



C/STLE
BIOSCIENCES

2021 Annual Report

Dear Fellow Stockholders,

2021 was an exceptional year for Castle, and I would be remiss if I did not begin by thanking our talented employees for their tireless dedication and commitment. Each new year brings new opportunities to improve health and guide patient care, and we are only able to achieve our goals through our combined and collaborative efforts.

2021 HIGHLIGHTS 2021 was a year of growth across our business. We exceeded our revenue expectations and delivered full-year 2021 revenue of \$94.1 million, a 50% increase over 2020. We successfully doubled our dermatology-facing commercial team and delivered more than 28,000 gene expression profile test reports, a 55% increase over our report volume in 2020. Our commercial team continued to build strong relationships with existing and new clinicians, which resulted in approximately 1,900 new ordering clinicians and approximately 5,900 total ordering clinicians for our dermatologic tests.

Continuing our theme of growth, we identified and executed on two strategic opportunities that we believe complement our existing business and allow us to impact patient care in areas of unmet clinical need. The first was the acquisition of the Myriad myPath® laboratory in May 2021, which added the myPath Melanoma test to our dermatologic portfolio, and the second was the acquisition of Cernostics in December 2021, which represents our decision to serve patients suffering from gastrointestinal diseases. Cernostics' TissueCypher® Barrett's Esophagus test represents our initial test offering in the gastroenterology market. We believe the spatialomics platform that underlies the TissueCypher test expands our R&D and clinical laboratory capabilities and enables us to consider new pipeline tests utilizing this advanced technology.

As a science-based company, expanding the body of scientific evidence supporting the value of our tests is an operating imperative. And in 2021, our world-class R&D team delivered on our aggressive goals, successfully generating 15 peer-reviewed articles supporting the value of our commercial tests and advancing our pipeline tests, including our initiative to develop a test to predict systemic therapy response in patients with moderate-to-severe psoriasis, atopic dermatitis and related inflammatory skin conditions.

MISSION, VISION AND VALUES Since our inception in 2008, we have built our business around innovation, transformation and by keeping people first. While we have continued to grow and evolve as an organization, these foundational principles have remained the guidepost for the direction of our company and the basis of our long-term value creation. Grounded in this firm foundation, we relaunched our Mission, Vision and Values in 2021, which depict who we are at our core and who we aspire to be, now and into the future.

Our Mission: Improving health through innovative tests that guide patient care

Our Vision: To transform disease management by keeping people first: patients, clinicians, employees and investors

Our Values: Trust, Excellence, Collaboration, Integrity, Innovation and Excitement

LOOKING FORWARD We believe our success in 2021 allows us to enter 2022 with momentum, a strong balance sheet and the potential to further position the company as an industry leader. Driven by strong execution and a focus on three key operational pillars - our strong core dermatology business, pipeline initiatives and strategic opportunities - we anticipate continued growth and value creation in the near- and long-term.

At Castle, we believe wholeheartedly that our success is due to our steadfast commitment to keeping people first: patients, clinicians, employees and you, our valued investors. Thank you for your continued support, as we strive to truly transform disease management in the years to come.

Sincerely,



Derek Maetzold
Founder, President & CEO

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**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549**

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

OR

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

For the transition period from _____ to _____

Commission File Number: 001-38984

CASTLE BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation or organization)

77-0701774

(I.R.S. Employer Identification No.)

**505 S. Friendswood Drive, Suite 401,
Friendswood, Texas**

(Address of principal executive offices)

77546

(Zip Code)

(866) 788-9007

(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.001 par value per share	CSTL	The Nasdaq Global Market

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit 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.

Large accelerated filer	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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 voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2021 (the last business day of the registrant’s most recently completed second fiscal quarter) was \$1.5 billion based on the closing price of the registrant’s common stock on June 30, 2021, as reported by the Nasdaq Global Market.

As of February 21, 2022, there were 25,410,602 shares of common stock, \$0.001 par value per share, issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant’s definitive proxy statement to be filed with the Securities and Exchange Commission, or SEC, subsequent to the date hereof pursuant to Regulation 14A in connection with the registrant’s 2022 Annual Meeting of Stockholders, are incorporated by reference into Part III of this Annual Report on Form 10-K. The registrant intends to file such proxy statement with the SEC not later than 120 days after the conclusion of its fiscal year ended December 31, 2021.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks and uncertainties. The forward-looking statements are contained principally in the sections entitled “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business.” These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- estimates of our total addressable market, future revenue, expenses, capital requirements and our needs for additional financing;
- expectations with respect to reimbursement for our products, including third-party payor reimbursement and coverage decisions;
- anticipated cost, timing and success of our product candidates, and our plans to research, develop and commercialize new tests;
- the impact of the COVID-19 pandemic on our business;
- our ability to obtain funding for our operations, including funding necessary to complete the expansion of our operations and development of our pipeline products;
- the implementation of our business model and strategic plans for our products, technologies and business;
- expectations with respect to acquisitions of businesses, assets, products or technologies;
- our ability to manage and grow our business by expanding our sales to existing customers or introducing our products to new customers;
- our ability to develop and maintain sales and marketing capabilities;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers;
- the success of competing diagnostic products that are or become available;
- our ability to attract and retain key personnel; and
- our expectations regarding our ability to obtain and maintain intellectual property protection for our products and our ability to operate our business without infringing on the intellectual property rights of others.

In some cases, you can identify these statements by terms such as “anticipate,” “believe,” “could,” “estimate,” “expects,” “intend,” “may,” “plan,” “potential,” “project,” “should,” “will,” “would” or the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes. These forward-looking statements reflect our management’s beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this Annual Report on Form 10-K and are subject to risks and uncertainties. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements. We discuss many of the risks associated with the forward-looking statements in this Annual Report on Form 10-K in greater detail in the section entitled “Risk Factors.” Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

RISK FACTORS SUMMARY

We face many risks and uncertainties, as more fully described in this Annual Report on Form 10-K under the heading “Risk Factors.” Some of these risks and uncertainties are summarized below. The summary below does not contain all of the information that may be important to you, and you should read this summary together with the more detailed discussion of these risks and uncertainties contained in “Risk Factors.”

Risk Related to our Financial Condition

- We rely upon a small number of third-party payors for a significant portion of our revenue.
- Our method of recognizing revenue may not reflect our underlying business.
- We have incurred significant losses since inception, and we may never achieve profitability.
- We are an early, commercial-stage company and have a limited operating history, which may make it difficult to evaluate our current business and predict our future performance.
- Our financial results could fluctuate in the future, causing the market price of our stock to decline substantially.
- If our internal control over financial reporting is ineffective, we may not be able to accurately report our financial results or file our periodic reports in a timely manner.
- We may need to raise additional capital to commercialize new products, to expand operations or to fund existing operations.

Risks Related to our Business

- We have been, and may continue to be, adversely impacted by the COVID-19 pandemic, which has, at times, caused decreased test report volume.
- Our revenue heavily relies upon the sale of a single product and our current or future products may not achieve or maintain significant commercial market acceptance.
- Billing for our products is complex and we require substantial time and resources to collect payment.
- We rely on third parties for sample collection, preparation and delivery.
- A depletion or loss of our sample database could significantly harm our business.
- If our primary clinical laboratory facility becomes damaged or inoperable or we are required to vacate our existing facility, our ability to conduct our laboratory work for our commercial products and pursue our research and development efforts may be jeopardized.
- New product development is lengthy and complex and our revenues could be limited if we are unable to increase and support adoption of our products by both physicians and other healthcare providers.
- We rely on limited or sole suppliers for some of the reagents, equipment, chips and other materials used by our products, and we may not be able to find replacements or transition to alternative suppliers if these suppliers are unable or unwilling to continue providing these materials.
- The sizes of the addressable markets for our current and future products have not been established with precision and may be smaller than we estimate.
- The diagnostic testing industry is subject to rapid change, which could make our current or future products obsolete.

Risks Related to Reimbursement and Government Regulation

- We currently have limited reimbursement coverage for our lead product, DecisionDx-Melanoma, and if third-party payors, including government and commercial payors, do not provide sufficient coverage of, or adequate reimbursement for, our products, our commercial success, including revenue, will be negatively affected.
- We conduct business in a heavily regulated industry and failure to comply with regulatory requirements, including those established by the Centers for Medicare & Medicaid Services (“CMS”), and the U.S. Food and Drug Administration (“FDA”) or changes in enforcement discretion for laboratory developed tests could harm our business.
- Data from our clinical studies may change materially, which could harm our business.
- Changes in healthcare policy, statutes or regulations, or our ability to comply with applicable healthcare requirements, could have a material adverse effect on our business and operations.

Risks Related to Intellectual Property

- If we are unable to obtain and maintain sufficient intellectual property protection for our technology, our ability to successfully commercialize our products may be impaired.
- Our commercial success depends significantly on our ability to operate without infringing upon the intellectual property rights of third parties.

- We rely on information technology systems that we license from third parties and other royalty-bearing license agreements.

