unlimited; however, the Company has a directors and officers insurance policy that limits its exposure and may enable it to recover a portion of any future amounts paid. The Company believes the fair value of these indemnification agreements is minimal. Accordingly, the Company has not recorded any liabilities for these agreements as of December 31, 2021 and 2020.

Reclassifications

Certain prior year amounts have been reclassified to conform to the current year presentation in the consolidated financial statements and accompanying notes to the consolidated financial statements.

(2) REVENUE

The following table presents the Company's revenues disaggregated by revenue source:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Screening			
Medicare Parts B & C	$ 438,646	$ 365,471	$ 404,331
Commercial	569,944	409,671	368,006
Other	53,718	39,925	37,783
Total Screening	1,062,308	815,067	810,120
Precision Oncology			
Medicare Parts B & C	$ 195,069	$ 157,166	$ 24,325
Commercial	189,198	186,043	29,976
International	109,913	77,484	11,444
Other	67,496	19,800	428
Total Precision Oncology	561,676	440,493	66,173
COVID-19 Testing	$ 143,103	$ 235,831	$ —
Total	$ 1,767,087	$ 1,491,391	$ 876,293

Screening revenue primarily includes laboratory service revenue from the Cologuard test while Precision Oncology revenue primarily includes laboratory service revenue from global Oncotype products.

The downward adjustment to revenue from changes in transaction price on tests completed in the prior year was $11.8 million for the year ended December 31, 2021 and revenue recognized from changes in transaction price on tests completed in the prior year was $9.6 million and $9.9 million for the years ended December 31, 2020 and 2019, respectively.

The Company had deferred revenue of $1.0 million and $25.0 million as of December 31, 2021 and 2020, respectively. As of December 31, 2020, $24.2 million of the Company's deferred revenue balance is a result of the billing terms pursuant to the existing COVID-19 LSAs with customers. Deferred revenue is reported in other current liabilities in the Company's consolidated balance sheets.

Revenue recognized for the years ended December 31, 2021 and 2020, which was included in the deferred revenue balance at the beginning of each period was $24.6 million and $0.2 million, respectively. Of the $24.6 million of revenue recognized for the year ended December 31, 2021, which was included in the deferred revenue balance at the beginning of the period, $24.2 million related to COVID-19 testing.

(3) MARKETABLE SECURITIES

The following table sets forth the Company's cash, cash equivalents, restricted cash, and marketable securities at December 31, 2021 and 2020:

(In thousands)	December 31, 2021	December 31, 2020
Cash, cash equivalents, and restricted cash		
Cash and money market	$ 247,335	$ 901,294
Cash equivalents	68,136	589,994
Restricted cash (1)	297	306
Total cash, cash equivalents and restricted cash	315,768	1,491,594
Marketable securities		
Available-for-sale debt securities	$ 711,669	$ 347,178
Equity securities	3,336	1,521
Total marketable securities	715,005	348,699
Total cash and cash equivalents, restricted cash and marketable securities	$ 1,030,773	$ 1,840,293

(1) Restricted cash is included in other long-term assets on the consolidated balance sheets.

Available-for-sale debt securities at December 31, 2021 consisted of the following:

(In thousands)	Amortized Cost	Gains in Accumulated Other Comprehensive Income (Loss) (1)	Losses in Accumulated Other Comprehensive Income (Loss) (1)	Estimated Fair Value
Cash equivalents				
U.S. government agency securities	$ 3,543	$ —	$ —	$ 3,543
Commercial paper	64,593	—	—	64,593
Total cash equivalents	68,136	—	—	68,136
Marketable securities				
Corporate bonds	$ 313,634	$ 13	$ (493)	$ 313,154
U.S. government agency securities	250,793	—	(873)	249,920
Asset backed securities	94,565	2	(107)	94,460
Certificates of deposit	47,147	2	(10)	47,139
Commercial paper	6,996	—	—	6,996
Total marketable securities	713,135	17	(1,483)	711,669
Total available-for-sale debt securities	$ 781,271	$ 17	$ (1,483)	$ 779,805

(1) Gains and losses in accumulated other comprehensive income (loss) ("AOCI") are reported before tax impact.

Available-for-sale debt securities at December 31, 2020 consisted of the following:

(In thousands)	Amortized Cost	Gains in Accumulated Other Comprehensive Income (Loss) (1)	Losses in Accumulated Other Comprehensive Income (Loss) (1)	Estimated Fair Value
Cash equivalents				
U.S. government agency securities	$ 589,986	$ 8	$ —	$ 589,994
Total cash equivalents	589,986	8	—	589,994
Marketable securities				
Corporate bonds	$ 132,301	$ 612	$ —	$ 132,913
U.S. government agency securities	207,119	52	—	207,171
Asset backed securities	7,070	24	—	7,094
Total marketable securities	346,490	688	—	347,178
Total available-for-sale debt securities	$ 936,476	$ 696	$ —	$ 937,172

(1) Gains and losses in AOCI are reported before tax impact.

The following table summarizes contractual underlying maturities of the Company's available-for-sale debt securities at December 31, 2021:

(In thousands)	Due one year or less Cost	Due one year or less Fair Value	Due after one year through five years Cost	Due after one year through five years Fair Value
Cash equivalents				
Commercial paper	$ 64,593	$ 64,593	$ —	$ —
U.S. government agency securities	3,543	3,543	—	—
Total cash equivalents	68,136	68,136	—	—
Marketable securities				
U.S. government agency securities	$ 48,113	$ 48,046	$ 202,680	$ 201,874
Corporate bonds	180,114	180,008	133,520	133,146
Asset backed securities	—	—	94,565	94,460
Certificates of deposit	47,147	47,139	—	—
Commercial paper	6,996	6,996	—	—
Total marketable securities	282,370	282,189	430,765	429,480
Total available-for-sale securities	$ 350,506	$ 350,325	$ 430,765	$ 429,480

The following table summarizes the gross unrealized losses and fair values of available-for-sale debt securities in an unrealized loss position as of December 31, 2021, aggregated by investment category and length of time those individual securities have been in a continuous unrealized loss position:

	Less than 12 months		12 months or greater		Total	
(In thousands)	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss
Marketable securities						
Corporate bonds	$ 299,448	$ (493)	$ —	$ —	$ 299,448	$ (493)
U.S. government agency securities	249,921	(873)	—	—	249,921	(873)
Asset backed securities	89,990	(107)	—	—	89,990	(107)
Certificates of deposit	24,137	(10)	—	—	24,137	(10)
Total available-for-sale securities	$ 663,496	$ (1,483)	$ —	$ —	$ 663,496	$ (1,483)

There were no available-for-sale debt securities in an unrealized loss position as of December 31, 2020.

The Company evaluates investments that are in an unrealized loss position for impairment as a result of credit loss. It was determined that no credit losses exist as of December 31, 2021 and 2020 because the change in market value for those securities in an unrealized loss position has resulted from fluctuating interest rates rather than a deterioration of the credit worthiness of the issuers.

The gains and losses recorded are included in investment income, net in the Company's consolidated statements of operations. The gains and losses recorded on available-for-sale debt securities and equity securities were not significant for the years ended December 31, 2021, 2020, and 2019.

(4) INVENTORY

Inventory consisted of the following:

	December 31,	
(In thousands)	2021	2020
Raw materials	$ 51,321	$ 43,083
Semi-finished and finished goods	53,673	49,182
Total inventory	$ 104,994	$ 92,265

(5) PROPERTY, PLANT AND EQUIPMENT

The carrying value and estimated useful lives of property, plant and equipment are as follows:

		December 31,	
(In thousands)	Estimated Useful Life	2021	2020
Property, plant and equipment			
Land	n/a	$ 4,716	$ 4,466
Leasehold and building improvements	(1)	147,083	117,865
Land improvements	15 years	5,206	4,864
Buildings	30 - 40 years	210,560	200,980
Computer equipment and computer software	3 years	109,119	75,519
Laboratory equipment	3 - 10 years	189,748	142,110
Furniture and fixtures	3 - 10 years	28,293	24,968
Assets under construction	n/a	100,339	18,751
Property, plant and equipment, at cost		795,064	589,523
Accumulated depreciation		(214,816)	(137,537)
Property, plant and equipment, net		$ 580,248	$ 451,986

(1) Lesser of remaining lease term, building life, or estimated useful life.

Depreciation expense for the years ended December 31, 2021, 2020, and 2019 was $85.3 million, $70.0 million, and $34.2 million, respectively.

At December 31, 2021, the Company had $100.3 million of assets under construction, which consisted of $41.5 million in buildings under construction, $27.6 million in leasehold improvements, $19.8 million in laboratory equipment under construction, $10.6 million of capitalized costs related to software projects, $0.6 million in land improvements, and $0.2 million in furniture and fixtures. Depreciation will begin on these assets once they are placed into service upon completion in 2022 and 2023.

(6) INTANGIBLE ASSETS AND GOODWILL

Intangible Assets

The following table summarizes the net-book-value and estimated remaining life of the Company's intangible assets as of December 31, 2021:

(In thousands)	Weighted Average Remaining Life (Years)	Cost	Accumulated Amortization	Net Balance at December 31, 2021
Finite-lived intangible assets				
Trade name	13.4	$ 104,700	$ (13,554)	$ 91,146
Customer relationships	9.6	6,700	(1,577)	5,123
Patents and licenses	3.6	10,942	(6,763)	4,178
Supply agreement	5.4	2,295	(101)	2,194
Acquired developed technology	8.6	918,171	(176,402)	741,769
Total finite-lived intangible assets		1,042,808	(198,397)	844,411
In-process research and development	n/a	1,250,000	—	1,250,000
Total intangible assets		$ 2,292,808	$ (198,397)	$ 2,094,411

The following table summarizes the net-book-value and estimated remaining life of the Company's intangible assets as of December 31, 2020:

(In thousands)	Weighted Average Remaining Life (Years)	Cost	Accumulated Amortization	Net Balance at December 31, 2020
Finite-lived intangible assets				
Trade name	14.9	$ 100,700	$ (7,258)	$ 93,442
Customer relationships	12.8	2,700	(404)	2,296
Patents	3.7	10,441	(5,422)	5,019
Supply agreement	6.5	30,000	(4,527)	25,473
Acquired developed technology	9.0	814,171	(93,278)	720,893
Total intangible assets		$ 958,012	$ (110,889)	$ 847,123

As of December 31, 2021, the estimated future amortization expense associated with the Company's finite-lived intangible assets for each of the five succeeding fiscal years is as follows:

(In thousands)	
2022	$ 98,614
2023	98,611
2024	98,277
2025	97,230
2026	96,169
Thereafter	355,510
	$ 844,411

The Company's acquired intangible assets are being amortized on a straight-line basis over the estimated useful life.

During the third quarter of 2021 and in connection with the preparation of the financial statements included in the Company's Form 10-Q for the period ended September 30, 2021, the Company recorded a non-cash, pre-tax impairment loss of $20.2 million related to the supply agreement intangible asset that was initially recorded as part of the combination with Genomic Health due to lower than anticipated performance of the underlying product. The Company utilized the income approach to measure the fair value of the supply agreement, which involves significant unobservable inputs (Level 3 inputs). The impairment is recorded in intangible asset impairment charge in the consolidated statement of operations for the year ended December 31, 2021.

During the third quarter of 2020, the Company began discussions with Biocartis regarding the termination of its agreements with Biocartis related to the development of an in vitro diagnostic ("IVD") version of the Oncotype DX Breast Recurrence Score® test. As a result, and in connection with the preparation of the financial statements included in the Company's Form 10-Q for the period ended September 30, 2020, the Company recorded a non-cash, pre-tax impairment loss of $200.0 million related to the in-process research and development intangible asset that was initially recorded as part of the combination with Genomic Health. The impairment is recorded in intangible asset impairment charge in the consolidated statement of operations for the year ended December 31, 2020. The agreements with Biocartis were terminated in November 2020.

During the third quarter of 2020, the Company abandoned certain research and development assets acquired in 2017 through an asset purchase agreement with Armune Biosciences, Inc. These assets were expected to complement the Company's product pipeline and were expected to have alternative future uses at the time of acquisition; however, due to changes in strategic priorities and efforts during the third quarter of 2020, these assets are no longer expected to be utilized to advance the Company's product pipeline. As a result, and in connection with the preparation of the financial statements included in the Company's Form 10-Q for the period ended September 30, 2020, the Company wrote-off the gross cost basis of the intangible asset of $12.2 million and accumulated amortization of $2.5 million as of September 30, 2020. This write-off resulted in a non-cash, pre-tax impairment loss of $9.7 million, which is recorded in intangible asset impairment charge in the consolidated statement of operations for the year ended December 31, 2020.

There were no impairment losses for the year ended December 31, 2019.

Goodwill

The change in the carrying amount of goodwill for the years ended December 31, 2021 and 2020 is as follows:

(In thousands)	
Balance, January 1, 2020 (1)	$ 1,203,197
Paradigm & Viomics acquisition	30,431
Genomic Health acquisition adjustment (2)	4,044
Balance, December 31, 2020	1,237,672
Thrive acquisition	948,105
Ashion acquisition	56,758
PreventionGenetics acquisition	92,637
Balance, December 31, 2021	$ 2,335,172

(1) The beginning balance represents the goodwill acquired from the acquisitions of Sampleminded, Inc., Biomatrica, Inc., and Genomic Health between 2017 and 2019 totaling $2.0 million, $15.3 million, and $1.19 billion, respectively.

(2) The Company recognized a measurement period adjustment to goodwill related to an increase in Genomic Health's pre-acquisition deferred tax liability due to finalization of certain income-tax related items.

There were no impairment losses for the years ended December 31, 2021, 2020, and 2019.

(7) FAIR VALUE MEASUREMENTS

The three levels of the fair value hierarchy established are as follows:

Level 1 Quoted prices (unadjusted) in active markets for identical assets or liabilities that the Company has the ability to access as of the reporting date. Active markets are those in which transactions for the asset or liability occur in sufficient frequency and volume to provide pricing information on an ongoing basis.

Level 2 Pricing inputs other than quoted prices in active markets included in Level 1, which are either directly or indirectly observable as of the reporting date. These include quoted prices for similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active.

Level 3 Unobservable inputs that reflect the Company's assumptions about the assumptions that market participants would use in pricing the asset or liability. Unobservable inputs shall be used to measure fair value to the extent that observable inputs are not available.

The following table presents the Company's fair value measurements as of December 31, 2021 along with the level within the fair value hierarchy in which the fair value measurements, in their entirety, fall.

(In thousands)	Fair value at December 31, 2021	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash, cash equivalents, and restricted cash				
Cash and money market	$ 247,335	$ 247,335	$ —	$ —
Commercial paper	64,593	—	64,593	—
U.S. government agency securities	3,543	—	3,543	—
Restricted cash	297	297	—	—
Marketable securities				
Corporate bonds	$ 313,154	$ —	$ 313,154	$ —
U.S. government agency securities	249,920	—	249,920	—
Asset backed securities	94,460	—	94,460	—
Certificates of deposit	47,139	—	47,139	—
Commercial paper	6,996	—	6,996	—
Equity securities	3,336	3,336	—	—
Non-marketable securities	$ 3,090	$ —	$ —	$ 3,090
Liabilities				
Contingent consideration	$ (359,021)	$ —	$ —	$ (359,021)
Total	$ 674,842	$ 250,968	$ 779,805	$ (355,931)

The following table presents the Company's fair value measurements as of December 31, 2020 along with the level within the fair value hierarchy in which the fair value measurements, in their entirety, fall.

(In thousands)	Fair Value at December 31, 2020	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash and cash equivalents				
Cash and money market	$ 901,294	$ 901,294	$ —	$ —
U.S. government agency securities	589,994	—	589,994	—
Restricted cash	306	306	—	—
Marketable securities				
Corporate bonds	$ 132,913	$ —	$ 132,913	$ —
Asset backed securities	7,094	—	7,094	—
U.S. government agency securities	207,171	—	207,171	—
Equity securities	1,521	1,521	—	—
Liabilities				
Contingent consideration	$ (2,477)	$ —	$ —	$ (2,477)
Total	$ 1,837,816	$ 903,121	$ 937,172	$ (2,477)

The equity securities held as of December 31, 2021 were subject to a short-term lock-up restriction after they were obtained in the second quarter of 2021, and the fair value was previously discounted from the observable market prices of the similar unrestricted equity securities, which the Company classified as a Level 2 investment. The lock-up restriction ended during the fourth quarter of 2021, and the equity securities are classified as a Level 1 investment as of December 31, 2021. There was no change in valuation techniques or transfers between fair value measurement levels during the year ended December 31, 2020. The fair value of Level 2 instruments classified as cash equivalents and marketable debt securities are valued using a third-party pricing agency where the valuation is based on observable inputs including pricing for similar assets and other observable market factors.