Risks Related to Employee Matters and Managing Growth and Other Risks Related to Our Business

- We are highly dependent on the services of our key personnel, including our President and Chief Executive Officer.
- Our employees and any current or potential commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.
- We have, and may continue to, engage in strategic transactions, such as the acquisition of businesses, assets, products or technologies, which could be disruptive to our existing operations, divert the attention of our management team and adversely impact our liquidity, cash flows, financial condition and results of operations.
- Our business may be negatively impacted by cyber-security threats, natural disasters and public health crises.
- Product or professional liability lawsuits against us could cause us to incur substantial liabilities and could limit our commercialization of our products.

Risks Related to Ownership of Our Common Stock.

- The price of our common stock may be volatile or may decline regardless of our operating performance, and you may lose all or part of your investment.
- We have broad discretion in the use of working capital and may not use it effectively or in ways that increase our share price.
- Related party transactions that create conflicts of interest, or the appearances of conflicts of interest, may harm our business and cause our stock price to decline.
- The concentration of our stock ownership will likely limit your ability to influence corporate matters, including the ability to influence the outcome of director elections and other matters requiring stockholder approval.
- Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock.
- Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

PART I

Item 1. Business.

As used in this Annual Report on Form 10-K, unless the context indicates or otherwise requires, “Castle Biosciences,” “the Company,” “we,” “us,” and “our” refer to Castle Biosciences, Inc., a Delaware Corporation.

Overview

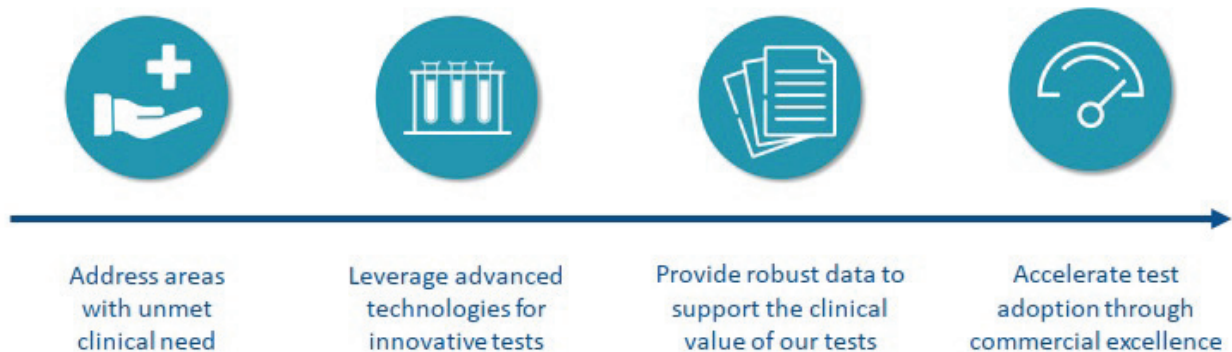
Castle Biosciences is improving health through innovative tests that guide patient care. For the diseases that our portfolio of tests cover, we believe the traditional approach to developing a treatment plan for cancers and other diseases using clinical and pathology factors alone is inadequate and can be improved by incorporating the personalized information our diagnostic and prognostic tests provide.

Vision and Foundational Strategy

Since our inception in 2008, it has been our vision to transform disease management by keeping people first: patients, clinicians, employees and investors. This foundational strategy remains the guidepost for the direction of our company and the basis of long-term value creation.

Castle Remains Focused On Transforming Disease Management

• Strategic priorities that create value for customers, patients and stockholders



Our foundational strategy focuses on executing four principles:

Address Areas With Unmet Clinical Need. Our commercial and pipeline tests address many treatment plan challenges facing physicians by providing physicians and their patients with a laboratory report that contains clinically actionable and personalized information from our proprietary tests to inform the treatment plan for each patient.

Leverage Advanced Technologies For Innovative Tests. We focus on multi-analyte assays with algorithmic analysis (“MAAAs”) that enable us to characterize an individual patient’s tissue biology to improve risk-stratification, improve diagnostic certainty and predict therapy response. Our expectation is that incorporating our personalized test results into the shared decision-making between a patient and their clinician should result in improved treatment plan decisions and lead to optimized health outcomes with a reduction in healthcare costs. Due to the biological complexity of the diseases we target, we believe that MAAAs are the optimal approach to precision testing.

Provide Robust Data To Support The Clinical Value Of Our Tests. We conduct extensive clinical utility and validity studies to support the adoption of, and reimbursement for, our products. This growing set of data is key in educating physicians and patients about the consistent value of our commercial products. Regarding our lead product, DecisionDx-Melanoma, in 2015, we published our initial two peer-reviewed manuscripts. As of February 28, 2022, we have more than 35 peer-reviewed publications supporting the clinical utility and validity of DecisionDx-Melanoma, including multiple prospective studies and two systematic reviews with meta-analyses involving over 6,000 unique patients. We anticipate analyzing more than 20,000 additional patients’ data in cutaneous melanoma studies in 2022. Across our testing portfolio, we currently have 16 ongoing clinical research studies and as of December 31, 2021 we had 341 committed/contributing clinical research sites and 7,800

patients enrolled in studies. In order to maintain our competitive advantage and increase sales of our products, we will continue to generate additional clinical data to support the use of our products.

Accelerate Test Adoption Through Commercial Excellence. Our commercial team focuses on educating clinicians on the value of incorporating the results of MAAA tests to make more informed treatment plan decisions. In the field of dermatology, this approach has resulted in established relationships with clinicians that allow us to optimize our interactions, increase adoption of our current products and identify areas of unmet clinical need to efficiently launch additional, complementary products. Our significant investment in developing evidence of the value of our tests has resulted in rigorous scientific support and peer-reviewed publications in leading journals, which allows our commercial team to have substantive, in-depth dialogues with physicians. Through these established relationships, we have been able to integrate our products into physicians’ workflows and identify further educational programs, which we believe fosters adoption of our products. We believe our history of commercial success in dermatology will translate into other markets, including ocular oncology and gastroenterology.

Our Test Portfolio

We map out the continuum of diagnostic test services as starting with (i) screening of healthy individuals, to (ii) supporting diagnostic clarity in patients with signs or symptoms of disease, to (iii) risk-stratification or prognosis, to (iv) response to treatment for specific treatment selection and to (v) late-stage testing for use in resistant metastatic disease. We currently focus our investments on innovative test services that assist in providing diagnostic clarity in patients with signs or symptoms of disease, risk-stratification and response to treatment. We have five commercially available proprietary tests that assist physicians and patients along this continuum and focus on answering clinical questions arising during the treatment of dermatologic cancers, uveal melanoma and Barrett’s esophagus (“BE”): DecisionDx-Melanoma, DecisionDx-SCC, DecisionDx DiffDx-Melanoma, myPath Melanoma, DecisionDx-UM and TissueCypher Barrett’s Esophagus Assay. Together, we believe these commercial products support an estimated total addressable market (“TAM”) of \$3.0 billion in the United States. Currently, our revenue is primarily generated by our DecisionDx®-Melanoma risk stratification test for cutaneous melanoma and our DecisionDx®-UM risk stratification test for uveal melanoma.

In 2021, we announced the launch of our innovative pipeline initiative to develop a genomic test aimed at predicting response to systemic therapy in patients with moderate to severe psoriasis, atopic dermatitis and related inflammatory skin conditions. If successful, this inflammatory skin pipeline test has the potential to add approximately \$1.9 billion to our current estimated U.S. TAM. In 2021, we formed a steering committee comprised of leading experts in the field, received Institutional Revenue Board (“IRB”) approval and enrolled our first patient in the development and validation study for this genomic test. We believe we are on track to launch this test by the end of 2025. We have initiated work on additional pipeline tests which branch out upstream, downstream and parallel to our commercial tests, within or adjacent to our established dermatology commercial call points.

Answering Clinical Questions to Guide Care Along The Patient Journey

- Our focus is on diagnostic, risk stratification and therapy response areas of the patient care continuum



Operational Pillars Supporting Castle's Growth

Our near and long-term growth plans are focused on three operational pillars: our strong core dermatology business, pipeline initiatives and strategic opportunities.

Pillars Of Our Growth Plan

Consistent execution furthers our leading position in dermatology and in the Dx space

Strong Core Derm Business



- Continuing provider education
- Optimizing commercial team
- Evolving our go-to-market strategy (EMA, VA)
- NCI/SEER collaboration

Pipeline Initiatives



- Ability to answer clinical questions/impact patient care
- Utilizing our areas of expertise (genomics, spatialomics, AI) to develop innovative tests
- Focusing on complementary/adjacent disease states

Strategic Opportunities



- Areas where we can utilize our commercial success
- Potential to create a suite of tests in a single call point
- Ability to answer clinical questions/impact patient care
- Early reimbursement wins

Strong Core Dermatology Business

The foundation of our business is our dermatologic cancer franchise, and our lead product is DecisionDx-Melanoma. DecisionDx-Melanoma is a proprietary multi-gene expression profile (“GEP”) risk stratification test that predicts the risk of metastasis, or recurrence, for patients diagnosed with invasive cutaneous melanoma, a deadly skin cancer. In the management of melanoma, as with nearly all diseases, treatment plans are directed by patient risk-stratification. This test has two distinct, complementary clinically actionable uses. The first revolves around predicting the likelihood of having a sentinel lymph node (“SLN”) negative biopsy result so that physicians and patients can discuss the risk and benefit of undergoing the SLN biopsy (“SLNB”) surgical procedure. The second use is to inform the appropriate treatment plan during the initial five years post-diagnosis, regardless of the decision to undergo or avoid invasive SLNB surgery. In a typical year, we estimate approximately 130,000 patients are diagnosed with invasive cutaneous melanoma in the United States. We launched DecisionDx-Melanoma in May 2013. Based on the substantial clinical evidence that we have developed, we have received Medicare coverage for DecisionDx-Melanoma, which represents approximately 50% of the addressable patient population for this test.

In 2021, we initiated a collaboration with the National Cancer Institute (“NCI”) to link Surveillance, Epidemiology, and End Results (“SEER”) Program registries’ data on cutaneous melanoma cases with DecisionDx-Melanoma testing data. The analysis of the first subset of data from patients 65 years and older confirmed the performance of our test to risk stratify the likelihood of progression. The analysis also showed that patients tested with DecisionDx-Melanoma had improved overall survival rates compared to untested patients. In addition to confirming results from previous studies, this data from a large, real-world and unselected patient population, confirmed that patients who received a DecisionDx-Melanoma test result lived longer than patients whose clinicians relied solely on traditional clinicopathologic factors. The first phase of the collaboration links SEER cutaneous melanoma registries that were diagnosed between 2013 and 2018 with DecisionDx-Melanoma results and additional clinicopathologic information from patients tested between 2013 and 2018. We expect that the peer-reviewed publication will be available in 2022. The next planned phase of the collaboration with the NCI is to link the SEER registries’ cutaneous melanoma cases diagnosed post-2018. We expect further data read outs later in 2022 and beyond.

On August 31, 2020, we commercially launched our cutaneous squamous cell carcinoma (“SCC”) proprietary GEP test, DecisionDx®-SCC, for use in patients with one or more risk factors (also referred to as “high-risk” SCC). On November 2, 2020, we commercially launched our proprietary GEP test for difficult-to-diagnose melanocytic lesions, DecisionDx® DiffDx™-Melanoma for use in patients with a melanocytic lesion and uncertainty related to the malignancy of the lesion. We

believe that these two additional skin cancer tests address areas of high clinical need in dermatological cancer and, together, represent an estimated addressable population of approximately 500,000 patients in the United States.

We further expanded our commercially available dermatologic portfolio in May 2021 when we acquired Myriad myPath, LLC (“Myriad myPath Laboratory”) from Myriad Genetics, Inc. for a cash purchase price of \$32.5 million. myPath Melanoma is a clinically validated GEP test that addresses the same unmet clinical need as our DecisionDx DiffDx-Melanoma test. Today, we offer both our myPath Melanoma test and our DecisionDx DiffDx-Melanoma test under an offering that we refer to as our comprehensive diagnostic offering (“CDO”) of molecular testing solutions. By offering both of these tests in a single offering, we believe we have demonstrated the ability to improve the test result performance for patients with difficult-to-diagnose melanocytic lesions.

Pipeline Initiatives

We identify areas of significant unmet clinical needs in the treatment of skin cancer and other diseases and leverage our expertise in genomics and other advanced technologies, data analytics and artificial intelligence to develop clinically actionable products. We focus first on confirming the unmet clinical needs of clinicians treating skin cancer and other diseases, which we gather from in-depth conversations with our customers and thought leaders as well as feedback our sales and medical affairs representatives receive from clinicians. Once we have generated a pipeline test that we believe will address an unmet clinical need, we work to validate the product candidate through extensive testing of patient tissue samples, many of which will be housed in Castle’s own biorepository and annotated with clinical outcomes data. We use our extensive data bank of patient tissue samples and clinical outcomes data to conduct development and validation studies, as well as clinical studies to collect new samples in additional diseases.

We have significant expertise in developing proprietary algorithms, conducting clinical studies and using the necessary instrumentation required for efficiently developing our pipeline products.

In 2021, we announced the launch of our innovative pipeline initiative to develop a genomic test aimed at predicting response to systemic therapy in patients with moderate to severe psoriasis, atopic dermatitis and related inflammatory skin conditions. In the U.S. alone, there are approximately 18 million patients diagnosed with psoriasis and atopic dermatitis. Approximately 450,000 of these patients annually are eligible for systemic therapies. If successful, this inflammatory skin disease pipeline test has the potential to add approximately \$1.9 billion to our current estimated U.S. TAM. In 2021, we initiated a 4,800 patient, prospective, multi-center clinical study to develop and validate this pipeline test, and have 50 committed centers, out of the initial target of 50. Based upon our current development and validation timelines, we expect to launch this pipeline test by the end of 2025.

Although we are still in the early stages of development, we believe that, utilizing our existing sales channels, we could launch three to five new tests by the end of 2025, potentially adding approximately \$1.7 billion to our current U.S. TAM.

Strategic Opportunities

A key pillar of our growth plan is to identify targeted, complementary strategic opportunities. Our M&A philosophy includes entering markets where we expect our history of commercial success in the field of dermatology will translate well. Further, we seek opportunities where we expect to leverage advanced technologies to bring innovative tests to clinicians and patients, where there is an opportunity to transform disease management in areas with unmet clinical need and provide actionable information to answer clinical questions, and where we have the potential to create a suite of tests for use by a single clinician.

We further expanded our commercially available dermatologic portfolio in May 2021, when we completed the acquisition of the Myriad myPath Laboratory, as mentioned above.

In December 2021, we extended our commercial portfolio of proprietary tests into the gastroenterology market through our acquisition of Cernostics, Inc. (“Cernostics”) and the TissueCypher® platform. The TissueCypher platform focuses on unlocking, in the case of the initial test for use in patients with BE, the importance of the location of the expression of proteins or lack thereof within the morphology of the disease (also known as spatialomics). This “spatialomic” information is then interpreted using artificial intelligence approaches to predict the likelihood of progression to high-grade dysplasia and/or esophageal cancer in patients with non-dysplastic, indefinite or low-grade dysplasia BE. We believe the addition of expertise in the spatialomics area positions us for continued growth and success in the diagnostics space, complementing our first-to-market dermatologic franchise and our proprietary test for uveal melanoma.

Our History of Transforming Disease Management

In addition to our dermatologic franchise and our initial entry into the gastroenterology market with our TissueCypher test for BE, we also market tests for patients diagnosed with uveal melanoma (“UM”), a rare cancer of the eye. DecisionDx®-UM is a proprietary GEP test that provides risk-stratification information for patients with UM.

We believe DecisionDx-UM is the standard of care in the management of newly diagnosed UM in the majority of ocular oncology practices in the U.S., and it is estimated that nearly 8 in 10 patients diagnosed with UM in the U.S. receive the DecisionDx-UM test as part of their diagnostic workup. We launched DecisionDx-UM in January 2010. Based on the substantial clinical evidence that we have developed, we received Medicare coverage for DecisionDx-UM, which represents approximately 50% of the addressable patient population as well as widespread commercial payor coverage.

Test Adoption

The number of test reports we generate is a key indicator that we use to assess our business. A test report is generated when we receive a sample in our laboratory, and then the relevant test information is entered into our Laboratory Information Management System, the expression of the biomarkers is measured, then a proprietary algorithmic analysis of the combined biomarkers is performed to generate a report providing the results of that analysis, which is sent to the clinician who ordered the test. The numbers of GEP test reports delivered by us and our net revenues during the past five years are presented in the table below:

	Years Ended December 31,				
	2021	2020	2019	2018	2017
DecisionDx-Melanoma	20,328	16,232	15,529	12,032	9,300
DecisionDx-SCC ⁽¹⁾	3,510	485	—	—	—
CDO ⁽²⁾	2,662	73	—	—	—
Dermatologic Total	26,500	16,790	15,529	12,032	9,300
DecisionDx-UM	1,618	1,395	1,526	1,413	1,314
Grand Total	28,118	18,185	17,055	13,445	10,614
Net Revenues (in thousands)	\$ 94,085	\$ 62,649	\$ 51,865	\$ 22,786	\$ 13,754

(1) We commercially launched DecisionDx-SCC on August 31, 2020.




(2) Includes DecisionDx DiffDx-Melanoma, which we commercially launched on November 2, 2020, and myPath Melanoma, which we began offering following our acquisition of Myriad myPath Laboratory on May 28, 2021. We offer both our myPath Melanoma and DecisionDx DiffDx-Melanoma under our CDO.