Contingent Consideration

The fair value of contingent consideration as of December 31, 2021 and 2020 was $359.0 million and $2.5 million, respectively, which was recorded in other long-term liabilities in the condensed consolidated balance sheets.

The following table provides a reconciliation of the beginning and ending balances of contingent consideration:

(In thousands)	Contingent consideration
Balance, January 1, 2020 (1)	$ (2,879)
Changes in fair value	325
Payments	77
Balance, December 31, 2020	(2,477)
Purchase price contingent consideration (2)	(350,348)
Changes in fair value	(6,359)
Payments	163
Balance, December 31, 2021	$ (359,021)

(1) The change in fair value of the contingent consideration liability during the year ended December 31, 2019 was not material to the consolidated financial statements.

(2) The increase in the contingent consideration liability is due to the contingent consideration associated with the acquisitions of Ashion Analytics, LLC ("Ashion") and Thrive. Refer to Note 19 for further information.

This fair value measurement of contingent consideration is categorized as a Level 3 liability, as the measurement amount is based primarily on significant inputs not observable in the market.

The fair value of the contingent consideration liability recorded related to regulatory and product development milestones associated with the Thrive and Ashion acquisitions was $357.8 million as of December 31, 2021. The Company evaluates the fair value of the regulatory and product development contingent consideration liabilities using the probability-weighted scenario based discounted cash flow model, which is consistent with the initial measurement of the expected contingent consideration liabilities. Probabilities of success are applied to each potential scenario and the resulting values are discounted using a rate that considers a present-value factor. The passage of time in addition to changes in projected milestone achievement timing, present-value factor, the degree of achievement if applicable, and probabilities of success may result in adjustments to the fair value measurement. The fair value measurements of contingent consideration for which a liability is recorded include significant unobservable inputs. As of December 31, 2021, the fair value of the contingent consideration liability recorded related to regulatory and product development milestones was determined using a weighted average probability of success of 90.5% and a weighted average present-value factor of 2.3%. The projected fiscal year of payment range is from 2024 to 2027. Unobservable inputs were weighted by the relative fair value of the contingent consideration liability.

The fair value of the contingent consideration earnout liability related to certain revenue milestones associated with the Biomatrica acquisition was $1.2 million as of December 31, 2021. The revenue milestone associated with the Ashion acquisition is not expected to be achieved and therefore no liability has been recorded for this milestone.

Non-Marketable Equity Investments

As of December 31, 2021 and 2020, the aggregate carrying amounts of the Company's non-marketable equity securities without readily determinable fair values were $25.3 million and $28.3 million, respectively, which are classified as a component of other long-term assets in the Company's consolidated balance sheets. There have been no downward or upward adjustments made on these investments since initial recognition.

The Company has committed capital to venture capital investment funds (the "Funds") of $17.5 million, of which $16.0 million remained callable through 2033 as of December 31, 2021. The aggregate carrying amount of the Funds, which are classified as a component of other long-term assets in the Company's consolidated balance sheets, were $1.5 million and $0.8 million as of December 31, 2021 and 2020, respectively.

Derivative Financial Instruments

As of December 31, 2021 and 2020, the Company had open foreign currency forward contracts with notional amounts of $46.7 million and $22.4 million, respectively. The Company's foreign exchange derivative instruments are classified as Level 2 within the fair value hierarchy as they are valued using inputs that are observable in the market or can be derived principally from or corroborated by observable market data. The fair value of the foreign currency forward contracts was zero at December 31, 2021 and 2020, and there were no gains or losses recorded for the years ended December 31, 2021 and 2020.

(8) ACCRUED LIABILITIES

Accrued liabilities at December 31, 2021 and 2020 consisted of the following:

	December 31,	
(In thousands)	2021	2020
Compensation	$ 183,517	$ 124,654
Pfizer Promotion Agreement related costs	91,436	46,937
Professional fees	50,077	36,203
Other	32,116	13,064
Assets under construction	22,611	2,118
Research and trial related expenses	15,534	6,111
Licenses	3,265	4,517
	$ 398,556	$ 233,604

(9) LONG-TERM DEBT

Construction Loan Agreement

During December 2017, the Company entered into a loan agreement with Fifth Third Bank (formerly MB Financial Bank, N.A.) (the "Construction Loan Agreement"), which provided the Company with a non-revolving construction loan (the "Construction Loan") of $25.6 million. The Company used the Construction Loan proceeds to finance the construction of an additional clinical laboratory and related facilities in Madison, Wisconsin. The Construction Loan was collateralized by the additional clinical laboratory and related facilities.

In November 2021, the Company entered into a revolving loan agreement (the "Revolving Loan Agreement") with PNC Bank, National Association ("PNC"). As part of the Revolving Loan Agreement, the Company agreed to repay in full all outstanding debt owed to Fifth Third Bank under the Construction Loan Agreement, and as of December 31, 2021, the remaining outstanding balance had been fully repaid in connection with the termination of the Construction Loan Agreement.

Prior to the repayment, the Construction Loan Agreement bore interest at a rate equal to the sum of the 1-month LIBOR rate plus 2.25%. Regular monthly payments were interest-only for the first 24 months, with further payments based on a 20-year amortization schedule. Amounts borrowed pursuant to the Construction Loan Agreement could be prepaid at any time without penalty, and the maturity date of the Construction Loan Agreement would have been December 10, 2022.

In November 2017, Fifth Third Bank, on behalf of the Company, issued an Irrevocable Standby Letter of Credit in the amount of $0.6 million in favor of the City of Madison, Wisconsin (the "City Letter of Credit"). The City Letter of Credit was deemed to have been issued pursuant to the Construction Loan Agreement. The amount of the City Letter of Credit reduced, dollar for dollar, the amount available for borrowing under the Construction Loan Agreement.

As a condition to Fifth Third's initial advance of loan proceeds under the Construction Loan Agreement, the Company was required to first invest at least $16.4 million of its own cash into the construction project. The Company fulfilled its required initial investment and made its first draw on the Construction Loan in June 2018. In December 2019, the Company began making monthly payments towards the outstanding principal balance plus accrued interest. As of December 31, 2020, the outstanding balance was $23.8 million from the Construction Loan, including $0.7 million of interest incurred, which was accrued for as an interest reserve and represents a portion of the loan balance. The Company capitalized the $0.7 million of interest to the construction project. The Company incurred approximately $0.2 million of debt issuance costs related to the Construction Loan, which were recorded as a direct deduction from the liability. The debt issuance costs were being amortized over the life of the Construction Loan, and any unamortized issuance costs were recorded as a loss as of the date of the repayment of the loan in November 2021.

The carrying amount of the Construction Loan approximated fair value due to the short maturity of this instrument. The Construction Loan was privately held with no public market for this debt and therefore was classified as a Level 3 fair value measurement. The change in the fair value during the years ended December 31, 2021 and December 31, 2020 was due to payments made on the loan resulting in a decrease in the liability.

Revolving Loan Agreement

During November 2021, the Company entered into the Revolving Loan Agreement with PNC. The Revolving Loan Agreement provides the Company with a revolving line of credit of up to $150.0 million (the "Revolver"). The Revolver is collateralized by the Company's marketable securities held by PNC, which must continue to maintain a minimum market value of $150.0 million. The Revolver is available for general working capital purposes and all other lawful corporate purposes. In addition, the Company may request, in lieu of cash advances, letters of credit with an aggregate stated amount outstanding not to exceed $20.0 million. The availability of advances under the line of credit will be reduced by the stated amount of each letter of credit issued and outstanding.

Borrowings under the Revolving Loan Agreement accrue interest at an annual rate equal to the sum of the daily Bloomberg Short-Term Bank Yield Index Rate plus the applicable margin of 0.60%. Loans under the Revolving Loan Agreement may be prepaid at any time without penalty. The Revolver's maturity date is November 5, 2023.

The Company has agreed in the Revolving Loan Agreement to various financial covenants, and as of December 31, 2021, the Company is in compliance with all covenants.

During the fourth quarter of 2021, PNC issued a letter of credit of $2.9 million, which reduced the amount available for cash advances under the line of credit to $147.1 million as of December 31, 2021. As of December 31, 2021, the Company has not drawn funds from, nor are any amounts outstanding under, the Revolving Loan Agreement.

Tax Increment Financing Loan Agreements

The Company entered into two separate Tax Increment Financing Loan Agreements ("TIFs") in February 2019 and June 2019 with the City of Madison, Wisconsin. The TIFs provide for $4.6 million of financing in the aggregate. In return for the loans, the Company is obligated to create and maintain 500 full-time jobs over a five-year period, starting on the date of occupancy of the buildings constructed. In the event that the job creation goals are not met, the Company would be required to pay a penalty.

The Company records the earned financial incentives as the full-time equivalent positions are filled. The amount earned is recorded as a liability and amortized as a reduction of operating expenses over a two-year period, which is the timeframe when the TIFs will be repaid through property taxes.

As of December 31, 2019, the Company had earned and received payment of the full $4.6 million from the City of Madison, and the corresponding liability became fully amortized in October 2020. In May 2021 the City of Madison confirmed that the Company had repaid the TIFs in full and released the Company from the loans and the related property liens.

(10) CONVERTIBLE NOTES

Convertible note obligations included in the consolidated balance sheet consisted of the following as of December 31, 2021:

				Fair Value (2)	
(In thousands)	Principal Amount	Unamortized Debt Discount and Issuance Costs	Net Carrying Amount	Amount	Leveling
2028 Convertible notes - 0.375%	$ 1,150,000	$ (18,826)	$ 1,131,174	$ 1,139,650	2
2027 Convertible notes - 0.375%	747,500	(11,691)	735,809	771,794	2
2025 Convertible notes - 1.000% (1)	315,005	(1,756)	313,249	415,473	2

Convertible note obligations included in the consolidated balance sheet consisted of the following as of December 31, 2020:

				Fair Value (2)	
(In thousands)	Principal Amount	Unamortized Debt Discount and Issuance Costs	Net Carrying Amount	Amount	Leveling
2028 Convertible notes - 0.375%	$ 1,150,000	$ (21,879)	$ 1,128,121	$ 1,526,625	2
2027 Convertible notes - 0.375%	747,500	(13,937)	733,563	992,306	2
2025 Convertible notes - 1.000% (1)	315,049	(2,333)	312,716	601,744	2

(1) Based on the Company's share price on the trading days leading up to December 31, 2020 and through the third quarter of 2021, holders of the 2025 Convertible Notes had the right to convert their debentures beginning on January 1, 2021 and ending on December 31, 2021. As a result, the 2025 Convertible Notes were included within convertible notes, net, current portion on the consolidated balance sheet as of December 31, 2020. Some holders did convert their debentures, resulting in a decrease of the principal amount of the 2025 Convertible Notes. As of December 31, 2021, the 2025 Convertible Notes are not convertible and included within long-term convertible notes, net on the consolidated balance sheet.

(2) The fair values are based on observable market prices for this debt, which is traded in less active markets and therefore is classified as a Level 2 fair value measurement.

Issuances and Settlements

In January 2018, the Company issued and sold $690.0 million in aggregate principal amount of 1.0% Convertible Notes (the “January 2025 Notes”) with a maturity date of January 15, 2025. The January 2025 Notes accrue interest at a fixed rate of 1.0% per year, payable semi-annually in arrears on January 15 and July 15 of each year, beginning on July 15, 2018. The net proceeds from the issuance of the January 2025 Notes were approximately $671.1 million, after deducting underwriting discounts and commissions and the offering expenses payable by the Company.

In June 2018, the Company issued and sold an additional $218.5 million in aggregate principal amount of 1.0% Convertible Notes (the “June 2025 Notes”). The June 2025 Notes were issued under the same indenture pursuant to which the Company previously issued the January 2025 Notes (the “Indenture”). The January 2025 Notes and the June 2025 Notes (collectively, the “2025 Notes”) have identical terms (including the same January 15, 2025 maturity date) and are treated as a single series of securities. The net proceeds from the issuance of the June 2025 Notes were approximately $225.3 million, after deducting underwriting discounts and commissions and the offering expenses payable by the Company.

In March 2019, the Company issued and sold $747.5 million in aggregate principal amount of 0.375% Convertible Notes (the “2027 Notes”) with a maturity date of March 15, 2027. The 2027 Notes accrue interest at a fixed rate of 0.375% per year, payable semi-annually in arrears on March 15 and September 15 of each year, beginning on September 15, 2019. The net proceeds from the issuance of the 2027 Notes were approximately $729.5 million, after deducting underwriting discounts and commissions and the offering expenses payable by the Company.

The Company utilized a portion of the proceeds from the issuance of the 2027 Notes to settle a portion of the 2025 Notes in privately negotiated transactions. In March 2019, the Company used cash of $494.1 million and an aggregate of 2.2 million shares of the Company’s common stock valued at $182.4 million for total consideration of $676.5 million to settle $493.4 million of the 2025 Notes, of which $0.7 million was used to pay off interest accrued on the 2025 Notes. The transaction resulted in a loss on settlement of convertible notes of $187.7 million, which is reflected in interest expense in the Company’s consolidated statement of operations. The loss represents the difference between (i) the fair value of the consideration transferred and (ii) the carrying value of the debt at the time of repurchase.

In February 2020, the Company issued and sold $1.15 billion in aggregate principal amount of 0.375% Convertible Notes (the “2028 Notes” and, collectively with the 2025 Notes and the 2027 Notes, the “Notes”) with a maturity date of March 1, 2028. The 2028 Notes accrue interest at a fixed rate of 0.375% per year, payable semi-annually in arrears on March 1 and September 1 of each year, beginning on September 1, 2020. The net proceeds from the issuance of the 2028 Notes were approximately $1.13 billion, after deducting underwriting discounts and commissions and the offering expenses payable by the Company.

In February 2020, the Company used $150.1 million of the proceeds from the issuance of the 2028 Notes to settle $100.0 million of the 2025 Notes, of which $0.1 million was used to pay off interest accrued on the 2025 Notes. The transaction resulted in a loss on settlement of convertible notes of $50.8 million, which is recorded in interest expense in the Company’s consolidated statement of operations. The loss represents the difference between (i) the fair value of the consideration transferred and (ii) the carrying value of the debt at the time of repurchase.

Summary of Conversion Features

Until the six-months immediately preceding the maturity date of the applicable series of Notes, each series of Notes is convertible only upon the occurrence of certain events and during certain periods, as set forth in the Indentures filed at the time of the original offerings. On or after the date that is six-months immediately preceding the maturity date of the applicable series of Notes until the close of business on the second scheduled trading day immediately preceding the maturity date, holders may convert such Notes at any time. The Notes will be convertible into cash, shares of the Company’s common stock (plus, if applicable, cash in lieu of any fractional share), or a combination of cash and shares of the Company’s common stock, at the Company’s election.

It is the Company’s intent and policy to settle all conversions through combination settlement. The initial conversion rate is 13.26, 8.96, and 8.21 shares of common stock per $1,000 principal amount for the 2025 Notes, 2027 Notes, and 2028 Notes, respectively, which is equivalent to an initial conversion price of approximately $75.43, $111.66, and $121.84 per share of the Company’s common stock for the 2025 Notes, 2027 Notes, and 2028 Notes, respectively. The 2025 Notes, 2027 Notes, and 2028 Notes may be convertible in up to 4.2 million, 6.7 million, and 9.4 million shares, respectively. The conversion rate is subject to adjustment upon the occurrence of certain specified events as set forth in the Indentures filed at the time of the original offerings but will not be adjusted for accrued and unpaid interest. In addition, holders of the Notes who convert their Notes in connection with a “make-whole fundamental change” (as defined in the Indenture), will, under certain circumstances, be entitled to an increase in the conversion rate.

If the Company undergoes a “fundamental change” (as defined in the Indenture), holders of the Notes may require the Company to repurchase for cash all or part 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.

Based on the closing price of the Company's common stock of $77.83 on December 31, 2021, the if-converted values on the Company's 2025 Notes exceed the principal amount by $10.0 million and the if-converted values of the 2027 Notes and 2028 Notes do not exceed the principal amount.

Ranking of Convertible Notes

The Notes are the Company’s senior unsecured obligations and (i) rank senior in right of payment to all of its future indebtedness that is expressly subordinated in right of payment to the Notes; (ii) rank equal in right of payment to each outstanding series thereof and to all of the Company’s future liabilities that are not so subordinated, unsecured indebtedness; (iii) are effectively junior to all of the Company's existing and future secured indebtedness and other secured obligations, to the extent of the value of the assets securing that indebtedness and other secured obligations; and (iv) are structurally subordinated to all indebtedness and other liabilities of the Company’s subsidiaries.