Dermatologic Franchise Overview

Skin cancer is the uncontrolled growth of abnormal skin cells. There are six types of pre-cancers and skin cancers that result in a total annual incidence of 5.5 million patients. The three most common forms of skin cancers are basal cell carcinomas, SCC and cutaneous melanoma. SCC, the second most common form of skin cancer, is an uncontrolled growth of abnormal cells arising from the squamous cells in the epidermis, the skin's outermost layer. Melanoma, an aggressive form of skin cancer, originates in the pigment-producing melanocytes in the basal layer of the epidermis. We do not, at this time, have an active focus on basal cell carcinomas.

Pre-cancers include suspicious pigmented lesions, which are unusual-looking lesions that may be melanoma, and actinic keratosis. The estimated TAM for our dermatologic commercial products, which is based on estimated patient population assuming average reimbursement rate among all payors, is set forth below:

Dermatologic Franchise

Cutaneous melanoma/ risk of metastasis	Cutaneous squamous cell carcinoma/ risk of metastasis	Suspicious pigmented lesions/melanoma status	Pipeline Test - Inflammatory	Additional Derm Pipeline Tests
~130k Patients classified as Stage I, II or III ¹	~200k Patients w/ high-risk features ¹	~300k Patients w/ indeterminant biopsy ¹	~450k Patients eligible for systemic therapies	To be announced
~\$540M	~\$820M	~\$600M	~\$1.9B	~\$1.7B
				

1. Annual U.S. incidence for Stage I, II or III melanoma estimated at 130,000; Annual U.S. incidence for squamous cell carcinoma estimated at 1,000,000 with addressable market limited to carcinomas with one or more high risk features; Annual U.S. incidence for suspicious pigmented lesion biopsies estimated at 2,000,000 with addressable market limited to the 15% with an indeterminant biopsy.

Cutaneous Melanoma

Melanoma tumors originate in the pigment-producing melanocytes in the basal layer of the epidermis. Published statistics suggest that there were nearly 300,000 new cases of melanoma diagnosed worldwide, with the U.S. Surveillance, Epidemiology, and End Results (“SEER”) database estimating that approximately 96,000 invasive cutaneous melanomas are diagnosed in the United States annually, however, multiple publications report that melanoma diagnoses are underreported by between 30% and 72% annually in the United States. Using the mean of the underreporting of these four studies, we estimate the annual incidence of cutaneous melanoma to be 130,000, representing an estimated U.S. TAM of \$540 million. According to these publications, the underreporting of melanoma diagnoses reflects the fact that the majority of diagnoses are made by community-based dermatologists and dermatopathologists rather than institutional-based specialists who more typically have tumor registry support. Based on currently available data, we estimate the targetable clinician base is between 11,000 and 15,000.

Additionally, the incidence of melanoma has steadily increased annually over the last several decades, with an estimated growth in the United States of more than 50% during the past ten years.

After a diagnosis of invasive cutaneous melanoma, healthcare providers have traditionally relied solely on clinical and pathology factors from the initial biopsy to estimate the patient’s risk of metastasis to then determine a risk-based treatment plan. This estimation or “staging” process is then used to determine nearly all treatment decisions. Invasive melanoma tumors are staged as Stage I through Stage IV. Stage I tumors have invaded the dermis but are thin, with less than or equal to 2.0 mm invasion into the dermis if not ulcerated, or less than or equal to 1.0 mm invasion into the dermis if ulcerated. Stage I tumors have the lowest population-based risk of metastasis and death from melanoma. Stage II tumors, though localized, are thicker than 2.0 mm if not ulcerated or greater than 1.0 mm if ulcerated. Stage III tumors have evidence of regional metastasis, such as palpable metastasis at the regional lymph node basin, in-transit or satellite disease, or melanoma cell(s) in the SLN tissue but without evidence of distant metastatic spread. Stage IV tumors are those in which distant metastasis, such as to the lung or brain, has been detected.

All patients who are diagnosed with an invasive cutaneous melanoma will undergo a wide local excision procedure with the surgical margins determined by the depth of the tumor. Invasive SLNB surgery is generally recommended to be considered for patients with melanomas greater than or equal to 0.8 mm thick or for thinner melanomas accompanied by an adverse pathologic feature such as ulceration, high mitotic rate or transected base. Tumors with these anatomic based features are believed to result in an SLN-positive biopsy result 5% or more of the time. If the SLNB surgery is performed, then the wide local excision is performed at that time. As noted above, an SLN-positive biopsy result, meaning that at least one melanoma cell was seen in the SLN tissue, leads to re-staging the patient as Stage III. Guideline committees do not recommend SLNB surgery if the likelihood of a positive SLN result is less than 5%. They recommend discussing and considering SLNB surgery if the likelihood of a

positive SLN result falls between 5% and 10%, and recommend discussing and offering SLNB surgery if the likelihood exceeds 10%. Guideline committees have generally converged on the 5% threshold due to a reported regional false negative rate of the SLNB surgery of 5% (meaning that 5% of the time, or more, the guideline committees expect a patient with an SLN-negative biopsy result will subsequently develop SLN metastasis). However, the published literature documents a median regional false negative rate of 18% and an 11% surgical complication rate. The “regional false negative rate” measures the rate that metastasis to the regional lymph node in patients with a negative SLNB surgical result.

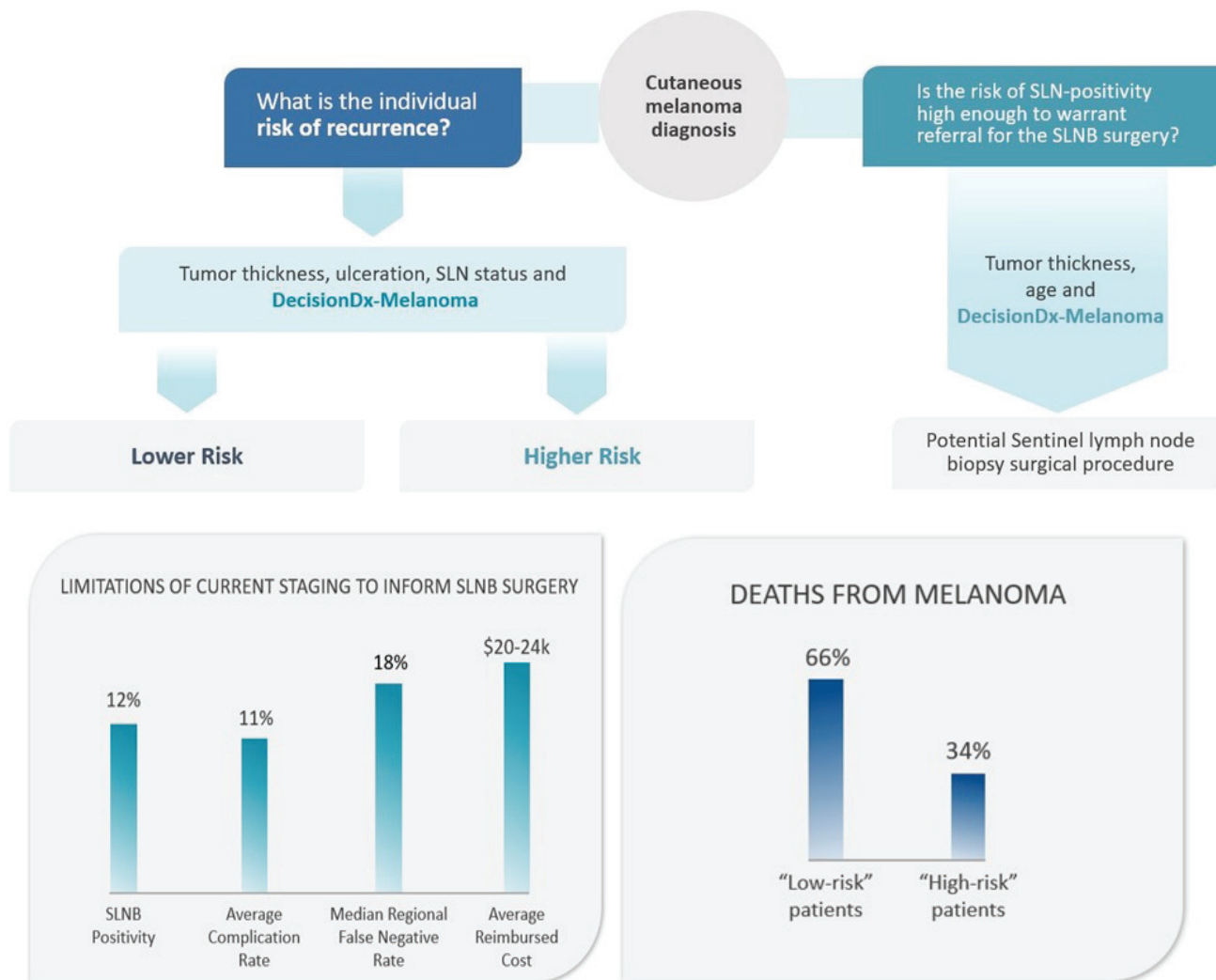
The traditional clinical and pathology staging system for invasive cutaneous melanoma is based upon the anatomic findings of the melanoma; that is what the pathologist can see under the microscope from an initial tumor biopsy and what the physician can feel or see during a clinical exam or upon imaging. While this staging system provides population-based risk of metastasis estimates based on clinical and pathology factors, it does not evaluate nor incorporate the biology of the patient’s primary tissue biology.

Importantly, while it was formerly believed that SLNB surgery improved melanoma specific survival, the NCI conducted a landmark, prospective, randomized multi-center study (“the MSLT-I study”) which showed that the death rate from melanoma was the same in patients who were randomized to the SLNB surgery and those who merely underwent observation, indicating that SLNB surgery is prognostic, and not therapeutic, as it relates to the risk of death from melanoma. On average, 12% of patients undergoing the SLNB surgery will have an SLN-positive biopsy result and 88% will not. Invasive SLNB surgery carries significant healthcare burden. For example, the overall complication rate of SLNB surgery was shown to be 11.3% in a systematic review of 21 articles representing 9,047 patients. A separate review reported that the regional false negative rate of the SLNB surgery ranged from 5% to 21%, with a median rate of 18%.

Both the complication and false negative rates are above the recommended 5% and 10% positivity rates proposed by guideline committees as thresholds at which physicians should either consider (5%) or offer (10%) the procedure to their patients. Further, the SLNB surgery requires the use of general anesthesia, and nearly half of these surgeries are performed in an in-patient setting, leading to an average reimbursed cost of \$20,000 to \$24,000. Finally, the 88% SLN-negative rate in these surgeries carries significant patient and healthcare system implications because 88% of patients undergoing an SLNB surgery will have no change in their treatment plan or their staging, but are still exposed to the complications from the surgery, including general anesthesia risks, high medical costs and a median false negative rate of 18%. Thus, while it is true that patients who are SLN positive, or re-staged to Stage III, have a higher population-based rate of metastasis and death from melanoma, invasive SLNB surgery does not improve melanoma-specific survival, carries risk of complications, a high false negative rate and significant costs.

In addition to the significant clinical issues involved in only using traditional clinical and pathology factors to evaluate the appropriateness of SLNB surgery, there is a discord between an individual’s “stage” and their actual risk of metastasis or death from melanoma. Based on data from SEER and the American Joint Committee on Cancer (“AJCC”), out of the cutaneous melanoma tumors diagnosed as Stage I, II or III, 80% are classified as Stage I (the lowest risk) and 12% are classified as Stage II (the next lowest risk). However, these data also show that melanomas initially diagnosed as Stage I or II under the traditional staging framework account for 60% of all deaths in patients receiving Stage I, II or III diagnoses. Furthermore, while patients with Stage III melanoma are at a higher population risk of metastasis and death from melanoma than Stage I or II, the five-year melanoma-specific survival rate for Stage II patients is 77%. We believe that the limitations of the current staging system not only result in unnecessary SLNB surgeries for certain low-risk patients, but also lead to overtreatment with adjuvant immunology and targeted therapies for certain patients with Stage III melanoma.

In summary, risk-stratification, or the risk of metastasis, determines the treatment plans in newly diagnosed patients, including the recommendation for the SLNB surgery, decisions around the initiation of advanced imaging for active surveillance, frequency and specialty for clinical follow-up, initiation of adjuvant therapy and discussion of clinical trial enrollment opportunities. The top portion of the graphic below summarizes the two decision points that DecisionDx-Melanoma impacts. The lower portion summarizes the limitations of relying on clinical and pathology factors alone to determine risk of metastasis that informs SLNB surgery and subsequent treatment plan decisions.



Source: AJCC v7 J Clin Oncol 2009; SEER data release 2017; Morton et al. N Engl J Med 2014; Whiteman et al. J Invest Dermatol 2015; Shaikh et al. J Natl Cancer Inst 2016; Poklepovic and Carvajal. Oncology 2018; Sondak and Zager. Ann Surg Oncol 2010. Moody et al. Euro Jml Surg Onc 2017.

Cutaneous Squamous Cell Carcinoma

Cutaneous SCC the second most common form of skin cancer, is an uncontrolled growth of abnormal cells arising from the squamous cells in the epidermis, the skin’s outermost layer. Approximately one million patients are diagnosed with SCC annually in the United States. While worldwide data on SCC diagnoses are inconsistently reported, the incidence outside the United States is estimated to be greater than two million diagnoses annually.

Historically, SCC has been classified as one of the “non-melanoma skin cancers” with a clinical focus on curative primary surgery. However, high risk SCC is now recognized as a significant cause of morbidity and mortality, and due to the rate of increased incidence, more patients are now estimated to die annually from SCC in the United States (approximately 15,000 patients) than from cutaneous melanoma. Similar to melanoma, treatment plan decisions are based solely upon clinical and pathology factors from the initial biopsy to estimate a patient’s risk of recurrence or metastasis. However, unlike melanoma, which uses population-based risk analysis of these factors, the estimates are based upon small patient cohorts, and our research shows that most clinicians rely upon individual clinical and pathologic features rather than a staging “group” for guiding treatment plan decisions. Our DecisionDx-SCC test, which we launched on August 31, 2020, is intended for guiding the

treatment of the estimated 20% of SCC patients, or 200,000 annually, who present with one or more high risk features, representing an estimated U.S. TAM of \$820 million.

Identifying high risk SCC presents challenges for physicians. Unlike in cutaneous melanoma, where longitudinal databases were developed in an attempt to align population-based risk of metastasis with particular clinical and pathology factors, the same level of organization has not been given to SCC. To date, there has been a lack of reliance on the two primary staging systems in the United States, the AJCC version 8 and the Brigham and Women's Hospital ("BWH") system, which are marked by widely divergent classifications for its two risk categories (high and low). Further, the National Comprehensive Cancer Network ("NCCN") staging method organizes clinical and pathology features into three risk categories (low, high and very high) based on their association with recurrence risk. A 2014 study compared the then-current AJCC version 7 and NCCN systems to assess concordance between the two. The AJCC system classified 82% as low risk while the NCCN system classified 13% as low risk. Because of the level of discordance among the risk assessment staging systems for SCC, and the lack of available databases, these staging systems end up minimally impacting treatment plans, with patients frequently being over- and under-treated, because of hesitancy by physicians to rely on them.

The two principal staging systems for SCC, AJCC (which is limited to head and neck SCC) and BWH, both classify patients according to the tumor (T), node (N) and metastasis (M) staging method and rely upon a combination of clinical or pathology factors to stage or classify risk of metastasis. The NCCN's staging method identifies the majority of patients who do go on to metastasize, but its system suffers from the lowest positive predictive value ("PPV") compared to the AJCC and BWH staging methods. Our initial clinical validation study of 321 patients was focused on patients with one or more high-risk features. Within this study cohort, using the risk criteria established within the NCCN guidelines demonstrated a sensitivity of 96% while PPV was 7% and negative predictive value ("NPV") was 90.5%. The low PPV means that 93 out of 100 SCC instances labeled as high risk by the NCCN criteria did not actually metastasize. The AJCC and BWH guidelines demonstrated a sensitivity of 38.5% and 25%, respectively, PPV of 33% and 35%, respectively and NPV of 88% and 86%, respectively. A physician that relies solely upon NCCN criteria, given the low PPV, may end up developing an adjuvant treatment plan that includes radiation, or chemotherapy or complete lymph surgical dissection, or a combination of these, for a "high-risk" patient that is ultimately appropriate for only one out of fourteen high-risk patients who will metastasize, but not for the remaining thirteen patients who would not have metastasized. The AJCC and BWH staging systems do demonstrate stronger PPV but would still recommend that two out of three patients undergo an adjuvant treatment plan who will not benefit. These accuracy metrics have created significant discordance in the approach to managing patients with high-risk features, from one end of the spectrum advocating surgical intervention for all high-risk patients to another extreme calling for a "watch and wait" approach for all high-risk patients. The end result is an unacceptable clinical discordance in the approach to treatment plans and significant over- and under-treatment for a diagnosis that leads to the most skin cancer deaths in the United States.

DecisionDx-SCC was developed to improve upon the PPV of the current staging systems for SCC. The test has been shown to be an accurate and independent predictor of recurrence risk in a cohort of 420 cutaneous SCC tumors and demonstrated a PPV of greater than 50% in that cohort. We believe that integrating DecisionDx-SCC can drive risk-appropriate treatment management decisions for physicians and patients.

Difficult-to-Diagnose Melanocytic Lesions

Difficult-to-diagnose melanocytic lesions are pigmented lesions are unusual-looking lesions that may be melanoma. There are approximately two million skin biopsies performed annually specifically to rule in or rule out a diagnosis of melanoma in the United States. Approximately 15% of these biopsies are classified as indeterminate, in which case a pathologist cannot make a definitive diagnosis as to whether the biopsy is benign or malignant. A pigmented lesion biopsy that is difficult to diagnose may lead to an indeterminate diagnosis, in which case the treating physician generally leans towards making a conservative decision and assumes that the lesion is melanoma. A definitive diagnosis of invasive cutaneous melanoma results in a treatment plan that involves wider margins for the definitive wide local excision surgery, consideration of the SLNB surgery and post-diagnosis management plans, including frequent, high intensity surveillance using advanced imaging, frequent clinical visits and encouragement to enroll in clinical studies. If the indeterminate lesion was benign, the recommendation in the majority of cases would be no additional intervention. Thus, the tendency of physicians to treat an indeterminate diagnosis as melanoma leads to significant over-treatment decisions, complications and increased healthcare costs.

myPath Melanoma and DecisionDx DiffDx-Melanoma are independent GEP tests that together comprise Castle's CDO of molecular testing solutions for difficult-to-diagnose melanocytic lesions.