Issuance costs are amortized to interest expense over the term of the Notes. The following table summarizes the original issuance costs at the time of issuance for each set of Notes:

(In thousands)	
January 2025 Notes	$ 10,284
June 2025 Notes	7,362
2027 Notes	14,285
2028 Notes	24,453

The Notes do not contain any financial or operating covenants or any restrictions on the payment of dividends, the issuance of other indebtedness or the issuance or repurchase of securities by the Company.

Interest expense includes the following:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Debt issuance costs amortization	$ 5,727	$ 5,303	$ 2,891
Debt discount amortization	147	131	(131)
Loss on settlement of convertible notes	—	50,819	187,698
Coupon interest expense	10,266	9,631	6,611
Total interest expense on convertible notes	16,140	65,884	197,069
Other interest expense	2,466	2,057	2,123
Total interest expense	$ 18,606	$ 67,941	$ 199,192

The effective interest rates on the 2025 Notes, 2027 Notes, and 2028 Notes for the year ended December 31, 2021 were 1.18%, 0.68%, and 0.64%, respectively. The effective interest rates on the 2025 Notes, 2027 Notes, and 2028 Notes for the year ended December 31, 2020 were 1.20%, 0.68%, and 0.54%, respectively. The effective interest rates on the 2025 Notes and 2027 Notes for the year ended December 31, 2019 were 1.27% and 0.55%, respectively. The remaining period over which the unamortized debt discount will be recognized as non-cash interest expense is 3.04 years, 5.21 years, and 6.17 years for the 2025 Notes, 2027 Notes and 2028 Notes, respectively.

(11) LICENSE AND COLLABORATION AGREEMENTS

The Company licenses certain technologies that are, or may be, incorporated into its technology under several license agreements, as well as the rights to commercialize certain diagnostic tests through collaboration agreements. Generally, the license agreements require the Company to pay single-digit royalties based on net revenues received using the technologies and may require minimum royalty amounts, milestone payments, or maintenance fees.

Mayo

In June 2009, the Company entered into a license agreement with the Mayo Foundation for Medical Education and Research (“Mayo”). The Company’s license agreement with Mayo was most recently amended and restated in September 2020. Under the license agreement, Mayo granted the Company an exclusive, worldwide license to certain Mayo patents and patent applications, as well as a non-exclusive, worldwide license with regard to certain Mayo know-how. The scope of the license covers any screening, surveillance or diagnostic test or tool for use in connection with any type of cancer, pre-cancer, disease or condition.

The licensed Mayo patents and patent applications contain both method and composition claims that relate to sample processing, analytical testing and data analysis associated with nucleic acid screening for cancers and other diseases. The jurisdictions covered by these patents and patent applications include the U.S., Australia, Canada, the European Union, China, Japan and Korea. Under the license agreement, the Company assumed the obligation and expense of prosecuting and maintaining the licensed Mayo patents and is obligated to make commercially reasonable efforts to bring to market products using the licensed Mayo intellectual property.

Pursuant to the Company’s agreement with Mayo, the Company is required to pay Mayo a single-digit royalty on the Company’s net sales of current and future products using the licensed Mayo intellectual property each year during the term of the Mayo agreement.

In addition to the royalties described above, the Company is required to pay Mayo cash of $0.2 million, $0.8 million and $2.0 million upon each product using the licensed Mayo intellectual property reaching $5.0 million, $20.0 million and $50.0 million in cumulative net sales, respectively.

As part of the most recent amendment, the Company agreed to pay Mayo an additional $6.3 million, payable in five equal annual installments, through 2024. The annual installments are recorded in research and development expenses in the Company's consolidated statements of operations.

The license agreement will remain in effect, unless earlier terminated by the parties in accordance with the agreement, until the last of the licensed patents expires in 2039 (or later, if certain licensed patent applications are issued). However, if the Company is still using the licensed Mayo know-how or certain Mayo-provided biological specimens or their derivatives on such expiration date, the term shall continue until the earlier of the date the Company stops using such know-how and materials and the date that is five years after the last licensed patent expires. The license agreement contains customary termination provisions and permits Mayo to terminate the license agreement if the Company sues Mayo or its affiliates, other than any such suit claiming an uncured material breach by Mayo of the license agreement.

In addition to granting the Company a license to the covered Mayo intellectual property, Mayo provides the Company with product development and research and development assistance pursuant to the license agreement and other collaborative arrangements. In September 2020, Mayo also agreed to make available certain personnel to provide such assistance through January 2025. In connection with this collaboration, the Company incurred charges of $5.0 million, $3.9 million, and $4.8 million for the years ended December 31, 2021, 2020, and 2019, respectively. The charges incurred in connection with this collaboration are recorded in research and development expenses in the Company's consolidated statements of operations.

Biocartis

In September 2017, Genomic Health entered into an exclusive license and development agreement with Biocartis, a molecular diagnostics company based in Belgium, to develop and commercialize an IVD version of the Oncotype DX Breast Recurrence Score test on the Biocartis Idylla platform. Under the terms of the license and development agreement, the Company had an exclusive, worldwide, royalty-bearing license to develop and commercialize an IVD version of the Oncotype DX Breast Recurrence Score test on the Biocartis Idylla platform, and certain options to expand the collaboration.

In October 2020, the Company and Biocartis agreed to terminate all agreements between them with a mutual release. As part of the termination, the Company made a payment of $12.0 million and returned certain equipment to Biocartis. The remaining net book value of the equipment was previously written off when it was determined that the agreement with Biocartis would be terminated. The termination payment and equipment write-off are both recorded in general and administrative expenses on the Company's consolidated statement of operations.

Johns Hopkins University (“JHU”)

Through the acquisition of Thrive, the Company acquired a worldwide exclusive license agreement with JHU for use of several JHU patents and licensed know-how. The license is designed to enable the Company to leverage JHU proprietary data in the development and commercialization of a blood-based, multi-cancer early detection test. The agreement terms include single-digit sales-based royalties and sales-based milestone payments of $10.0 million, $15.0 million, and $20.0 million upon achieving calendar year licensed product revenue using JHU proprietary data of $0.50 billion, $1.00 billion, and $1.50 billion, respectively.

(12) PFIZER PROMOTION AGREEMENT

In August 2018, the Company entered into a Promotion Agreement (the “Original Promotion Agreement”) with Pfizer, Inc. (“Pfizer”), which was amended and restated in October 2020 (the “Restated Promotion Agreement”). The Restated Promotion Agreement extended the relationship between the Company and Pfizer and restructured the manner in which the Company compensated Pfizer for promotion of the Cologuard test through a service fee, and provision of certain other sales and marketing services related to the Cologuard test. The Restated Promotion Agreement included fixed and performance-related fees, some of which retroactively went into effect on April 1, 2020. In November 2021, the Company and Pfizer entered into an amendment to the Restated Promotion Agreement (the “November 2021 Amendment”), which provides that after November 30, 2021, Pfizer will no longer promote the Cologuard test to healthcare providers. The November 2021 Amendment provides that the Company will pay Pfizer a total of $35.9 million in three installments during the second, third, and fourth quarters of 2022. The November 2021 Amendment eliminates the Company's obligation to pay Pfizer royalties or other fees except for certain media fees, advertising fees, and any detail fees owed to Pfizer for promoting the Cologuard test prior to November 30, 2021. The $35.9 million fee incurred as a result of the November 2021 Amendment was recognized in full during the fourth quarter of 2021. All payments to Pfizer are recorded in sales and marketing expenses in the Company's consolidated statements of operations.

Under the Original Promotion Agreement, the service fee was calculated based on incremental gross profits over specified baselines during the term. Under the Restated Promotion Agreement (and prior to giving effect to the November 2021 Amendment), the service fee provided a fee-for-service model that included certain fixed fees and performance-related bonuses. The performance-related bonuses were contingent upon the achievement of certain annual performance criteria with any applicable expense being recognized ratably upon achievement of the payment becoming probable. The Company incurred charges of $81.3 million, $51.2 million, and $68.5 million for the service fee during the years ended December 31, 2021, 2020 and 2019, respectively. The Company incurred charges of $121.0 million, $85.3 million, and $68.9 million for promotion, sales and marketing services performed by Pfizer on behalf of the Company during the years ended December 31, 2021, 2020 and 2019, respectively.

(13) STOCKHOLDERS' EQUITY

Amendment to Certificate of Incorporation

In July 2020, the Company filed a Certificate of Amendment (the “Certificate of Amendment”) to its Sixth Amended and Restated Certificate of Incorporation with the Secretary of State of the State of Delaware to increase the number of authorized shares of the Company’s common stock from 200 million to 400 million shares. The Certificate of Amendment was approved by the Company’s stockholders at the Company’s 2020 annual meeting in July 2020.

PreventionGenetics LLC (“PreventionGenetics”) Acquisition Stock Issuance

In December 2021, the Company completed its acquisition of PreventionGenetics. In connection with the acquisition, which is further described in Note 19, the Company issued 1.1 million shares of the Company's common stock that had a fair value of $84.2 million.

Ashion Acquisition Stock Issuance

In April 2021, the Company completed its acquisition of Ashion. In connection with the acquisition, which is further described in Note 19, the Company issued 0.1 million shares of the Company's common stock that had a fair value of $16.2 million.

Thrive Acquisition Stock Issuance

In January 2021, the Company completed its acquisition of Thrive. In connection with the acquisition, which is further described in Note 19, the Company issued 9.3 million shares of the Company's common stock that had a fair value of $1.19 billion.

Targeted Digital Sequencing (“TARDIS”) License Acquisition Stock Issuance

In January 2021, the Company acquired a worldwide exclusive license to the TARDIS technology from The Translational Genomics Research Institute (“TGen”), which is further described in Note 19. As part of the consideration transferred, the Company issued 0.2 million shares of the Company's common stock that had a fair value of $27.3 million.

Registered Direct Offering

In October 2020, the Company entered into securities purchase agreements with a limited number of institutional investors for the registered direct offering of 8.6 million shares of common stock at a price of $101.00 per share. The Company received, in the aggregate, approximately $861.7 million of net proceeds from the offering, after deducting $7.5 million for the offering expenses and other stock issuance costs paid by the Company.

Paradigm Diagnostics, Inc. ("Paradigm") and Viomics, Inc. ("Viomics") Acquisition Stock Issuance

In March 2020, the Company completed the acquisitions of Paradigm and Viomics. The purchase price for these acquisitions consisted of cash and stock with a fair value of $40.4 million. Of the $40.4 million purchase price, $32.2 million is expected to be settled through the issuance of 0.4 million shares of common stock. Of the $32.2 million that will be settled through the issuance of common stock, $28.8 million was issued as of December 31, 2021, and the remainder was withheld and may become issuable as additional merger consideration subject to the terms and conditions of the acquisition agreements.

Changes in Accumulated Other Comprehensive Income (Loss)

The amount recognized in AOCI for the years ended December 31, 2021, 2020 and 2019 were as follows:

(In thousands)	Cumulative Translation Adjustment	Unrealized Gain (Loss) on Securities	Accumulated Other Comprehensive Income (Loss)
Balance at January 1, 2019	$ (25)	$ (1,397)	$ (1,422)
Other comprehensive income (loss) before reclassifications	—	681	681
Amounts reclassified from accumulated other comprehensive income (loss)	—	641	641
Net current period change in accumulated other comprehensive income (loss) (1)	—	1,322	1,322
Balance at December 31, 2019	$ (25)	$ (75)	$ (100)
Other comprehensive income (loss) before reclassifications	—	771	771
Amounts reclassified from accumulated other comprehensive income (loss)	25	—	25
Net current period change in accumulated other comprehensive income (loss)	25	771	796
Income tax expense related to items of other comprehensive income (loss)	—	(170)	(170)
Balance at December 31, 2020	$ —	$ 526	$ 526
Other comprehensive income (loss) before reclassifications	23	(1,648)	(1,625)
Amounts reclassified from accumulated other comprehensive income (loss)	—	(514)	(514)
Net current period change in accumulated other comprehensive income (loss)	23	(2,162)	(2,139)
Income tax expense related to items of other comprehensive income (loss)	—	170	170
Balance at December 31, 2021	$ 23	$ (1,466)	$ (1,443)

(1) There was no tax impact from the amounts recognized in AOCI for the year ended December 31, 2019.

Amounts reclassified from accumulated other comprehensive income (loss) for the years ended December 31, 2021, 2020 and 2019 were as follows:

Details about AOCI Components (In thousands)	Affected Line Item in the Statements of Operations	Year Ended December 31, 2021	2020	2019
Change in value of available-for-sale investments				
Sales and maturities of available-for-sale investments	Investment income	$ (514)	$ —	$ 641
Foreign currency adjustment	General and administrative	—	25	—
Total reclassifications		$ (514)	$ 25	$ 641

(14) STOCK-BASED COMPENSATION

Stock-Based Compensation Plans

The Company maintains the following plans for which awards were granted from or had shares outstanding in 2021: the 2010 Omnibus Long-Term Incentive Plan (As Amended and Restated Effective July 27, 2017), the 2019 Omnibus Long-Term Incentive Plan, the 2010 Employee Stock Purchase Plan, and the 2016 Inducement Award Plan. These plans are collectively referred to as the "Stock Plans".

The Stock Plans are administered by the Human Capital Committee of the Company's Board of Directors. The 2019 Omnibus Long-Term Incentive Plan provides that upon an acquisition of the Company, all equity will accelerate by a period of one year. In addition, upon the termination of an employee without cause or for good reason prior to the first anniversary of the completion of the acquisition, all equity awards then outstanding under the respective plan held by that employee will immediately vest.

2019 Omnibus Long-Term Incentive Plan. The Company adopted the 2019 Omnibus Long-Term Incentive Plan (the "2019 Stock Plan") on July 25, 2019 to grant share-based awards to employees, officers, directors, consultants and advisors. Awards granted under the 2019 Stock Plan may include incentive stock options, as defined under the Internal Revenue Code, non-qualified options, restricted stock awards and other stock awards in amounts and with terms and conditions determined by the human capital committee of the Company's Board of Directors, subject to the provisions of the 2019 Stock Plan. The 2019 Stock Plan will expire on July 25, 2029 and after such date no further awards may be granted under the plan. Options granted under the 2019 Stock Plan expire ten years from the date of grant. Grants made from the 2019 Stock Plan generally vest over a period of three to four years. At December 31, 2021, options to purchase 395,584 shares were outstanding under the 2019 Stock Plan and 3,573,014 shares of restricted stock and restricted stock units were outstanding. At December 31, 2021, there were 8,491,176 shares available for future grant under the 2019 Stock Plan.

2010 Omnibus Long-Term Incentive Plan. The Company adopted the 2010 Omnibus Long-Term Incentive Plan (the "2010 Stock Plan") on July 16, 2010 to grant share-based awards to employees, officers, directors, consultants and advisors. Awards granted under the 2010 Stock Plan may include incentive stock options, as defined under the Internal Revenue Code, non-qualified options, restricted stock awards and other stock awards in amounts and with terms and conditions determined by the human capital committee of the Company's Board of Directors, subject to the provisions of the 2010 Stock Plan. The 2010 Stock Plan expired on July 16, 2020 and after such date no further awards may be granted under the plan. Options granted under the 2010 Stock Plan expire ten years from the date of grant. Grants made from the 2010 Stock Plan generally vest over a period of three to four years. At December 31, 2021, options to purchase 1,474,505 shares were outstanding under the 2010 Stock Plan and 1,230,807 shares of restricted stock and restricted stock units were outstanding. At December 31, 2021, there were no shares available for future grant under the 2010 Stock Plan.

2016 Inducement Award Plan. The Company adopted the 2016 Inducement Award Plan (the "2016 Inducement Plan") on January 25, 2016 to grant share-based awards to employees who were not previously an employee of the Company or any of its Subsidiaries. Awards granted under the 2016 Inducement Plan may include grant incentive stock options, as defined under the Internal Revenue Code, non-qualified options, restricted stock awards and other stock awards in amounts and with terms and conditions determined by the Human Capital committee of the Company's Board of Directors, subject to the provisions of the 2016 Inducement Plan. The 2016 Inducement Plan expired on July 27, 2017, and after such date no further awards could be granted under the plan. Options granted under the 2016 Inducement Plan expire ten years from the date of grant. Grants made from the 2016 Inducement Plan generally vest over a period of three to four years. At December 31, 2021, there were no shares of restricted stock and restricted stock units outstanding under the 2016 Inducement Award Plan. At December 31, 2021, there were no shares available for future grant under the 2016 Inducement Plan.

2010 Employee Stock Purchase Plan. The 2010 Employee Stock Purchase Plan (the "2010 Purchase Plan") was adopted by the Company on July 16, 2010 to provide participating employees the right to purchase shares of common stock at a discount through a series of offering periods. The 2010 Purchase Plan will expire on October 31, 2030. The Company's stockholders approved amendments to the 2010 Employee Stock Purchase Plan to increase the number of shares available for purchase thereunder by 500,000 shares and 2,000,000 shares on July 24, 2014 and July 28, 2016, respectively. At December 31, 2021, there were 427,246 shares of common stock available for purchase by participating employees under the 2010 Purchase Plan.

Generally, all employees whose customary employment is more than 20 hours per week and more than five months in any calendar year are eligible to participate in the 2010 Purchase Plan. Participating employees authorize an amount, between 1% and 15% of the employee's compensation, to be deducted from the employee's pay during the offering period. On the last day of the offering period, the employee is deemed to have exercised the employee's option to purchase shares of Company common stock, at the option exercise price, to the extent of accumulated payroll deductions. Under the terms of the 2010 Purchase Plan, the option exercise price is an amount equal to 85% of the fair market value, as defined under the 2010 Purchase Plan, and no employee can purchase more than $25,000 of Company common stock under the 2010 Purchase Plan in any calendar year. Rights granted under the 2010 Purchase Plan terminate upon an employee's voluntary withdrawal from the 2010 Purchase Plan at any time or upon termination of employment. At December 31, 2021, there were 2,372,754 cumulative shares issued under the 2010 Purchase Plan.

Stock-Based Compensation Expense

The Company records stock-based compensation expense in connection with the amortization of restricted stock and restricted stock unit awards ("RSUs"), stock purchase rights granted under the Company's employee stock purchase plan and stock options granted to employees, non-employee consultants and non-employee directors. A summary of non-cash stock-based compensation expense by expense category included in the Company's consolidated statements of operations for the years ended December 31, 2021, 2020, and 2019 is as follows:

(In thousands)	Year Ended December 31, 2021	2020	2019
Cost of sales	$ 16,835	$ 12,852	$ 5,799
Research and development	49,723	19,976	17,196
General and administrative	216,952	75,999	64,222
Sales and marketing	55,716	44,079	21,266
Total stock-based compensation	$ 339,226	$ 152,906	$ 108,483

As of December 31, 2021, there was approximately $368.5 million of expected total unrecognized compensation cost related to non-vested share-based compensation arrangements granted under all equity compensation plans. The Company expects to recognize that cost over a weighted average period of 2.40 years.

In connection with the acquisition of Thrive, the Company accelerated the vesting of shares of previously unvested stock options and restricted stock units for employees with qualifying termination events. During the year ended December 31, 2021, the Company accelerated 139,096 shares of previously unvested stock options and 58,171 shares of previously unvested restricted stock awards and restricted stock units and recorded $19.0 million of non-cash stock-based compensation for the accelerated awards. As further discussed in Note 19, the Company also recorded $86.2 million in stock-based compensation related to accelerated vesting of awards held by Thrive employees in connection with the acquisition.

In connection with the combination with Genomic Health, the Company accelerated the vesting of shares of previously unvested stock options and restricted stock units for employees with qualifying termination events. During the year ended December 31, 2020, the Company accelerated 83,593 shares of previously unvested stock options and 93,770 shares of previously unvested restricted stock units and recorded $9.7 million of non-cash stock-based compensation for the accelerated awards. During the year ended December 31, 2019, the Company accelerated 364,281 shares of previously unvested stock options and 70,138 shares of previously unvested restricted stock units and recorded $21.6 million of non-cash stock-based compensation for the accelerated awards. There was an immaterial amount of accelerated unvested stock options and restricted stock during the year ended December 31, 2021.

Stock Options

The Company determines the fair value of each service-based option award on the date of grant using the Black-Scholes option-pricing model, which utilizes several key assumptions which are disclosed in the following table:

	Year Ended December 31		
	2021	2020	2019
Option Plan Shares			
Risk-free interest rates	(1)	1.26% - 1.47%	2.54% - 2.59%
Expected term (in years)	(1)	6.15	6.28
Expected volatility	(1)	65.67% - 65.71%	64.95% - 64.99%
Dividend yield	(1)	0%	0%

(1) The Company did not grant stock options under its 2010 Omnibus Long-Term Incentive Plan or 2019 Omnibus Long-Term Incentive Plan during the period.

A summary of stock option activity under the Stock Plans is as follows:

Options	Shares	Weighted Average Exercise Price (1)	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (2)
(Aggregate intrinsic value in thousands)				
Outstanding, January 1, 2021	2,231,059	$ 39.67	6.0	
Granted	—	—		
Assumed through acquisition	1,393,748	5.51		
Exercised	(1,295,400)	11.17		
Forfeited	(45,131)	56.66		
Outstanding, December 31, 2021	2,284,276	$ 34.65	5.5	$ 107,586
Vested and expected to vest, December 31, 2021	2,284,276	$ 34.65	5.5	$ 107,586
Exercisable, December 31, 2021	1,780,838	$ 25.59	4.8	$ 96,789

(1) The weighted average grant date fair value of options granted during the years ended December 31, 2020 and 2019 was $58.57 and $57.11, respectively.

(2) The total intrinsic value of options exercised during the years ended December 31, 2021, 2020, and 2019 was $155.8 million, $40.6 million, and $52.0 million, respectively, determined as of the date of exercise.

The Company received approximately $14.4 million, $27.1 million, and $8.8 million from stock option exercises during the years ended December 31, 2021, 2020 and 2019, respectively.

Restricted Stock and Restricted Stock Units

The fair value of restricted stock and restricted stock units is determined on the date of grant using the closing stock price on that day.

A summary of restricted stock and restricted stock unit activity is as follows:

	Restricted Shares	Weighted Average Grant Date Fair Value (2)
Outstanding, January 1, 2021	3,968,214	$ 79.38
Granted	2,333,213	129.16
Assumed through acquisition	242,123	127.79
Released (1)	(1,697,643)	73.18
Forfeited	(524,997)	101.20
Outstanding, December 31, 2021	4,320,910	$ 108.84

(1) The fair value of restricted stock units vested and converted to shares of the Company's common stock was $219.4 million, $152.4 million, and $173.8 million for the years ended December 31, 2021, 2020, and 2019, respectively.

(2) The weighted average grant date fair value of the restricted stock units granted during the years ended December 31, 2020 and 2019 was $92.55 and $93.20, respectively.

Performance Share Units

The Company has issued performance-based equity awards to certain employees which vest upon the achievement of certain performance goals, including financial performance targets and operational milestones.

In June 2020 and December 2020, the Company modified certain of the operational milestones and financial performance targets, respectively, within the outstanding performance-based equity awards, which were not deemed to have an impact on vesting and no incremental stock-based compensation expense was recorded for the year ended December 31, 2021. This modification impacted awards held by 36 employees.

A summary of performance share unit activity is as follows:

	Performance Share Units (2)	Weighted Average Grant Date Fair Value
Outstanding, January 1, 2021	618,515	$ 93.22
Granted	270,665	138.09
Released (1)	—	—
Forfeited	(11,066)	83.15
Outstanding, December 31, 2021	878,114	$ 107.18

(1) The fair value of performance share units vested and converted to shares of the Company's common stock was $183.8 million for the year ended December 31, 2019. There were no performance share units vested and converted to shares of the Company's common stock during the years ended December 31, 2021 and 2020.

(2) The performance share units listed above assumes attainment of maximum payout rates as set forth in the performance criteria. Applying actual or expected payout rates, the number of outstanding performance share units as of December 31, 2021 was 45,312.

(3) The weighted average grant date fair value of the performance share units granted during the years ended December 31, 2020 and 2019 was $90.17 and $93.40, respectively.

Employee Stock Purchase Plan ("ESPP")

A summary of ESPP activity is as follows:

	Year Ended December 31,		
(in thousands, except share and per share amounts)	2021	2020	2019
Shares issued under the 2010 Purchase Plan	331,769	301,064	176,458
Cash received under the 2010 Purchase Plan	$ 23,070	$ 18,355	$ 8,396
Weighted average fair value per share of stock purchase rights granted during the period	$ 34.93	$ 32.57	$ 29.21

The 331,769 shares issued during the year ended December 31, 2021 were as follows:

Offering period ended	Number of Shares	Average price per Share
April 30, 2021	173,717	$ 69.31
November 1, 2021	158,052	$ 69.71

The fair value of ESPP shares is based on the assumptions in the following table:

	Year Ended December 31,		
	2021	2020	2019
ESPP Shares			
Risk-free interest rates	0.04% - 0.16%	0.11% - 0.20%	1.60% - 2.40%
Expected term (in years)	0.5 - 2	0.5 - 2	0.4 - 2
Expected volatility	43.00% - 68.51%	61.59% - 89.00%	43.20% - 57.60%
Dividend yield	0%	0%	0%

Shares Reserved for Issuance

The Company has reserved shares of its authorized common stock for issuance pursuant to its employee stock purchase and equity plans, including all outstanding stock option grants noted above at December 31, 2021, as follows:

Shares reserved for issuance	
2019 Stock Plan	8,491,176
2010 Purchase Plan	427,246
	8,918,422

(15) COMMITMENTS AND CONTINGENCIES

Leases

The components of lease expense were as follows:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Finance lease cost			
Amortization of right-of-use assets	$ 5,731	$ 1,935	$ 27
Interest on lease liabilities	1,018	383	2
Operating lease cost	31,730	22,551	9,200
Short-term lease cost	628	356	219
Variable lease cost	5,212	2,703	896
Total lease Cost	$ 44,319	$ 27,928	$ 10,344

Supplemental disclosure of cash flow information related to the Company's cash and non-cash activities with its leases are as follows:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Cash paid for amounts included in the measurement of lease liabilities:			
Operating cash flows from operating leases	$ 27,461	$ 17,531	$ 9,641
Operating cash flows from finance leases	938	381	1
Finance cash flows from finance leases	5,290	1,756	15
Non-cash investing and financing activities:			
Right-of-use assets obtained in exchange for new operating lease liabilities (1)	74,369	13,261	51,030
Right-of-use assets obtained in exchange for new finance lease liabilities	5,460	20,349	237
Weighted-average remaining lease term - operating leases (in years)	8.33	8.75	9.80
Weighted-average remaining lease term - finance leases (in years)	2.95	3.68	1.20
Weighted-average discount rate - operating leases	6.11 %	6.80 %	6.80 %
Weighted-average discount rate - finance leases	5.36 %	5.67 %	5.60 %

(1) For the year ended December 31, 2021, this includes right-of-use assets acquired as part of the business combinations described in Note 19 of $39.6 million. For the year ended December 31, 2019, this includes right-of-use assets obtained from the initial adoption of ASC 842 of $17.9 million.

As of December 31, 2021 and 2020, the Company’s right-of-use assets from operating leases are $174.2 million and $125.9 million, respectively, which are reported in operating lease right-of-use assets in the Company’s consolidated balance sheet. As of December 31, 2021, the Company has outstanding operating lease obligations of $201.9 million, of which $19.7 million is reported in operating lease liabilities, current portion and $182.2 million is reported in operating lease liabilities, less current portion in the Company’s consolidated balance sheet. As of December 31, 2020, the Company had outstanding operating lease obligations of $132.6 million, of which $11.5 million is reported in operating lease liabilities, current portion and $121.1 million is reported in operating lease liabilities, less current portion in the Company’s consolidated balance sheet.

As of December 31, 2021 and 2020, the Company's right-of-use assets from finance leases are $18.2 million and $18.6 million, respectively, which are reported in other long-term assets, net in the Company's consolidated balance sheets. As of December 31, 2021, the Company has outstanding finance lease obligations of $18.7 million, of which $6.2 million is reported in other current liabilities and $12.5 million is reported in other long-term liabilities in the Company's consolidated balance sheets. As of December 31, 2020, the Company had outstanding finance lease obligations of $18.7 million, of which $4.7 million is reported in other current liabilities and $14.0 million is reported in other long-term liabilities in the Company's consolidated balance sheets.

Maturities of operating lease liabilities on an annual basis as of December 31, 2021 were as follows:

(In thousands)	
2022	$ 30,706
2023	31,793
2024	32,209
2025	30,446
2026	29,890
Thereafter	106,967
Total minimum lease payments	262,011
Imputed interest	(60,135)
Total	$ 201,876

Maturities of finance lease liabilities on an annual basis as of December 31, 2021 were as follows (amounts in thousands):

(In thousands)	
2022	$ 7,040
2023	6,930
2024	5,253
2025	911
2026	51
Thereafter	—
Total minimum lease payments	20,185
Imputed interest	(1,449)
Total	$ 18,736

Legal Matters

The Company records reserves and accrues costs for certain legal proceedings and regulatory matters to the extent that it determines an unfavorable outcome is probable and the amount of the loss can be reasonably estimated. While such reserves and accrued costs reflect the Company's best estimate of the probable loss for such matters, the recorded amounts may differ materially from the actual amount of any such losses. In some cases, no estimate of the possible loss or range of loss in excess of amounts accrued, if any, can be made because of the inherently unpredictable nature of legal and regulatory proceedings, which may be exacerbated by various factors, including but not limited to, they may involve indeterminate claims for monetary damages or may involve fines, penalties or punitive damages; present novel legal theories or legal uncertainties; involve disputed facts; represent a shift in regulatory policy; involve a large number of parties, claimants or regulatory bodies; are in the early stages of the proceedings; involve a number of separate proceedings and/or a wide range of potential outcomes; or result in a change of business practices.

As of the date of this Annual Report on Form 10-K, amounts accrued for legal proceedings and regulatory matters were not material except for the amounts accrued related to the Medicare Date of Service Rule Investigation (the "DOS Rule Investigation") discussed below. However, it is possible that in a particular quarter or annual period the Company's financial condition, results of operations, cash flow and/or liquidity could be materially adversely affected by an ultimate unfavorable resolution of, or development in, legal and/or regulatory proceedings, including as described below. Except for the proceedings discussed below, the Company believes that the ultimate outcome of any of the regulatory and legal proceedings that are currently pending against it should not have a material adverse effect on financial condition, results of operations, cash flow or liquidity.

The Company is currently responding to civil investigative demands and administrative subpoenas issued pursuant to the Health Insurance Portability and Accountability Act of 1996 by the United States Department of Justice ("DOJ") concerning Genomic Health's compliance with the Medicare Date of Service billing regulations. The Company has been cooperating with these inquiries and has produced documents in response thereto.

During the second quarter of 2021, as part of ongoing discussions between the DOJ and the Company regarding the DOS Rule Investigation, the DOJ presented an estimate of civil damages in the amount of $48.2 million relating to alleged non-compliance with the Medicare Date of Service billing regulations from 2007 to 2020. The civil damages estimate does not include potential treble damages, civil or criminal penalties or other remedies that the DOJ could seek against the Company. Based on the Company's review and analysis of the DOJ presentation, ongoing discussions held with the DOJ, the civil damages estimate, and range of potential exposure, the Company recorded an accrual of approximately $10 million for the year ended December 31, 2021.

As noted above, litigation outcomes are difficult to predict, and the estimation of probable losses requires an analysis of multiple possible outcomes that often depend on judgments about potential actions by third parties. Accordingly, the recorded accrual of approximately $10 million for the year ended December 31, 2021 is based on several factors, considerations, and judgments, and the ultimate resolution of this matter could result in a loss in excess of the recorded accrual.

On June 24, 2019, Niles Rosen M.D. filed a sealed ex parte qui tam lawsuit against the Company in the United States District Court for the Middle District of Florida, that alleged a violation of the Federal Anti-Kickback Statute and False Claims Act for offering gift cards to patients in exchange for returning the Cologuard screening test (the "Qui Tam Suit"). Dr. Rosen seeks on behalf of the U.S. government and himself an award of civil penalties, treble damages and fees and costs. On February 25, 2020, the Company received a civil investigative demand by the DOJ related to the Company's gift card program. The Company produced documents in response thereto. On March 25, 2021, the DOJ filed a notice of its election to decline intervention in the Qui Tam Suit. This election does not prevent Dr. Rosen from continuing the Qui Tam Suit. On April 12, 2021, Dr. Rosen filed an amended complaint against the Company, alleging violations of the Federal Anti-Kickback Statute and False Claims Act. The Company first learned of the Qui Tam Suit and the DOJ's election to decline intervention in July 2021. The Company intends to vigorously defend itself against Dr. Rosen's claims and seek, among other things, the Company's attorneys' fees and costs incurred in defending this action. Although the Company denies Dr. Rosen's allegations and believes that it has meritorious defenses to his False Claims Act claims, neither the outcome of the litigation nor can a reasonable estimate or an estimated range of loss associated with the litigation be determined at this time.