Our CDO has robust diagnostic resolution for melanocytic lesions with unknown malignant potential, with validation studies demonstrating accurate diagnosis of benign and malignant lesions for 97% of cases tested.

We estimate the U.S. TAM at \$600 million for our CDO, comprised of myPath Melanoma and DecisionDx DiffDx-Melanoma.

Uveal Melanoma Overview

The incidence of uveal melanoma has remained relatively constant over time with approximately 2,000 patients diagnosed annually in the United States, representing an estimated U.S. TAM of \$8.0 million. Uveal melanomas arise from the three tissues comprising the uveal tract and vary by location with approximately 90% occurring in the choroid, 5% in the ciliary body and 5% in the iris. Uveal melanoma may also be referred to as ocular melanoma.

Approximately 97% of patients with uveal melanoma have no evidence of metastatic disease at the time of diagnosis and the success rate for definitive treatment of the primary tumor is over 90%. However, within three years, approximately 30% of all patients will experience metastases. Prior to commercial availability of DecisionDx-UM, other clinical staging and molecular diagnostic tests for uveal melanoma had been commercialized, but due to the lack of prospective studies, coupled with their low accuracy, tests were primarily used for research purposes rather than for clinical management of patients in the United States. As a result, nearly all U.S. centers grouped patients into a single, high-risk treatment plan that included frequent, high intensity surveillance using advanced imaging, frequent clinical visits and encouragement to enroll in clinical studies.

DecisionDx-UM is our proprietary GEP test that helps healthcare providers predict the risk of metastasis in patients with uveal melanoma. The test has been shown to have higher prognostic accuracy than chromosomal testing, mutation analysis or clinical features of the tumor, and is recommended by the NCCN for prognosis of uveal melanoma tumors.

Barrett's Esophagus Overview

There are approximately 4 million patients in the U.S. currently diagnosed with BE and approximately 400,000 endoscopies are performed annually on BE patients—either for initial diagnosis or repeat endoscopy for assessing possible progression of BE (active surveillance). We estimate the U.S. TAM at \$1 billion for our TissueCypher Barrett's Esophagus Assay test, which we acquired through our acquisition of Cernostics on December 3, 2021.

GI Franchise

Barrett's esophagus/
risk of progression to
esophageal cancer

384K

Patients receiving upper GI
endoscopies/year w/
confirmed Dx of BE¹

~\$1B

tissuecypher
BARRETT'S ESOPHAGUS ASSAY

1. 384,000 upper GI endoscopies/year with confirmed dx of BE (ND, IND, LGD) x \$2,513 = U.S. only TAM of ~\$1 billion

The TissueCypher Barrett's Esophagus Assay is a protein-based MAAA test that was designed and developed to address these limitations in the current standard of care for risk stratification of patients with BE. TissueCypher guides clinical management of BE by:

1. Identifying patients who are at high risk of developing EAC but are currently missed due to reliance on traditional histopathology and clinical variables. This should enable early therapeutic intervention to prevent EAC, or increase surveillance for early detection of EAC at a treatable stage; and
2. Identifying patients who are at low risk of developing EAC, enabling extension of surveillance intervals and reduction in unnecessary procedures.

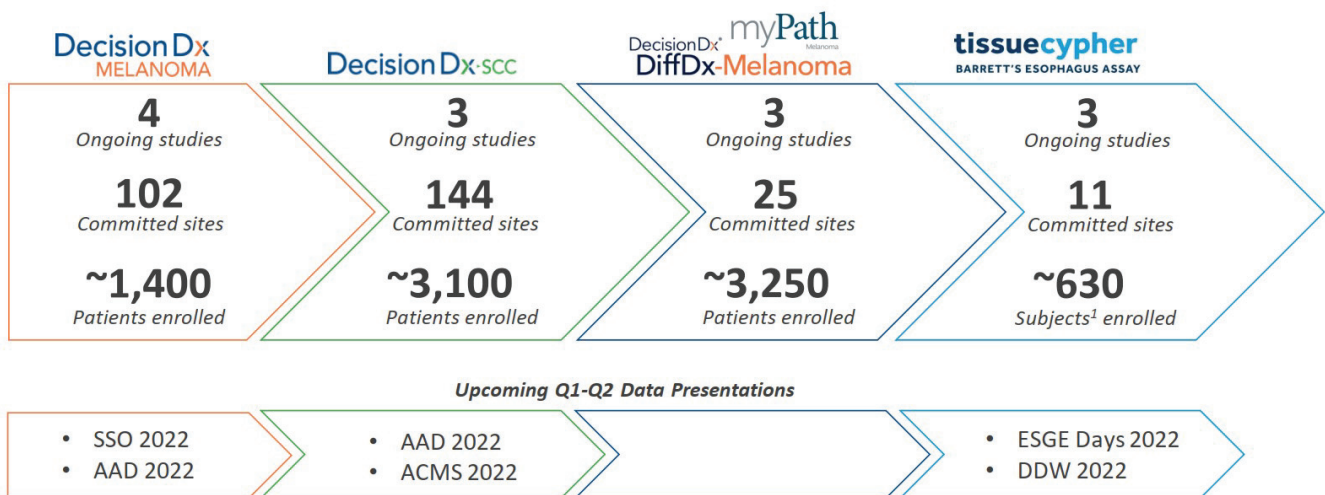
Our Testing Solutions

We use MAAA to characterize an individual patient’s tissue biology to inform specific prognosis of tumor development, death due to disease, metastasis or recurrence and aid the decision-making process of the treating physician and their patient to help optimize health outcomes and reduce healthcare costs. Due to the biological complexity of diseases, developing accurate products takes scientific diligence, stringent clinical protocols, machine learning expertise, proprietary algorithms and significant investments of time and capital. In addition, the underlying tissue samples and associated clinical outcomes data required to develop and validate these products are difficult to obtain. Once successfully developed and validated, commercial success requires generating ongoing evidence, such as clinical use documentation, to support appropriate physician adoption, reimbursement success and guideline inclusion.

We currently market five proprietary MAAA tests for use in the dermatologic, ocular and gastroenterology fields: DecisionDx-Melanoma, DecisionDx-SCC, our CDO, DecisionDx-UM and TissueCypher Barrett’s Esophagus Assay. The accuracy of each product in our portfolio is supported by multiple studies published in peer-reviewed journals since completion of the initial clinical validation studies. Also, multiple clinical impact studies have demonstrated a significant impact on physician decisions to alter their treatment plan when the results of our tests are considered in concert with the traditional clinical and pathology factors. DecisionDx-Melanoma, DecisionDx-UM, TissueCypher and myPath Melanoma are currently reimbursed by Medicare. In addition, we have received widespread positive private payor coverage and positive guideline inclusion for DecisionDx-UM, our first melanoma test, launched in January 2010. Since our inception, we have processed more than 100,000 clinical patient samples across our product portfolio.

Accelerating Investments In Clinical Development

- Generating data that supports the clinical value of our tests and supports provider and payer adoption



Our products are designed to provide the following benefits:

- Clinically Actionable Information for Physicians.** Our commercial tests provide physicians and their patients with reports that contain clinically actionable information to inform the treatment plan for each individual patient. Our reports are updated as new clinical data is generated that may enable additional clinical decisions to be made. Studies show that clinicians use our test results to make treatment plan changes. For example, four studies were initially conducted to evaluate the clinical actionability of our DecisionDx-Melanoma test, physicians utilizing the results of our test reports changed a patient’s treatment in approximately 50% of cases, indicating physician confidence in the evidence underlying our reports.
- Informed Patient Care.** The clinical evidence shows that our products are accurate predictors of a patient’s specific risk of progression to cancer, or metastasis or recurrence of their cancer based upon the gene expression profile of an ocular or dermatologic tumor or, in the case of our BE test, the spatial assessment of biomarkers, independent of available clinical and pathology factors. Physicians use this information to identify patients who are likely to benefit from an escalation of care as well as those who may avoid unnecessary treatments, such as medical, surgical and radiation interventions.

- **Reduced Healthcare Costs for Payors.** We believe our products have the potential to reduce overall healthcare costs by enabling physicians and their patients to avoid unnecessary medical and surgical interventions. As an example, without DecisionDx-Melanoma, 88% of patients who receive the SLNB surgery, which has an average in-patient reimbursed cost of \$20,000 to \$24,000, are found to be SLN-negative and remain classified as low risk. If all patients eligible for the SLNB surgery were tested with DecisionDx-Melanoma and their test results were acted upon, we estimate the potential savings to the U.S. healthcare system could be up to \$250 million, after considering the cost of DecisionDx-Melanoma.