Adverse outcomes from the DOS Rule Investigation and the Qui Tam Suit could include the Company being required to pay treble damages, incur civil and criminal penalties, paying attorneys' fees, entering into a corporate integrity agreement, being excluded from participation in government healthcare programs, including Medicare and Medicaid, and other adverse actions that could materially affect the Company's business, financial condition, and results of operation.

In connection with the Company's combination with Genomic Health, on June 22, 2020, Suzanne Flannery, a purported former stockholder of Genomic Health, filed a Verified Individual and Class Action Complaint in the Delaware Court of Chancery, captioned Flannery v. Genomic Health, Inc., et al., C.A. No. 2020-0492. Flannery amended her complaint on November 23, 2020. The amended complaint asserted individual and class action claims, including: (i) a violation of 8 Del. C. § 203 by Genomic Health, Exact Sciences and a purported controlling group of former Genomic Health stockholders; (ii) conversion by Genomic Health, Exact Sciences and Spring Acquisition Corp.; (iii) breach of fiduciary duty by Genomic Health's former directors; (iv) breach of fiduciary duty by the purported controlling group; and (v) aiding and abetting breach of fiduciary duty against Exact Sciences, Spring Acquisition and Goldman Sachs & Co. LLC, Genomic Health's financial advisor in the combination. The amended complaint sought, among other things, declaratory relief, unspecified monetary damages and attorneys' fees and costs. All defendants moved to dismiss the amended complaint. Oral argument on defendants' motions to dismiss the amended complaint occurred in May 2021, and in September 2021 the case was officially dismissed by the court.

(16) EMPLOYEE BENEFIT PLAN

The Company maintains a qualified 401(k) retirement savings plan for Exact Sciences employees (the "401(k) Plan"). The Company also maintains additional retirement savings plans that are acquired as a result of business combinations. These plans are maintained for a period of time before being merged into the 401(k) Plan. Under the terms of the 401(k) Plan, participants may elect to defer a portion of their compensation into the 401(k) Plan, subject to certain limitations. Company matching contributions may be made at the discretion of the Board of Directors.

The Company's Board of Directors approved 401(k) Plan matching contributions for the years ended December 31, 2021, 2020 and 2019 in the form of Company common stock equal to 100% up to 6% of the participant's eligible compensation for that year. The Company recorded compensation expense of approximately $30.0 million, $22.8 million, and $12.5 million, respectively, in the statements of operations for the years ended December 31, 2021, 2020 and 2019.

(17) NEW MARKET TAX CREDIT

During the fourth quarter of 2014, the Company received approximately $2.4 million in net proceeds from financing agreements related to working capital and capital improvements at one of its Madison, Wisconsin facilities. This financing arrangement was structured with an unrelated third-party financial institution (the "Investor"), an investment fund, and its majority owned community development entity in connection with the Company's participation in transactions qualified under the federal New Markets Tax Credit ("NMTC") program, pursuant to Section 45D of the Internal Revenue Code of 1986, as amended. Through its participation in this program, the Company has secured low interest financing and the potential for future debt forgiveness related to certain of the Company's Madison, Wisconsin facilities. The Company was required to be in compliance through December 2021 with various regulations and contractual provisions that apply to the NMTC arrangement. Noncompliance with applicable requirements could have resulted in the Investor's projected tax benefits not being realized and, therefore, require the Company to indemnify the Investor for any loss or recapture of NMTC related to the financing until such time as the recapture provisions have expired under the applicable statute of limitations.

The Investor and its majority owned community development entity were considered Variable Interest Entities ("VIEs") and the Company was the primary beneficiary of the VIEs. This conclusion was reached based on the following:

- the ongoing activities of the VIEs—collecting and remitting interest and fees and NMTC compliance—were all considered in the initial design and are not expected to significantly affect performance throughout the life of the VIE;
- contractual arrangements obligate the Company to comply with NMTC rules and regulations and provide various other guarantees to the Investor and community development entity;
- the Investor lacks a material interest in the underlying economics of the project; and
- the Company is obligated to absorb losses of the VIEs.

Because the Company was the primary beneficiary of the VIEs, they were included in the Company's consolidated financial statements as of December 31, 2020. There are no other assets, liabilities or transactions in these VIEs outside of the financing transactions executed as part of the NMTC arrangement. The $2.4 million was recorded in other long-term liabilities on the Company's balance sheet. The benefit of this net $2.4 million contribution was recognized as a decrease in expenses, included in cost of sales, as the Company amortized the contribution liability over the seven-year compliance period as it was being earned through the Company's on-going compliance with the conditions of the NMTC program. The seven-year term ended in December 2021, at which point the Company entered into a loan forgiveness agreement with the Investor, which forgives, cancels, and terminates the debt from the original financing agreements. As of December 31, 2021, there are no outstanding balances related to the NMTC financing agreements.

(18) WISCONSIN ECONOMIC DEVELOPMENT TAX CREDITS

During February 2015, the Company entered into an agreement with the WEDC ("Original WEDC Agreement") to earn $9.0 million in refundable tax credits on the condition that the Company expends $26.3 million in capital investments and establishes and maintains 758 full-time positions over a seven-year period.

During December 2021, the Company amended its agreement with the WEDC ("Amended WEDC Agreement") to earn an additional $18.5 million in refundable tax credits on the condition that the Company expends $350.0 million in capital investments and establishes and maintains 1,300 additional full-time positions over a five-year period. The capital investment credits are earned at a rate of 10% of eligible capital investments up to a maximum of $7.0 million, while the jobs creation credits are earned annually pursuant to the agreement.

The tax credits earned are first applied against the tax liability otherwise due, and if there is no such liability present, the claim for tax credits will be reimbursed in cash to the Company. The maximum amount of the refundable tax credit to be earned for each year is fixed, and the Company earns the credits by meeting certain capital investment and job creation thresholds over the term of the agreement. Should the Company earn and receive the job creation tax credits but not maintain those full-time positions through the end of the agreement, the Company may be required to pay those credits back to the WEDC.

Under the Original WEDC Agreement, the Company recorded the earned tax credits as job creation and capital investments occurred. The tax credits earned from capital investment are being recognized as an offset to depreciation expense over the expected life of the acquired capital assets. The tax credits earned related to job creation were recognized as an offset to operational expenses through December 31, 2020.

As of December 31, 2021, the Company has earned all $9.0 million of the refundable tax credits and has received payment of $7.5 million from the WEDC under the Original WEDC Agreement. The unpaid portion is $1.5 million, which is reported in prepaid expenses and other current assets, reflecting when collection of the refundable tax benefits is expected to occur.

During the years ended December 31, 2020 and 2019, the Company recognized $2.2 million and $2.4 million, respectively, of the tax credits earned as a reduction of operating expenses.

Under the Amended WEDC Agreement, the Company records the earned tax credits as job creation and capital investments occurs. The tax credits earned from capital investment are recognized as a reduction to capital expenditures at the time the costs are incurred, and then as an offset to depreciation expense over the expected life of the acquired capital assets. The tax credits earned related to job creation are recognized as an offset to operational expenses in the period in which the credits are earned. The credits recognized will be required to be repaid if the Company does not maintain minimum cumulative job requirements.

As of December 31, 2021, the Company has earned $8.0 million of the refundable tax credits under the Amended WEDC Agreement. The unpaid portion is $8.0 million as of December 31, 2021, of which $1.7 million is reported in prepaid expenses and other current assets and $6.3 million is reported in other long-term assets, reflecting when collection of the refundable tax credits is expected to occur.

During the year ended December 31, 2021, the Company recorded $7.0 million as a reduction to capital expenditures and $1.0 million as a reduction to operational expenses for the credits earned for capital investments and job creation, respectively.

(19) BUSINESS COMBINATIONS AND ASSET ACQUISITIONS

Business Combinations

PreventionGenetics LLC

On December 31, 2021, the Company completed the acquisition (the "PreventionGenetics Acquisition") of all of the outstanding equity interests of PreventionGenetics, LLC. The PreventionGenetics Acquisition provided the Company a Clinical Laboratory Improvement Amendments ("CLIA") certified and College of American Pathologist ("CAP") accredited sequencing lab based in Marshfield, Wisconsin. PreventionGenetics provides more than 5,000 predefined genetic tests for nearly all clinically relevant genes, additional custom panels, and comprehensive germline, whole exome ("PGxome®"), and whole genome ("PGnome®") sequencing tests. The Company has included the financial results of PreventionGenetics in the consolidated financial statements from the date of the combination.

The combination date fair value of the consideration transferred for PreventionGenetics was approximately $185.5 million, which consisted of the following:

(In thousands)		
Cash	$	101,255
Common stock issued		84,252
Total purchase price	$	185,507

The fair value of the 1,070,410 common shares issued as part of consideration transferred was determined on the basis of the average of the high and low market price of the Company's shares on the acquisition date, which was $78.71.

Of the total $101.3 million of consideration to be settled through the payment of cash, $85.8 million was paid as of December 31, 2021. The remaining $15.5 million represents withheld cash consideration that will be used to cover working capital adjustments or seller claims, if any, that arise following the completion of the acquisition. The withheld cash consideration will be held by the Company until settlement and was recorded in other current liabilities in the consolidated balance sheet.

The following table summarizes the preliminary estimated fair values of the assets acquired and liabilities assumed at the acquisition date.

(In thousands)		
Cash and cash equivalents	$	1,574
Accounts receivable		6,261
Inventory		1,697
Prepaid expenses and other current assets		30
Property, plant and equipment		12,793
Developed technology		65,000
Customer relationships		4,000
Trade name		4,000
Total identifiable assets acquired		95,355
Accounts payable		(1,493)
Accrued liabilities		(992)
Total liabilities assumed		(2,485)
Net identifiable assets acquired		92,870
Goodwill		92,637
Net assets acquired	$	185,507

Developed technology represents purchased technology that had reached technological feasibility and for which PreventionGenetics had substantially completed development as of the date of combination. The developed technology is associated with PreventionGenetics' ability to perform next-generation sequencing and use its developed software solutions and infrastructure to report on the sequencing process. The fair value of the developed technology has been determined using the income approach multi-period excess earnings method, which involves significant unobservable inputs (Level 3 inputs). These inputs include projected sales, margin, obsolescence factor, and discount rate. The developed technology intangible is amortized on a straight-line basis over its estimated useful life of 13 years.

Customer relationships represent agreements and relationships with existing PreventionGenetics customers. The fair value of customer relationships has been determined using the excess earnings distributor model, which involves significant unobservable inputs (Level 3 inputs). These inputs include projected sales, margin, attrition rate, and discount rate. The customer relationship intangible is amortized on a straight-line basis over its estimated useful life of 9 years.

Trade names represent the value associated with the PreventionGenetics trade name in the market. The fair value of trade names has been determined using the relief-from-royalty method, which involves significant unobservable inputs (Level 3 inputs). These inputs include projected sales, royalty rate, and discount rate. The trade name intangible is amortized on a straight-line basis over its estimated useful life of 4 years.

The calculation of the excess of the purchase price over the estimated fair value of the tangible net assets and intangible assets acquired was recorded to goodwill, which is primarily attributed to the acquired workforce's genetic sequencing, informatics, and counseling expertise, as well as expected sales force synergies. The total goodwill related to this combination is deductible for tax purposes.

The total purchase price allocation is preliminary and based upon estimates and assumptions that are subject to change within the measurement period as additional information for the estimates is obtained. The measurement period remains open pending the completion of valuation procedures related to certain acquired assets and liabilities assumed, primarily in connection with the intangible assets.

Pro forma impact and results of operations disclosures have not been included due to immateriality.

During 2021, the Company incurred $2.7 million of acquisition-related costs recorded in general and administrative expenses in the consolidated statement of operations. These costs include fees associated with financial, legal, accounting and other advisors incurred to complete the merger.

Ashion Analytics, LLC

On April 14, 2021, the Company completed the acquisition ("Ashion Acquisition") of all of the outstanding equity interests of Ashion Analytics, LLC from PMed Management, LLC ("PMed"), which is a subsidiary of TGen. The Ashion Acquisition provided the Company a CLIA-certified and CAP-accredited sequencing lab based in Phoenix, Arizona. Ashion developed GEM ExTra®, a comprehensive genomic cancer test, and provides access to whole exome, matched germline, and transcriptome sequencing capabilities. The Company has included the financial results of Ashion in the consolidated financial statements from the date of the combination.

The combination date fair value of the consideration transferred for Ashion was approximately $110.0 million, which consisted of the following:

(In thousands)		
Cash	$	74,775
Common stock issued		16,224
Contingent consideration		19,000
Total purchase price	$	109,999

The fair value of the 125,444 common shares issued as part of consideration transferred was determined on the basis of the average of the high and low market price of the Company's shares on the acquisition date, which was $129.33.

The contingent consideration arrangement requires the Company to pay $20.0 million of additional cash consideration to PMed upon the Company's commercial launch, on or before the tenth anniversary of the Ashion Acquisition, of a test for minimal residual disease ("MRD") detection and/or treatment (the "Commercial Launch Milestone"). The fair value of the Commercial Launch Milestone at the acquisition date was $19.0 million. The contingent consideration arrangement also requires the Company to pay $30.0 million of additional cash upon the Company's achievement, on or before the fifth anniversary of the Ashion Acquisition, of cumulative revenues from MRD products of $500.0 million (the "MRD Product Revenue Milestone"). No value was ascribed to the MRD Product Revenue Milestone based on probability assessments as of the acquisition date. The fair value of the Commercial Launch Milestone and MRD Product Revenue Milestone was estimated using a probability-weighted scenario based discounted cash flow model. This fair value measurement is based on significant inputs not observable in the market and thus represents a Level 3 measurement as defined in ASC 820. The key assumptions are described in Note 7.

The following table summarizes the preliminary estimated fair values of the assets acquired and liabilities assumed at the acquisition date.

(In thousands)	
Cash and cash equivalents	$ 2,474
Accounts receivable	2,349
Inventory	1,811
Prepaid expenses and other current assets	425
Property, plant and equipment	9,947
Operating lease right-of-use assets	548
Developed technology	39,000
Total identifiable assets acquired	56,554
Accounts payable	(1,477)
Accrued liabilities	(1,190)
Operating lease liabilities, current portion	(343)
Other current liabilities	(98)
Operating lease liabilities, less current portion	(205)
Total liabilities assumed	(3,313)
Net identifiable assets acquired	53,241
Goodwill	56,758
Net assets acquired	$ 109,999

The Company recorded $39.0 million of identifiable intangible assets related to the developed technology associated with GEM ExTra. Developed technology represents purchased technology that had reached technological feasibility and for which Ashion had substantially completed development as of the date of combination. The fair value of the developed technology has been determined using the income approach multi-period excess earnings method, which involves significant unobservable inputs (Level 3 inputs). These inputs include projected sales, margin, and required rate of return and tax rate. Cash flows were discounted to their present value as of the closing date. Developed technology is amortized on a straight-line basis over its estimated useful life of 13 years.

The calculation of the excess of the purchase price over the estimated fair value of the tangible net assets and intangible assets acquired was recorded to goodwill, which is primarily attributed to the acquired workforce expertise, the capabilities in the advancement of creating and launching new products, including an MRD product, and expected sales force synergies related to the developed technology. The total goodwill related to this combination is deductible for tax purposes.

The total purchase price allocation is preliminary and based upon estimates and assumptions that are subject to change within the measurement period as additional information for the estimates is obtained. The measurement period remains open pending the completion of valuation procedures related to certain acquired assets and liabilities assumed, primarily in connection with the developed technology intangible asset.

Pro forma impact and results of operations disclosures have not been included due to immateriality.

During the year ended December 31, 2021, the Company incurred $1.6 million of acquisition-related costs recorded in general and administrative expenses in the consolidated statement of operations. These costs include fees associated with financial, legal, accounting and other advisors incurred to complete the merger.

Thrive Earlier Detection Corporation

On January 5, 2021, the Company completed the acquisition (“Thrive Merger”) of all of the outstanding capital stock of Thrive Earlier Detection Corporation. Thrive, headquartered in Cambridge, Massachusetts, is a healthcare company dedicated to incorporating earlier cancer detection into routine medical care. The Company expects that combining Thrive's early-stage multi-cancer early detection test with the Company’s scientific platform, clinical organization, and commercial infrastructure will bring an accurate blood-based, multi-cancer early detection test to patients faster. The Company has included the financial results of Thrive in the consolidated financial statements from the date of the combination.

The combination date fair value of the consideration transferred for Thrive was approximately $2.19 billion, which consisted of the following:

(In thousands)	
Common stock issued	$ 1,175,431
Cash	584,996
Contingent consideration	331,348
Fair value of replaced equity awards	52,245
Previously held equity investment fair value	43,034
Total purchase price	$ 2,187,054

The Company issued 9,323,266 common shares that had a fair value of $1.19 billion based on the average of the high and low market price of the Company's shares on the acquisition date, which was $127.79. Of the total consideration for common stock issued, $1.18 billion was allocated to the purchase consideration and $16.0 million was recorded as compensation within general and administrative expenses in the consolidated statement of operations on the acquisition date due to accelerated vesting of legacy Thrive restricted stock awards (“RSA”) and RSU awards in connection with the acquisition.

The Company paid $590.2 million in cash on the acquisition date. Of the total consideration for cash, $585.0 million was allocated to the purchase consideration and $5.2 million was recorded as compensation within general and administrative expenses on the acquisition date due to accelerated vesting of legacy Thrive RSU and restricted stock awards (“RSA”) that were cash-settled in connection with the acquisition.

The contingent consideration arrangement requires the Company to pay up to $450.0 million of additional cash consideration to Thrive’s former shareholders upon the achievement of two discrete events, U.S. Food and Drug Administration (“FDA”) approval and CMS coverage, for $150.0 million and up to $300.0 million, respectively. The fair value of the contingent consideration arrangement at the acquisition date was $352.0 million. The fair value of the contingent consideration was estimated using a probability-weighted scenario based discounted cash flow model. This fair value measurement is based on significant inputs not observable in the market and thus represents a Level 3 measurement as defined in ASC 820. The key assumptions are described in Note 7. Of the total fair value of the contingent consideration, $331.3 million was allocated to the consideration transferred, $6.4 million was allocated to the Company’s previous ownership interest in Thrive, and $14.3 million was deemed compensatory as participation is dependent on replaced unvested equity awards vesting which requires future service. Compensation expense related to the milestones could be up to $18.2 million undiscounted and will be recognized in the future once probable and payable.

The Company replaced unvested stock options, RSUs, and RSAs and vested stock options with a combination-date fair value of $197.0 million. Of the total consideration for replaced equity awards, $52.2 million was allocated to the consideration transferred and $144.8 million was deemed compensatory as it was attributable to post acquisition vesting. Of the total compensation related to replaced awards, $65.0 million was expensed on the acquisition date due to accelerated vesting of stock options in connection with the acquisition and $79.8 million relates to future services and will be expensed over the remaining service periods of the unvested stock options, RSUs, and RSAs on a straight-line basis. Including expense recognized for accelerated vesting of RSUs and RSAs described above, total expected stock-based compensation expense is $166.0 million, of which $86.2 million was recognized immediately to general and administrative expenses in the consolidated statement of operations due to accelerated vesting.

The fair value of the stock options assumed by the Company was determined using the Black-Scholes option pricing model. The fair value of the RSA and RSUs assumed by the Company was determined based on the average of the high and low market price of the Company's shares on the acquisition date. The share conversion ratio of 0.06216 was applied to convert Thrive's outstanding equity awards for Thrive's common stock into equity awards for shares of the Company's common stock.

The fair value of options assumed were based on the assumptions in the following table:

Option Plan Shares Assumed	
Risk-free interest rates	0.11% - 0.12%
Expected term (in years)	1.26 - 1.57
Expected volatility	65.54% - 71.00%
Dividend yield	0%
Weighted average fair value per share of options assumed	$109.74 - $124.89

The Company previously held a preferred stock investment of $12.5 million in Thrive and recognized a gain of approximately $30.5 million on the transaction within investment income (expense), net on the Company's consolidated statement of operations, which represented the adjustment of the Company's historical investment to the acquisition date fair value. The fair value of the Company's previous ownership in Thrive was determined based on the pro-rata share payout applied to the Company's interest combined with the fair value of the Company's share of the contingent consideration arrangement, as discussed above.

The purchase price was allocated to the underlying assets acquired and liabilities assumed based upon their estimated fair values as follows:

(In thousands)	Preliminary Allocation January 5, 2021	Measurement Period Adjustments	Final Allocation December 31, 2021
Cash and cash equivalents	$ 241,748	$ —	$ 241,748
Prepaid expenses and other current assets	3,939	—	3,939
Property, plant and equipment	29,977	—	29,977
Operating lease right-of-use assets	39,027	—	39,027
Other long-term assets	67	—	67
In-process research and development (IPR&D)	1,250,000	—	1,250,000
Total identifiable assets acquired	1,564,758	—	1,564,758
Accounts payable	(3,222)	—	(3,222)
Accrued liabilities	(6,218)	(1,862)	(8,080)
Operating lease liabilities, current portion	(2,980)	—	(2,980)
Operating lease liabilities, less current portion	(38,622)	—	(38,622)
Deferred tax liability	(272,905)	—	(272,905)
Total liabilities assumed	(323,947)	(1,862)	(325,809)
Net identifiable assets acquired	1,240,811	(1,862)	1,238,949
Goodwill	946,243	1,862	948,105
Net assets acquired	$ 2,187,054	$ —	$ 2,187,054

IPR&D represents the fair value assigned to research and development assets that have not reached technological feasibility. The primary basis for determining technological feasibility of these projects is obtaining regulatory approval to market the underlying product and expected commercial release. The amounts capitalized are accounted for as indefinite-lived intangible assets, subject to impairment testing, until completion or abandonment of the research and development efforts associated with the projects. The Company recorded $1.25 billion of IPR&D related to a project associated with the development of an FDA approved blood-based, multi-cancer early detection test. The IPR&D asset was valued using the multiple-period excess earnings method approach, which involves significant unobservable inputs (Level 3 inputs). These inputs include inputs such as projected revenues, gross margin, required rate of return, tax rate, probability of commercial success, and obsolescence factor.

The calculation of the excess of the purchase price over the estimated fair value of the tangible net assets and intangible assets acquired was recorded to goodwill, which is primarily attributed to the research and development workforce expertise, next generation sequencing capabilities, and expected synergies. The total goodwill related to this combination is not deductible for tax purposes.

The net loss before tax of Thrive included in the Company's consolidated statement of operations from the combination date of January 5, 2021 to December 31, 2021 was $255.0 million.

The following unaudited pro forma financial information summarizes the combined results of operations for the Company and Thrive, as though the companies were combined as of the beginning of January 1, 2020.

	Year Ended December 31,	
(In thousands)	2021	2020
Total revenues	$ 1,767,087	$ 1,491,391
Net loss before tax	$ (761,337)	$ (1,014,352)

The unaudited pro forma financial information for all periods presented above has been calculated after adjusting the results of Thrive to reflect the business combination accounting effects resulting from this combination. The Company incurred $86.2 million of stock-based compensation expense related to accelerated vesting in connection with the acquisition, $13.5 million of stock-based compensation expense related to accelerated vesting for employees with qualifying termination events, and $10.3 million of transaction costs incurred to execute the acquisition during the first quarter of 2021. These expenses are included in general and administrative expenses on the consolidated statement of operations for the year ended December 31, 2021 and are reflected in pro forma earnings for the year ended December 31, 2020 in the table above. The Company recorded a realized gain of $30.5 million during the first quarter of 2021 in investment income (expense), net on the Company's consolidated statement of operations relating to the Company's pre-acquisition investment in Thrive. This gain has been reduced to $7.6 million due to the Company's smaller ownership interest in Thrive on January 1, 2020, and is reflected in pro forma earnings for the year ended December 31, 2020 in the table above. The Company recorded a remeasurement of contingent consideration of $7.2 million related to Thrive in general and administrative expenses in the consolidated statement of operations for the year ended December 31, 2021. This expense is reflected in the year ended December 31, 2020 in the table above. The historical consolidated financial statements have been adjusted in the unaudited pro forma combined financial information to give effect to pro forma events that are directly attributable to the business combination and factually supportable. The unaudited pro forma financial information is for informational purposes only and is not indicative of the results of operations that would have been achieved if the combination had taken place as of January 1, 2020.

During the year ended December 31, 2021, the Company incurred $10.3 million of acquisition-related costs recorded in general and administrative expenses in the consolidated statement of operations. These costs include fees associated with financial, legal, accounting and other advisors incurred to complete the merger.

In connection with acquisition-related severances, the Company recorded $19.0 million of expense related to vesting of previously unvested equity awards and $3.9 million of additional benefit charges for the year ended December 31, 2021.

Paradigm Diagnostics, Inc. and Viomics, Inc.

On March 3, 2020, the Company acquired all of the outstanding capital stock of Paradigm Diagnostics, Inc. and Viomics, Inc., two related party companies of one another headquartered in Phoenix, Arizona, in transactions that are deemed to be a single business combination in accordance with ASC 805, Business Combinations, ("the Paradigm Acquisition"). Paradigm provides comprehensive genomic-based profiling tests that assist in the diagnosis and therapy recommendations for late-stage cancer. Viomics provides a platform for identification of biomarkers.

The Company entered into this acquisition to enhance its product portfolio in cancer diagnostics and to enhance its capabilities for biomarker identification.

The acquisition date fair value of the consideration to be transferred for Paradigm and Viomics was $40.4 million, which consists of $32.2 million payable in shares of the Company's common stock and $8.2 million which was settled through a cash payment. Of the $32.2 million to be settled through the issuance of common stock, $28.8 million was issued as of December 31, 2021 and December 31, 2020, and the remaining $3.4 million, which was withheld and may become payable as additional merger consideration, is included in other current liabilities in the consolidated balance sheet as of December 31, 2021. The purchase price was allocated to the underlying assets acquired and liabilities assumed based upon their estimated fair values as follows:

(In thousands)	Preliminary Allocation March 3, 2020	Measurement Period Adjustments	Final Allocation March 3, 2021
Net operating assets	$ 6,133	$ (760)	$ 5,373
Goodwill	29,695	736	30,431
Developed technology	7,800	—	7,800
Net operating liabilities	(3,123)	(80)	(3,203)
Total purchase price	$ 40,505	$ (104)	$ 40,401

The fair value of identifiable intangible assets has been determined using the income approach, which involves significant unobservable inputs (Level 3 inputs). These inputs include projected sales, margin, weighted average cost of capital and tax rate.

Developed technology represents purchased technology that had reached technological feasibility and for which development had been completed as of the acquisition date. Fair value was determined using future discounted cash flows related to the projected income stream of the developed technology for a discrete projection period. Cash flows were discounted to their present value as of the closing date. Developed technology is amortized on a straight-line basis over its estimated useful life of 15 years.

The calculation of the excess of the purchase price over the estimated fair value of the tangible net assets and intangible assets acquired was recorded to goodwill, which is primarily attributed to the assembled workforce and expected synergies. The total goodwill related to this acquisition is not deductible for tax purposes.

The Company agreed to issue to the previous investors in Viomics equity interests with an acquisition-date fair value of up to $8.4 million in Viomics, vesting over 4 years based on certain retention arrangements. Payment is contingent upon continued employment with the Company over the four year vesting period and is recognized as stock-based compensation expense in general and administrative expense in the consolidated statement of operations.

Genomic Health, Inc.

On November 8, 2019, the Company acquired all of the outstanding capital stock of Genomic Health, Inc. Genomic Health, headquartered in Redwood City, California, provides genomic-based diagnostic tests that address both the overtreatment and optimal treatment of early and late stage cancer. The Company entered into this combination to create a leading global cancer diagnostics company and provide a robust platform for continued growth. The Company has included the financial results of Genomic Health in the consolidated financial statements from the date of the combination.

The combination date fair value of the consideration transferred for Genomic Health was approximately $2.47 billion, which consisted of the following:

(In thousands)	
Cash	$ 1,061,489
Common stock issued	1,389,266
Fair value of replacement stock options and restricted stock awards	17,813
Total purchase price	$ 2,468,568

The fair value of the common stock issued as part of consideration was determined on the basis of the closing market price of the Company's shares at the acquisition date. The fair value of the stock options assumed by the Company was determined using the Black-Scholes option pricing model. The share conversion ratio of 0.76534 was applied to convert Genomic Health's outstanding equity awards for Genomic Health's common stock into equity awards for shares of the Company's common stock.

The fair value of options assumed were based on the assumptions in the following table:

Option Plan Shares Assumed	
Risk-free interest rates	0.88% - 2.90%
Expected term (in years)	3.28 - 6.73
Expected volatility	63.54% - 69.09%
Dividend yield	0%
Weighted average fair value per share of options assumed	$45.75 - $57.44

During 2019, the Company incurred $22.5 million of acquisition-related costs recorded in general and administrative expense. These costs include fees associated with financial, legal, accounting and other advisors incurred to complete the combination.

In connection with the combination, the Company decided to terminate certain Genomic Health executives in the fourth quarter of 2019 and recorded $32.1 million in severance benefits charges.

The amounts of revenue and net loss before tax of Genomic Health included in the Company's consolidated statement of operations from the combination date of November 8, 2019 to December 31, 2019.

(In thousands)	2019
Total revenues	$ 66,174
Net loss before tax	$ (40,446)

The following unaudited pro forma financial information summarized the combined results of operations for the Company and Genomic Health, as though the companies were combined as of January 1, 2018.

(In thousands)	2019
Total revenues	$ 1,266,591
Net loss before tax	$ (389,795)

The unaudited pro forma financial information for the period presented above has been calculated after adjusting the results of Genomic Health to reflect the business combination accounting effects resulting from this combination, including the amortization expense from acquired intangible assets and the stock-based compensation expense for unvested stock options and restricted stock awards assumed as though the combination occurred as of January 1, 2018. The historical consolidated financial statements have been adjusted in the unaudited pro forma combined financial information to give effect to pro forma events that are directly attributable to the business combination and factually supportable. The unaudited pro forma financial information is for informational purposes only and is not indicative of the results of operations that would have been achieved if the combination had taken place as of January 1, 2018.

As described in Note 15, the Company identified a pre-acquisition contingency relating to the DOJ investigation. The Company assigned a fair value estimate of zero to this pre-acquisition contingency. Subsequent to the Company's final determination of the pre-acquisition contingency's estimated value, changes to this estimate could have a material impact on the Company's results of operations and financial position. As of December 31, 2021, the Company has accrued approximately $10 million related to this investigation.

Asset Acquisitions

PFS Genomics Inc.

On May 3, 2021, the Company acquired 90% of the outstanding capital stock of PFS Genomics Inc. ("PFS"). On June 23, 2021, the Company completed the acquisition of the remaining 10% interest in PFS. The Company paid cash of $33.6 million for 100% of the outstanding capital stock in PFS. PFS is a healthcare company focused on personalizing treatment for breast cancer patients to improve outcomes and reduce unnecessary treatment. The Company expects this acquisition to expand its ability to help guide early-stage breast cancer treatment through individualized radiotherapy treatment decisions.

The transaction was treated as an asset acquisition under GAAP because substantially all of the fair value of the gross assets acquired were deemed to be associated with the acquired technology.

The assets acquired and liabilities assumed were substantially comprised of the IPR&D asset as shown in the table below. The IPR&D asset acquired was recorded to research and development expense in the consolidated statement of operations immediately after acquisition as the asset was deemed to be incomplete and had no alternative future use at the time of acquisition.

The Company accounted for the acquisition in accordance with the accounting standards codification guidance for business combinations, whereby the total purchase price was allocated to the acquired net tangible and intangible assets based on their estimated fair values as of the closing date.

Acquisition related costs were not material in this asset acquisition.