DecisionDx-Melanoma

Decision Dx-MELANOMA

Overview

DecisionDx-Melanoma is our proprietary risk stratification GEP test developed to identify the risk of metastasis for patients diagnosed with invasive cutaneous melanoma. As of February 28, 2022, we have received orders from more than 9,300 clinicians for an aggregate of more than 90,000 tests. Under the traditional staging methods, melanomas are classified into low or and high-risk categories based on population-wide clinical and pathology features, and risk of recurrence guides a physician’s treatment plan recommendations about whether or not to offer invasive SLNB surgery, frequency and use of clinical imaging and follow-up, and/or adjuvant therapy consideration. Limitations of the current AJCC staging recommendations, and the NCCN recommendations for patient management, are demonstrated by the statistic that nearly 60% of the patients who die each year from melanoma are initially diagnosed with Stage I or II melanoma (the two lowest categories of risk). This reflects a need for better risk-stratification or prognostic markers to identify high-risk patients.

To address this need for a more accurate predictor of metastatic risk, we discovered, developed, validated and continue to support the performance of the DecisionDx-Melanoma test. This product is designed to help physicians identify high-risk tumors from among patients receiving a Stage I, II or III diagnosis based on the expression of 31 genes in the primary tissue. DecisionDx-Melanoma does not change the standard diagnostic workflow followed when performing a biopsy of a suspicious lesion, and utilizes the formalin-fixed, paraffin embedded biopsy or wide local excision tissue used to diagnose melanoma and determine AJCC stage. An additional biopsy is not needed. Test results are reported as GEP main classes (Class 1 (low risk) or Class 2(high risk)) or as subclasses (Class 1A represents the lowest risk group, Class 1B/2A represents an increased risk group and Class 2B represents the highest risk group), based on a continuous score ranging from 0-1.

In March 2021, we announced that DecisionDx-Melanoma utilizes an Integrated Test Result (“ITR”), designed to provide more precise risk prediction for patients with Stage I, II or III melanoma. The ITR is calculated by an independently validated algorithm (“i31-GEP”) that uses the DecisionDx-Melanoma continuous score in combination with clinical and pathology factors to provide a precise and personalized prediction of SLN positivity. In October 2021, we announced the completion of independent validation of a new, separate algorithm that integrates the DecisionDx-Melanoma continuous score to provide a prediction of an individual patient’s risk of metastasis and recurrence (“ROR”). This new i31-GEP algorithm for ROR includes the additional endpoints of recurrence-free survival (“RFS”) and distant metastasis-free survival, which are not currently provided by the American Joint Committee on Cancer Eighth Edition staging system. These endpoints are anticipated to be helpful when determining appropriate treatment pathways for each patient’s disease. Results generated by the i31-GEP algorithm guide discussions and recommendations, within current risk-based guidelines, for the SLNB surgical procedure or for surveillance methodologies. i31-GEP to predict SLN metastasis is an artificial intelligence-based neural network algorithm (independently validated in a cohort of 1,674 prospective, consecutively tested patients with T1-T4 cutaneous melanoma) that integrates the DecisionDx-Melanoma test result with the patient’s traditional clinical and pathology features, such as Breslow thickness, ulceration, mitotic rate and age. i31-GEP for ROR combines the 31-GEP continuous score with tumor thickness, ulceration status, mitotic rate, SLN status, age and tumor location to predict likelihood of recurrence, distant metastasis and melanoma specific death within 5 years of the melanoma diagnosis. The algorithm was developed using 1,581 tumors from patients diagnosed with melanoma and was validated in 523 patients. We expect to launch an app based on i31-GEP and the ITR later in 2022.

Clinical Validation

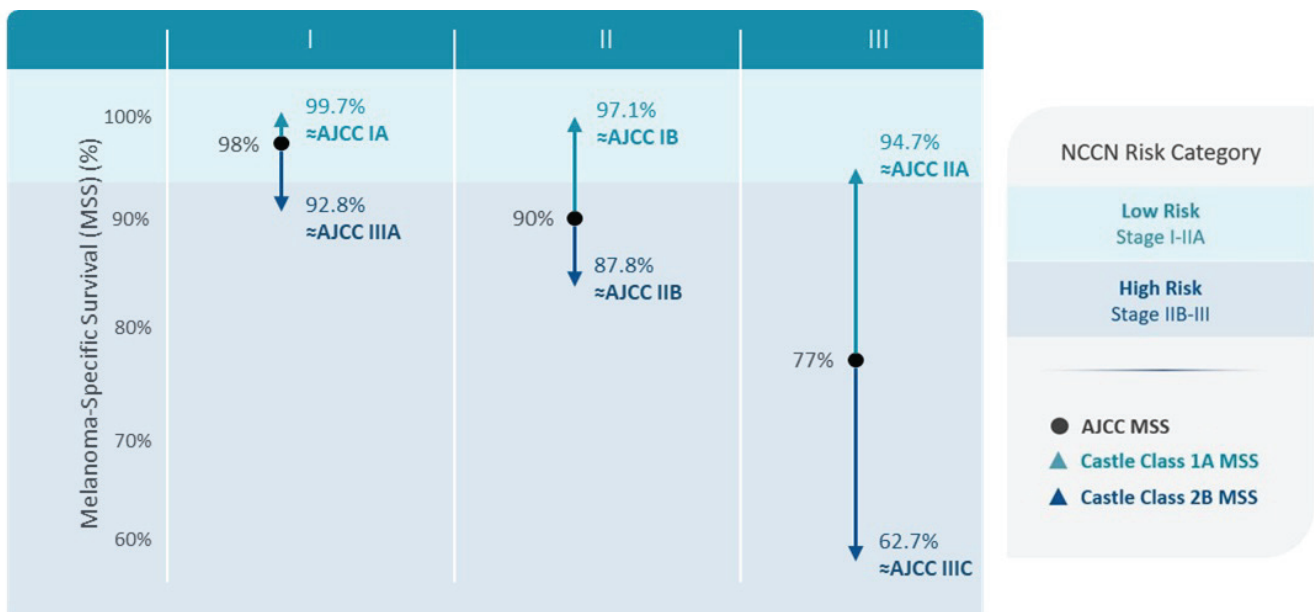
We have published more than 35 peer-reviewed articles demonstrating the analytical validity, clinical validity and clinical utility of DecisionDx-Melanoma, and we believe the clinical validation studies represent the largest clinical validation program of the metastatic risk of cutaneous melanoma ever conducted. Based on our published data, we have shown that DecisionDx-Melanoma is an accurate independent predictor of the risk of metastasis or recurrence.

Our first study, published in January 2015, analyzed 104 patients with Stage I, II and III melanoma from an independent cohort with long-term outcomes data. This study reported a five-year disease-free survival rate of 98% for patients with Stage I and II melanoma who received a DecisionDx-Melanoma Class 1 test result. In addition, the study also reported that only 2% of patients with a Class 1 test result were SLN-positive.

Our January 2019 study published in the Journal of the American Academy of Dermatology reviewed data on 690 patients with Stage I, II and III melanoma from three previously published long-term archival publications, and enabled analysis of clinically important subgroups considered low-risk based on staging criteria. Overall, the study reported a five-year melanoma specific survival rate of 99% for patients with Stage I, II or III melanoma who received a DecisionDx-Melanoma Class 1A test result.

Our long-term outcomes study data shows that DecisionDx-Melanoma can provide a more specific individual risk of metastasis and death from melanoma that is distinct from the AJCC staging approach that limits prediction to clinical and pathology factors. The only endpoint reported by the AJCC staging approach is death from melanoma. Within patients diagnosed with Stage I melanoma, a DecisionDx-Melanoma Class 2B result predominantly identifies a patient with a risk of death that is similar to a patient with Stage IIIA melanoma (see graph below). By comparison, DecisionDx-Melanoma Class 1A results indicate a 99.7% likelihood of survival from melanoma at five years. Within patients diagnosed with Stage II melanoma, DecisionDx-Melanoma can distinguish between patients who have a very low risk of death from melanoma (>97.1% likelihood of survival at 5-years) from those who have a higher risk of death from melanoma that is similar to a patient with Stage IIB melanoma. Within patients diagnosed with Stage III melanoma, DecisionDx-Melanoma can identify patients who have a likelihood of death from melanoma similar to a patient with Stage IIA melanoma, with the remainder having a risk similar to a patient with Stage IIIC melanoma.

The ability of DecisionDx-Melanoma to accurately reclassify the risk of recurrence or risk of death is clinically significant because NCCN guidelines recommend that the duration and frequency of follow-up and intensity of cross-sectional imaging be based on a patient's individual conditional probability of recurrence. The NCCN guideline cut-point for these decisions is between Stage I-IIA versus Stage IIB-III. For example, the chart below demonstrates that a patient diagnosed with Stage I melanoma but who has received a DecisionDx-Melanoma Class 2B test result has a melanoma specific survival rate of 92.8%, which is similar to the risk for a patient diagnosed with Stage IIIA melanoma. Today, patients diagnosed with Stage III melanoma are recommended to have an increased follow-up schedule, undergo routine cross-sectional imaging, consider initiation of adjuvant therapy, such as an anti-PD1 inhibitor, and consider enrollment in a clinical trial.