The following table summarizes the allocation of the purchase price to the fair values assigned to the assets acquired and liabilities assumed:

(In thousands)	
Consideration	
Cash paid for acquisition of PFS Genomics outstanding shares	$ 33,569
Assets acquired and liabilities assumed	
Cash	496
IPR&D asset	33,074
Other assets and liabilities	(1)
Net assets acquired	$ 33,569

TARDIS License Agreement

On January 11, 2021, the Company entered into a worldwide exclusive license to the proprietary TARDIS technology from TGen, an affiliate of City of Hope. Under the agreement, the Company acquired a royalty-free, worldwide exclusive license to proprietary TARDIS patents and know-how. The Company intends to develop and commercialize the TARDIS technology as a minimal residual disease test. The Company accounted for this transaction as an asset acquisition. In connection with the asset acquisition, the Company paid upfront fair value consideration of $52.3 million comprised of $25.0 million in cash and issuance of 0.2 million shares of common stock valued at $27.3 million based on the average of the high and low market price of the Company's shares on the acquisition date. In addition, the Company is obligated to make milestone payments to TGen of $10.0 million and $35.0 million upon achieving cumulative product revenue related to MRD detection and/or treatment totaling $100.0 million and $250.0 million, respectively. These payments are contingent upon achievement of these cumulative revenues on or before December 31, 2030. The upfront consideration was recorded to research and development expense in the consolidated statement of operations immediately after acquisition as the asset was deemed to be incomplete and had no alternative future use at the time of acquisition. The Company will record the sales milestones once achievement is deemed probable. No acquisition related costs were incurred in this asset acquisition during the year ended December 31, 2021.

Base Genomics, Limited

On October 26, 2020, The Company acquired all of the outstanding capital stock of Base Genomics, Limited ("Base Genomics") in a cash transaction totaling $416.5 million. Base Genomics, headquartered in Oxford, England, exclusively licenses from Ludwig a non-bisulfite technology for the detection of methylated DNA and other epigenetic modifications. This technology ("TAPS") simultaneously generates both genetic and epigenetic information at base resolution. TAPS overcomes the issues of the current gold standard for DNA methylation detection of bisulfite sequencing. The Company has included the financial results of Base Genomics in the consolidated statements from the date of the acquisition and not disclosed separately due to immateriality. Pro forma disclosures have not been included due to immateriality.

While the acquisition was treated legally as a merger of the two entities, for accounting purposes, the transaction was treated as an asset acquisition under GAAP because substantially all of the fair value of the gross assets acquired were deemed to be associated with the TAPS technology.

The assets and liabilities acquired in the merger were recorded at fair value as determined as of October 26, 2020, and were substantially comprised of the TAPS IPR&D asset as shown in the table below. The Company incurred approximately $4.6 million of direct transaction costs during 2020 associated with this acquisition. These acquisition-related transaction costs were capitalized to the acquired tangible and intangible assets based on their estimated fair values as of the closing date. The IPR&D asset acquired was recorded to research and development expense in the consolidated statement of operations immediately after acquisition as the asset was deemed to be incomplete and had no alternative future use at the time of acquisition.

The Company accounted for the merger in accordance with the accounting standards codification guidance for business combinations, whereby the total purchase price was allocated to the acquired net tangible and intangible assets based on their estimated fair values as of the closing date.

The following table summarizes the total consideration for the acquisition and the value of assets acquired and liabilities assumed as of October 26, 2020, the Merger closing date. These values are based on internal Company and independent external third-party valuations:

(In thousands)	
Consideration	
Cash paid for acquisition of Base Genomics outstanding shares	$ 416,525
Transaction costs	4,600
Total consideration	421,125
Assets acquired and liabilities assumed	
Cash	9,704
IPR&D asset	412,568
Other assets and liabilities	(1,147)
Net assets acquired	$ 421,125

(20) SEGMENT INFORMATION

Management determined that the Company functions as a single operating segment, and thus reports as a single reportable segment. This operating segment is focused on the development and global commercialization of clinical laboratory services allowing healthcare providers and patients to make individualized treatment decisions. Management assessed the discrete financial information routinely reviewed by the Company's Chief Operating Decision Maker, its President and Chief Executive Officer, to monitor the Company's operating performance and support decisions regarding allocation of resources to its operations. Performance is continuously monitored at the consolidated level to timely identify deviations from expected results.

The following table summarizes total revenue from customers by geographic region. Product revenues are attributed to countries based on ship-to location.

	Year Ended December 31,		
(In thousands)	2021	2020	2019
United States	$ 1,657,174	$ 1,413,907	$ 864,849
Outside of United States	109,913	77,484	11,444
Total revenues	$ 1,767,087	$ 1,491,391	$ 876,293

Long-lived assets located in countries outside of the United States are not significant.

(21) INCOME TAXES

Under financial accounting standards, deferred tax assets or liabilities are computed based on the differences between the financial statement and income tax bases of assets and liabilities using the enacted tax rates. Deferred income tax expense or benefit represents the change in the deferred tax assets or liabilities from period to period. At December 31, 2021, the Company had federal net operating loss, state net operating loss, and foreign net operating loss carryforwards of approximately $2.15 billion, $1.04 billion, and $15.9 million, respectively for financial reporting purposes, which may be used to offset future taxable income. The Tax Cuts and Jobs Act (H.R. 1) of 2017 limits the deduction for net operating losses to 80% of current year taxable income and provides for an indefinite carryover period for federal net operating losses. Both provisions are applicable for losses arising in tax years beginning after December 31, 2017. As of December 31, 2021 the Company has $1.32 billion of federal net operating loss carryovers incurred after December 31, 2017 with an unlimited carryover period and $835.6 million of federal net operating loss carryovers expiring at various dates through 2041. State and foreign net operating loss carryovers expire at various dates through 2041. All net operating loss carryforwards are subject to review and possible adjustment by federal, state and foreign taxing jurisdictions. The Company also had federal and state research tax credit carryforwards of $63.0 million and $39.8 million, respectively which may be used to offset future income tax liability. The federal credit carryforwards expire at various dates through 2041 and are subject to review and possible adjustment by the Internal Revenue Service. The state credit carryforwards expire at various dates through 2036 with the exception of $23.5 million of California

research and development tax credits that have an indefinite carryforward period. All state tax credits are subject to review and possible adjustment by local tax jurisdictions. In the event of a change of ownership, the federal and state net operating loss and research and development tax credit carryforwards may be subject to annual limitations provided by the Internal Revenue Code and similar state provisions.

Income (loss) before provision for taxes consisted of the following:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Income (loss) before income taxes:			
Domestic	$ (801,536)	$ (423,025)	$ (405,425)
Foreign	(40,970)	(406,038)	(1,019)
Total income (loss) before income taxes	$ (842,506)	$ (829,063)	$ (406,444)

The expense (benefit) for income taxes consists of:

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Current expense (benefit):			
Federal	$ —	$ (3)	$ —
State	1,388	802	314
Foreign	4,898	933	(63)
Deferred tax expense (benefit):			
Federal	(222,693)	(3,050)	(173,521)
State	(30,528)	(4,260)	(20,099)
Foreign	54	120	15
Total income tax expense (benefit)	$ (246,881)	$ (5,458)	$ (193,354)

The Company recorded an income tax benefit for the year ended December 31, 2021 of $246.9 million primarily as a result of the change in the deferred tax asset valuation allowance resulting from the Thrive Merger.

The components of the net deferred tax asset with the approximate income tax effect of each type of carryforward, credit and temporary differences are as follows:

	December 31,	
(In thousands)	2021	2020
Deferred tax assets:		
Operating loss carryforwards	$ 516,344	$ 369,642
Tax credit carryforwards	72,959	64,760
Compensation related differences	74,127	48,349
Lease liabilities	48,201	31,938
Capitalized research and development	23,035	—
Other temporary differences	20,087	6,136
Tax assets before valuation allowance	754,753	520,825
Less - Valuation allowance	(262,238)	(293,397)
Total deferred tax assets	492,515	227,428
Deferred tax liabilities		
Amortization	$ (464,748)	$ (197,847)
Property, plant and equipment	(4,756)	(4,580)
Lease assets	(45,781)	(30,312)
Other temporary differences	(6,012)	(3,995)
Total deferred tax liabilities	(521,297)	(236,734)
Net deferred tax liabilities	$ (28,782)	$ (9,306)

A valuation allowance to reduce the deferred tax assets is reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. The Company has incurred significant losses since its inception and due to the uncertainty of the amount and timing of future taxable income and the realization of deferred tax liabilities, management has determined that a valuation allowance of $262.2 million and $293.4 million at December 31, 2021 and 2020, respectively, is necessary to reduce the tax assets to the amount that is more likely than not to be realized. Given the future limitations on and expiration of certain federal and state deferred tax assets, the recording of a valuation allowance resulted in a deferred tax liability of approximately $28.8 million remaining at the end of 2021, which is included in other long-term liabilities on the Company's consolidated balance sheet. The overall change in valuation allowance for December 31, 2021 and 2020 was a decrease of $31.2 million and an increase of $98.0 million, respectively.

Activity associated with the Company's valuation allowance is as follows:

	December 31,		
(In thousands)	2021	2020	2019
Balance as of January 1,	$ (293,397)	$ (195,401)	$ (265,587)
Valuation allowances established	(206,574)	(94,589)	(113,522)
Changes to existing valuation allowances	(1,500)	2,151	(22)
Acquisition and purchase accounting	239,233	(5,558)	183,730
Balance as of December 31,	$ (262,238)	$ (293,397)	$ (195,401)

During the year ended December 31, 2021, the Company recorded an increase to the valuation allowance of $206.6 million primarily related to losses from continuing operations. Offsetting the increase, the Company recorded a decrease to the valuation allowance of $239.2 million related to the Thrive Merger offset against goodwill.

During the year ended December 31, 2020, the Company recorded an increase to the valuation allowance of $94.6 million primarily related to losses from continuing operations. Additionally, the Company recorded an increase to the valuation allowance of $5.6 million related to the Genomic Health combination offset against goodwill.

During the year ended December 31, 2019, the Company recorded an increase to the valuation allowance of $113.5 million primarily related to losses from continuing operations. Additionally, the Company recorded a decrease to the valuation allowance of $183.7 million related to the Genomic Health combination offset against goodwill.

The effective tax rate differs from the statutory tax rate due to the following:

	December 31,		
	2021	2020	2019
U.S. Federal statutory rate	21.0 %	21.0 %	21.0 %
State taxes	3.6	1.7	3.4
Federal and state tax rate changes	(0.3)	—	0.1
Foreign tax rate differential	(0.6)	(1.0)	0.4
Acquired IPR&D asset expense	(0.8)	(9.4)	—
Research and development tax credits	0.7	1.6	0.7
Stock-based compensation expense	1.1	1.1	14.6
Non-deductible executive compensation	(0.2)	(0.8)	(2.7)
Transaction costs	(0.1)	(0.1)	(0.5)
Loss on extinguishment - convertible notes	—	—	(9.2)
Other adjustments	1.2	(2.2)	(0.5)
Valuation allowance	3.7	(11.3)	20.2
Effective tax rate	29.3 %	0.6 %	47.5 %

For the year ended December 31, 2021, the Company recognized an income tax benefit, representing an effective tax rate of 29.3%. The difference between the expected statutory federal tax rate of 21.0% and the effective tax rate of 29.3% for the year ended December 31, 2021, was primarily attributable to an income tax benefit of $239.2 million recorded as a result of a change in the deferred tax asset valuation allowance resulting from the Thrive Merger.

For the year ended December 31, 2020, the Company recognized an income tax benefit, representing an effective tax rate of 0.6%. The difference between the expected statutory federal tax rate of 21.0% and the effective tax rate of 0.6% for the year ended December 31, 2020, was primarily attributable to the valuation allowance established against the Company's current period losses generated and the non-deductible IPR&D expense related to the Base Genomics acquisition.

For the year ended December 31, 2019, the Company recognized an income tax benefit, representing an effective tax rate of 47.5%. The difference between the expected statutory federal tax rate of 21.0% and the effective tax rate of 47.5% for the year ended December 31, 2019, was primarily attributable to an income tax benefit of $193.6 million recorded as a result of a change in the deferred tax asset valuation allowance resulting from the Genomic Health combination, as well as excess tax benefits on vested stock-based compensation awards.

The Company had unrecognized tax benefits related to federal and state research and development tax credits of $21.8 million, $16.6 million, and $10.3 million as of December 31, 2021, 2020, and 2019, respectively. These amounts have been recorded as a reduction to the Company's deferred tax asset, if recognized they would not have an impact on the effective tax rate due to the existing valuation allowance. Certain of the Company's unrecognized tax benefits could change due to activities of various tax authorities, including possible settlement of audits, or through normal expiration of various statutes of limitations. The Company does not expect a material change in unrecognized tax benefits in the next twelve months.

The following is a tabular reconciliation of the amounts of unrecognized tax benefits:

	December 31,		
(In thousands)	2021	2020	2019
January 1,	$ 16,629	$ 10,276	$ 1,926
Increase due to current year tax positions	5,363	3,600	2,142
Increase due to prior year tax positions	—	2,753	6,208
Decrease due to prior year tax positions	(212)	—	—
Settlements	—	—	—
December 31,	$ 21,780	$ 16,629	$ 10,276

As of December 31, 2021, due to the carryforward of unutilized net operating losses and research and development credits, the Company is subject to U.S. federal income tax examinations for the tax years 2002 through 2021, and to state income tax examinations for the tax years 2002 through 2021. There were no interest or penalties related to income taxes that have been accrued or recognized as of and for the years ended December 31, 2021, 2020 and 2019.

(22) QUARTERLY RESULTS OF OPERATIONS (UNAUDITED)

The following table sets forth unaudited quarterly statements of operations data for each of the eight quarters ended December 31, 2021 and 2020. In the opinion of management, this information has been prepared on the same basis as the audited consolidated financial statements and contains all adjustments, consisting only of normal recurring adjustments, considered necessary for a fair statement of the unaudited quarterly results for the periods presented. The quarterly data should be read in conjunction with the Company's audited consolidated financial statements and the notes to the consolidated financial statements appearing elsewhere in this Form 10-K.

	Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
	(Amounts in thousands, except per share data)			
2021				
Revenue	$ 402,077	$ 434,819	$ 456,379	$ 473,812
Cost of sales (exclusive of amortization of acquired intangible assets)	109,993	113,968	115,738	119,058
Amortization of acquired intangible assets (1)	20,555	21,188	21,214	21,216
Gross profit	271,529	299,663	319,427	333,538
Operating expenses, net (2)	572,070	471,327	481,450	554,988
Interest income and interest expense	26,572	(1,223)	(8,773)	(3,404)
Income tax benefit (expense)	242,805	(4,025)	3,858	4,243
Net loss	$ (31,164)	$ (176,912)	$ (166,938)	$ (220,611)
Net loss per share—basic and diluted	$ (0.18)	$ (1.03)	$ (0.97)	$ (1.28)
Weighted average common shares outstanding—basic and diluted	169,434	171,494	171,978	172,446
2020				
Revenue	$ 347,821	$ 268,868	$ 408,363	$ 466,339
Cost of sales (exclusive of amortization of acquired intangible assets)	81,606	77,892	95,061	99,765
Amortization of acquired intangible assets (1)	20,464	20,555	20,555	20,553
Gross profit	245,751	170,421	292,747	346,021
Operating expenses (2)	328,124	237,430	496,082	761,000
Interest income and interest expense (3)	(54,507)	(1,388)	(1,955)	(3,517)
Income tax benefit (3)	2,237	305	2,752	164
Net loss	$ (134,643)	$ (68,092)	$ (202,538)	$ (418,332)
Net loss per share—basic and diluted	$ (0.91)	$ (0.45)	$ (1.35)	$ (2.67)
Weighted average common shares outstanding—basic and diluted	148,151	149,727	150,155	156,470

(1) Includes only amortization of acquired intangible assets identified as developed technology assets through purchase accounting transactions, which otherwise would have been allocated to cost of sales.

(2) Consists of research and development, sales and marketing, general and administrative, and amortization of acquired intangible assets excluding acquired developed technology, which is included in the gross profit calculation above. This also includes intangible asset impairment charges and funding received as part of the CARES Act in the second quarter of 2020. Refer to Note 6 for further discussion on the intangible asset impairment charges recorded in the third quarters of 2020 and 2021. Refer to Note 1 for further discussion on the funding received as part of the CARES Act in the second quarter of 2020.

(3) As a result of the adoption of ASU 2020-06, *Debt - Debt with Conversion and Other Options (subtopic 470-20) and Derivatives and Hedging - Contracts in Entity's Own Equity (Subtopic 815-40)*, using the full retrospective method of adoption, the balances for interest expense and income tax benefit have been restated. Refer to Note 1 for further discussion on the adoption of this ASU.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

There have been no disagreements with accountants on accounting or financial disclosure matters.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures.

As required by Rule 13a-15(b) under the Securities Exchange Act of 1934 (the "Exchange Act"), our management, including our principal executive officer and principal financial officer, conducted an evaluation as of the end of the period covered by this report, of the effectiveness of our disclosure controls and procedures as defined in Rule 13a-15(e) under the Exchange Act. Based on that evaluation, our principal executive officer and principal financial officer have concluded that our disclosure controls and procedures were effective as of December 31, 2021 to provide reasonable assurance that information required to be disclosed by us in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported, within the time periods specified in Securities and Exchange Commission rules and forms and that material information relating to the Company is accumulated and communicated to management, including our principal executive officer and our principal financial officer, as appropriate to allow timely decisions regarding required disclosures.

Changes in Internal Control over Financial Reporting.

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) under the Exchange Act during the quarter ended December 31, 2021, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting.

Management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) under the Exchange Act. The Company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

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

We conducted an evaluation, under the supervision and with the participation of our management, of the effectiveness of our internal control over financial reporting as of December 31, 2021. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control—Integrated Framework (2013).* Based on our assessment, management, including our principal executive officer and principal financial officer, concluded that, as of December 31, 2021, our internal control over financial reporting was effective based on those criteria.

The effectiveness of the Company's internal control over financial reporting as of December 31, 2021 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears herein.

Item 9B. Other Information

On February 22, 2022, Kevin Conroy, Chief Executive Officer, and Jeffrey Elliott, Chief Financial Officer and Chief Operating Officer, agreed to accept performance vesting stock units ("PSUs") in lieu of one-half of their bonus opportunity for 2022. The amount of the PSUs that ultimately vest will be equal to the percentage of the bonus opportunity that is paid to bonus plan participants based on the achievement of corporate goals established for such plan.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required under this item is incorporated by reference to the following sections of our proxy statement for our 2022 Annual Meeting of Stockholders: "Information Concerning Directors and Nominees for Director," "Information Concerning Executive Officers," "Section 16(a) Beneficial Ownership Reporting Compliance," "Corporate Governance Principles and Board Matters," and "The Board of Directors and Its Committees."

Item 11. Executive Compensation

The information required under this item is incorporated by reference to the following sections of our proxy statement for our 2022 Annual Meeting of Stockholders: "Compensation and Other Information Concerning Directors and Officers," "The Board of Directors and Its Committees," and "Report of The Human Capital Committee."

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required under this item is incorporated by reference to the following sections of our proxy statement for our 2022 Annual Meeting of Stockholders: "Equity Compensation Plan Information" and "Securities Ownership of Certain Beneficial Owners and Management."

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required under this item is incorporated by reference to the following sections of our proxy statement for our 2022 Annual Meeting of Stockholders: "Certain Relationships and Related Transactions" and "Corporate Governance Principles and Board Matters."

Item 14. Principal Accountant Fees and Services

The information required under this item is incorporated by reference to the following sections of our proxy statement for our 2022 Annual Meeting of Stockholders: "Independent Registered Public Accounting Firm" and "Pre-Approval Policies and Procedures."

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Form 10-K:

(1) Financial Statements (see "Consolidated Financial Statements and Supplementary Data" at Item 8 and incorporated herein by reference).

(2) Financial Statement Schedules (Schedules to the Financial Statements have been omitted because the information required to be set forth therein is not applicable or is shown in the accompanying Financial Statements or notes thereto).

(3) Exhibits

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Registration Number
2.1	Agreement and Plan of Merger, dated July 28, 2019, by and among the Registrant, Spring Acquisition Corp. and Genomic Health, Inc.		8-K (Exhibit 2.1)	7/30/2019	001-35092
2.2	Agreement and Plan of Merger, dated October 26, 2020, by and among the Registrant, certain subsidiaries of the Registrant, Thrive Earlier Detection Corp. and Shareholder Representative Services LLC		8-K (Exhibit 2.1)	10/27/2020	001-35092
2.3	First Amendment to Agreement and Plan of Merger, dated December 23, 2020, by and among the Registrant, certain subsidiaries of the Registrant, Thrive Earlier Detection Corp. and Shareholder Representative Services LLC		8-K (Exhibit 2.1)	1/5/2021	001-35092
2.4	Second Amendment to Agreement and Plan of Merger, dated January 4, 2021, by and among the Registrant, certain subsidiaries of the Registrant, Thrive Earlier Detection Corp. and Shareholder Representative Services LLC		8-K (Exhibit 2.2)	1/5/2021	001-35092
3.1	Sixth Amended and Restated Certificate of Incorporation of the Registrant		S-1 (Exhibit 3.3)	12/4/2000	333-48812
3.2	Amendment to Sixth Amended and Restated Certificate of Incorporation of the Registrant		8-K (Exhibit 3.1)	7/24/2020	001-35092
3.3	Sixth Amended and Restated By-Laws of the Registrant		8-K (Exhibit 3.1)	1/28/2022	001-35092
4.1	Specimen certificate representing the Registrant's Common Stock		S-1 (Exhibit 4.1)	12/26/2000	333-48812
4.2	Indenture, dated January 17, 2018, by and between the Registrant and U.S. Bank Trust Company, National Association (as successor to U.S. Bank National Association), as Trustee		8-K (Exhibit 4.1)	1/17/2018	001-35092
4.3	First Supplemental Indenture, dated January 17, 2018, by and between the Registrant and U.S. Bank Trust Company, National Association (as successor to U.S. Bank National Association), as Trustee (including the form of 1.0% Convertible Senior Notes due 2025)		8-K (Exhibit 4.2)	1/17/2018	001-35092
4.4	Second Supplemental Indenture, dated March 8, 2019, by and between the Registrant and U.S. Bank Trust Company, National Association (as successor to U.S. Bank National Association), as Trustee (including the form of 0.3750% Convertible Senior Notes due 2027)		8-K (Exhibit 4.2)	3/8/2019	001-35092
4.5	Third Supplemental Indenture, dated February 27, 2020, by and between the Registrant and U.S. Bank Trust Company, National Association (as successor to U.S. Bank National Association), as Trustee (including the form of 0.3750% Convertible Senior Notes due 2028)		8-K (Exhibit 4.2)	2/27/2020	001-35092
4.6	Description of Common Stock		10-K (Exhibit 10.1)	2/16/2021	001-35092
Lease Agreements					
10.1	Second Amended and Restated Lease Agreement, dated September 28, 2018, by and between University Research Park Incorporated and the Registrant		10-K (Exhibit 10.1)	2/21/2019	001-35092
10.2	Lease Agreement, dated June 25, 2013, by and between Tech Building I, LLC and Exact Sciences Laboratories, Inc.		10-Q (Exhibit 10.2)	8/2/2013	001-35092
10.3	Lease Agreement, dated November 11, 2015, by and between Metropolitan Life Insurance Company and Genomic Health, Inc.		10-K (Exhibit 10.3)	2/21/2020	001-35092
10.4	First Amendment to Lease Agreement, dated October 4, 2019, by and between Metropolitan Life Insurance Company and Genomic Health, Inc.		10-K (Exhibit 10.4)	2/21/2020	001-35092
10.5	Lease Agreement, dated September 23, 2005, by and between Metropolitan Life Insurance Company and Genomic Health, Inc.		10-K (Exhibit 10.5)	2/21/2020	001-35092
10.6	First Amendment to Lease Agreement, dated September 5, 2006, by and between Metropolitan Life Insurance Company and Genomic Health, Inc.		10-K (Exhibit 10.6)	2/21/2020	001-35092
10.7	Second Amendment to Lease Agreement, dated November 30, 2010, by and between Metropolitan Life Insurance Company and Genomic Health, Inc.		10-K (Exhibit 10.7)	2/21/2020	001-35092

10.8	Third Amendment to Lease Agreement, dated November 11, 2015, by and between Metropolitan Life Insurance Company and Genomic Health, Inc.		10-K (Exhibit 10.8)	2/21/2020	001-35092
10.9	Fourth Amendment to Lease Agreement, dated October 4, 2019, by and between Metropolitan Life Insurance Company and Genomic Health, Inc.		10-K (Exhibit 10.9)	2/21/2020	001-35092
Agreements with Executive Officers and Directors					
10.10*	Employment Agreement, dated March 18, 2009, by and between Kevin T. Conroy and the Registrant		8-K (Exhibit 10.1)	3/18/2009	000-32179
10.11*	Employment Agreement, dated November 8, 2016, by and between Jeffrey T. Elliott and the Registrant		10-K (Exhibit 10.9)	2/21/2017	001-35092
10.12*	Employment Agreement, dated October 30, 2015, by and between Scott Coward and the Registrant		10-K (Exhibit 10.13)	2/24/2016	001-35092
10.13*	Employment Agreement, dated February 18, 2019, by and between Jacob Orville and the Registrant		10-K (Exhibit 10.17)	2/21/2020	001-35092
10.14*	Employment Agreement, dated August 22, 2017, by and between Sarah Condella and the Registrant		10-K (Exhibit 10.16)	2/16/2021	001-35092
10.15*	Employment Agreement, dated November 11, 2021, by and between Everett Cunningham and the Registrant	X			
Equity Compensation Plans and Policies					
10.16*	The Registrant’s 2010 Employee Stock Purchase Plan		DEF 14A (Appendix B)	4/30/2010	000-32179
10.17*	First Amendment to the Registrant’s 2010 Employee Stock Purchase Plan		DEF 14A (Appendix A)	6/20/2014	001-35092
10.18*	Second Amendment to the Registrant’s 2010 Employee Stock Purchase Plan		DEF 14A (Appendix A)	4/29/2016	001-35092
10.19*	The Registrant’s 2016 Inducement Award Plan		10-Q (Exhibit 10.3)	5/3/2016	001-35092
10.20*	The Registrant’s 2016 Inducement Award Plan Form Restricted Stock Unit Award Agreement		S-8 (Exhibit 4.7)	5/3/2016	333-211099
10.21*	The Registrant’s 2010 Omnibus Long-Term Incentive Plan (As Amended and Restated Effective July 27, 2017)		10-Q (Exhibit 10.1)	10/30/2017	001-35092
10.22*	The Registrant's Non-Employee Director Compensation Policy dated October 22, 2020		10-K (Exhibit 10.25)	2/16/2021	001-35092
10.23*	The Registrant’s Executive Deferred Compensation Plan dated January 1, 2019		10-K (Exhibit 10.22)	2/21/2019	001-35092
10.24*	Third Amendment to the Registrant's 2010 Employee Stock Purchase Plan		10-Q (Exhibit 10.1)	7/30/2019	001-35092

10.25*	The Registrant's 2019 Omnibus Long-Term Incentive Plan		S-8 (Exhibit 4.4)	7/31/2019	333-23916
10.26*	The Registrant's 2019 Omnibus Long-Term Incentive Plan Form Stock Option Award Agreement		10-K (Exhibit 10.29)	2/21/2020	001-35092
10.27*	The Registrant's 2019 Omnibus Long-Term Incentive Plan Form Restricted Stock Unit Award Agreement		10-K (Exhibit 10.30)	2/21/2020	001-35092
10.28*	The Registrant's 2019 Omnibus Long-Term Incentive Plan Form Restricted Stock Award Agreement		10-K (Exhibit 10.31)	2/21/2020	001-35092
10.29*	Genomic Health, Inc. Amended and Restated 2005 Stock Incentive Plan, as amended		S-8 (Exhibit 4.4)	11/8/2019	333-234608
10.30*	Thrive Earlier Detection Corp. 2019 Stock Option and Grant Plan		S-8 (Exhibit 4.6)	1/5/2021	333-251900
Other					
10.31**	Technology License Agreement dated as of October 14, 2009 by and among Hologic, Inc., Third Wave Technologies, Inc., and the Registrant		10-K (Exhibit 10.39)	3/12/2010	000-32179
10.32**	Amendment dated December 7, 2012 to Technology License Agreement dated October 14, 2009 by and among Hologic, Inc., Third Wave Technologies, Inc., and the Registrant		10-K (Exhibit 10.37)	3/1/2013	001-35092
10.32**	Second Amended and Restated License Agreement dated effective January 1, 2020, by and between the Registrant and Mayo Foundation for Medical Education and Research		10-Q (Exhibit 10.1)	10/27/2020	001-35092
21	Subsidiaries of the Registrant	X			
23.1	Consent of PricewaterhouseCoopers, LLP	X			
23.2	Consent of BDO USA, LLP	X			
24.1	Power of Attorney (included on signature page)	X			
31.1	Certification Pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934	X			
31.2	Certification Pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934	X			
32	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			

101	The following materials from the Annual Report on Form 10-K of Exact Sciences Corporation for the year ended December 31, 2021 filed with the Securities and Exchange Commission on February 22, 2022, formatted in Inline eXtensible Business Reporting Language ("iXBRL"): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statement of Changes in Stockholders' Equity, (iv) Consolidated Statements of Cash Flows and (v) related notes to these financial statements	X
104	The cover page from the Annual Report on Form 10-K of Exact Sciences Corporation for the year ended December 31, 2021 filed with the Securities and Exchange Commission on February 22, 2022, formatted in Inline eXtensible Business Reporting Language ("iXBRL")	X

(*) Indicates a management contract or any compensatory plan, contract or arrangement.

(**) Confidential Treatment requested for certain portions of this Agreement.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

EXACT SCIENCES CORPORATION

Date: February 22, 2022

By: /s/ Kevin T. Conroy
Kevin T. Conroy
President & Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

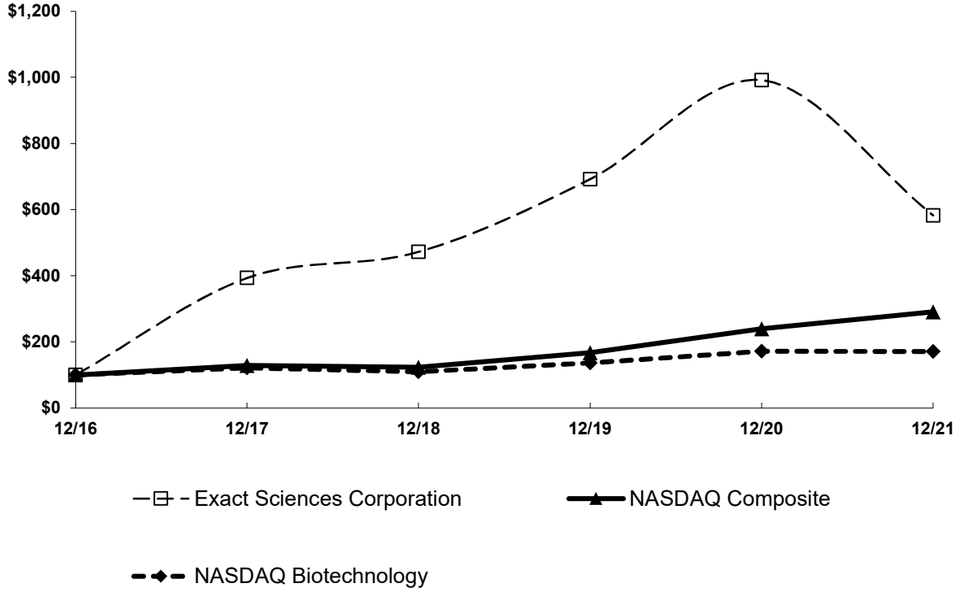
We, the undersigned officers and directors of Exact Sciences Corporation, hereby severally constitute and appoint Kevin T. Conroy our true and lawful attorney, with full power to him to sign for us and in our names in the capacities indicated below, any amendments to this Annual Report on Form 10-K, and generally to do all things in our names and on our behalf in such capacities to enable Exact Sciences Corporation to comply with the provisions of the Securities Exchange Act of 1934, as amended, and all the requirements of the Securities Exchange Commission.

Pursuant to the requirements of the Securities and Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Name	Title	Date
s/ Kevin T. Conroy Kevin T. Conroy	President and Chief Executive Officer (Principal Executive Officer) and Chairman of the Board	February 22, 2022
/s/ Jeffrey T. Elliott Jeffrey T. Elliott	Executive Vice President, Chief Financial Officer, and Chief Operating Officer (Principal Financial Officer and Principal Accounting Officer)	February 22, 2022
/s/ Paul Clancy Paul Clancy	Director	February 22, 2022
/s/ James E. Doyle James E. Doyle	Lead Independent Director	February 22, 2022
/s/ Freda Lewis-Hall Freda Lewis-Hall	Director	February 22, 2022
/s/ Pierre Jacquet Pierre Jacquet	Director	February 22, 2022
/s/ Daniel J. Levangie Daniel J. Levangie	Director	February 22, 2022
/s/ Shacey Petrovic Shacey Petrovic	Director	February 22, 2022
/s/ Kathleen Sebelius Kathleen Sebelius	Director	February 22, 2022
/s/ Katherine S. Zanotti Katherine S. Zanotti	Director	February 22, 2022

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*

Among Exact Sciences Corporation, The NASDAQ Composite Index,
and The NASDAQ Biotechnology Index



*$100 invested on 12/31/16 in stock or index including reinvestment of dividends.