The first prospective, multi-center study of 322 patients diagnosed with Stage I, II and III melanoma was published in August 2017. This initial analysis reported a RFS rate of 97% and overall survival rate of 99% for patients with Stage I, II and III

melanoma who received a DecisionDx-Melanoma Class 1 test result. Since that time, six prospective studies have been published and each consistently demonstrate the accurate and independent prognostic value provided by DecisionDx-Melanoma for identifying low- and high-risk melanoma tumors.

When evaluating DecisionDx-Melanoma, one of the most important criteria is whether the test adds new information that is independent of the traditional clinical and pathology factors. The formal statistical method used to evaluate independence is the Cox multivariate analysis. Outputs of the Cox multivariate analysis include statistical significance, measured by p-value, as well as the power of the result, measured by Hazard Ratio (“HR”). A p-value of less than 0.05 indicates statistical significance and thus independence. If statistical significance is reached, then the HR indicates the power of the result, with a higher HR indicating greater outcome prediction. For example, an HR of nine means that patients with a high-risk test result are nine times more likely to experience metastasis or death than a low-risk test result. The table below shows the Cox multivariate analysis of the disease-free survival, melanoma-specific survival and recurrence free survival from the four performance studies noted above.

Cox Multivariate analyses showing the strengthen of independence of DecisionDx-Melanoma over traditional clinical and pathology factors											
Gerami, CCR 2015 Endpoint: Disease Free Survival, Stage I and II			Gastman, JAAD 2019 Endpoint: Melanoma Specific Survival, Stage I, II and III			Hsueh Jrnl Hem/Onc 2017 Endpoint: Recurrence Free Survival, Stage I, II and III			Podlipnik JEAVD 2019 Endpoint: Recurrence Free Survival, Stage I, II		
	HR	p-value		HR	p-value		HR	p-value		HR	p-value
AJCC high risk	5.40	0.002	Tumor thickness	1.16	0.05	Tumor thickness	1.43	0.001	AJCC high risk	1.52	0.58
Decision-Melanoma Class 2	9.55	0.002	Mitotic rate	0.97	0.34	Mitotic rate	1.05	0.005	Age	3.7	0.9
			Ulceration present	0.77	0.47	Ulceration present	1.89	0.17	DecisionDx-Melanoma Class 2	28.37	0.01
			SLN positivity	3.38	0.0003	SLN positivity	2.46	0.035			
			DecisionDx-Melanoma Class 2B	9.02	0.004	DecisionDx-Melanoma Class 2	7.15	0.003			

AJCC = Stage IIB – III
Mitotic rate = # of dividing cancers cells

The American Academy of Dermatology and other organizations use the Strength of Recommendation Taxonomy (“SORT”) system to evaluate prognostic tests such as DecisionDx-Melanoma. The SORT system ranks evidence of clinical validity as levels 1, 2 or 3, and assigns a strength of recommendation as levels A, B or C. A SORT level 1A is the highest level and 3C is the lowest. For SORT ranking, “a systematic review or meta-analysis of good quality studies” or “a prospective study with good follow-up” represents a level 1 for good quality evidence of clinical validity. For SORT strength of recommendation, “consistent, good quality evidence” represents a level A recommendation. A systematic review and meta-analysis was published in the Journal of the American Academy of Dermatology in 2020 in an article titled “Molecular risk prediction in cutaneous melanoma: a meta-analysis of the 31-gene expression profile prognostic test in 1,479 patients.” This meta-analysis reviewed multiple peer-reviewed published clinical validation studies of DecisionDx-Melanoma, including prospective studies. The meta-analysis and the prospective studies satisfied the level 1 ranking of good quality studies and the consistency of DecisionDx-Melanoma data across these studies satisfied the level A strength of recommendation. Thus, the authors concluded that DecisionDx-Melanoma achieved a 1A level of evidence of clinical validity and strength of recommendation under the SORT system. Furthermore, as shown below, the multi-variate analysis for RFS found DecisionDx-Melanoma to be the strongest predictor of ROR compared to the evaluable clinical and pathology factors.

Multi-variate Analysis Output of Meta-Analysis for Random Effects	
Factors	Hazard Ratio for Recurrence Free Survival
Breslow thickness Random effects	1.12 (1.03 – 1.22)
Ulceration Random effects	1.63 (1.18 – 2.25)
Age Random effects	1.01 (0.99 – 1.03)
SLNB Random effects	2.42 (1.88 – 3.10)
DecisionDx-Melanoma Random effects	2.83 (2.01 – 4.19)

In addition, we conducted a prospective, multi-center study of 1,421 patients, which was published in *Future Oncology* in January 2019, that focused on the performance of DecisionDx-Melanoma to predict metastasis to the SLN. This study found that patients with a DecisionDx-Melanoma Class 1A test result with melanomas less than or equal to 2.0 mm thick, which represents 86% of all melanomas, have a 95% probability for an SLN-negative biopsy result. Analyzing this data by age shows that patients 65 years of age or older have a 98% NPV, those between 64 and 55 years of age have a 95% NPV and patients under 55 years of age have a 92% NPV. For physicians and patients evaluating whether to use DecisionDx-Melanoma to guide decision-making on the SLNB surgery, the impact on melanoma specific survival is an important consideration if the SLN status is not known. To address this, we analyzed the long-term outcome data from our Gastman 2019 publication and showed that patients of all ages with a melanoma less than or equal to 2.0 mm thick and a DecisionDx-Melanoma Class 1A test result had a five-year melanoma specific survival rate of 99.6%, while similar patients 55 years or older had a melanoma specific survival rate of 99.3%. This study showed that use of DecisionDx-Melanoma for patients with melanomas of less than or equal to 2.0 mm thick could potentially result in 74% fewer SLNB surgeries.

Clinical Utility

We completed and published four consecutive studies between September 2016 and March 2018 documenting how DecisionDx-Melanoma impacts treatment plan decisions. Based on the results of our DecisionDx-Melanoma test reports, physicians changed their treatment plan recommendations approximately 50% of the time. This change in the management of patient treatment plan recommendations compares favorably to leading molecular diagnostic tests as well as to the SLNB surgery, which only changes clinical decision-making approximately 12% of the time.

Study	Design	# of Patients	% Change in Management
Berger et al. CMRO 2016	Prospectively tested cohort, multi-center. Retrospective pre-test / post-test management.	156	53%
Dillon et al. SKIN J Cutan Med 2018	Prospective, multi-center: pre-test / post-test management.	247	49%
Farberg et al. J Drugs Derm 2017	169 physician impact study: patient vignettes with pre-test / post-test management.	n/a	47-50%
Schuitevoerder et al. J Drugs Derm 2018	Prospectively tested cohort, single center. Retrospective pre-test / post-test management; and modeling of prospective cohort.	91	52%

Building on our clinical utility evidence, in October 2020, the publication in *Future Oncology* of a retrospective study, titled “Integrating the melanoma 31-gene expression profile test to surgical oncology practice within national guideline and staging recommendations,” showed that DecisionDx-Melanoma impacted management decisions for patients diagnosed with Stage I – III melanoma under the AJCC framework. Study authors developed a recommended melanoma patient care algorithm that incorporates DecisionDx-Melanoma to help inform frequency and duration of follow-up visits, blood work and surveillance imaging in line with predicted metastatic risk. The patients’ DecisionDx-Melanoma test result was found to have an impact on the number and duration of follow-up and surveillance visits, and patients assessed as having a high risk of metastasis (designated by a DecisionDx-Melanoma Class 2 test result) received more intensive management than patients assessed as having a low risk (designated by a DecisionDx-Melanoma Class 1 test result). Clinicians using the test were shown to adjust patient management in a risk-appropriate direction, within recommendations of national guidelines.

These studies illustrate how physicians use DecisionDx-Melanoma to inform the treatment pathway for patients who have been diagnosed with invasive cutaneous melanoma. Our DecisionDx-Melanoma test informs two initial treatment decisions: (1) to determine whether to offer and recommend the SLNB surgery to patients with melanomas less than or equal to 2.0 mm thick, and (2) following this decision, to guide the appropriate post-SLNB surgery treatment plan for their patients, including decision-making regarding advanced imaging, frequency of clinical visits, referral to medical oncology, adjuvant therapy, clinical trial enrollment, and watchful waiting.

Health Economics

We believe our products have the potential to reduce overall healthcare costs by enabling physicians and their patients to avoid unnecessary medical and surgical interventions. As an example, without DecisionDx-Melanoma, 88% of patients who receive the SLNB surgery, which has an average in-patient reimbursed cost of \$20,000 to \$24,000, are found to be SLN-negative and remain classified as low risk under the AJCC framework. If all patients eligible for the SLNB surgery were tested using DecisionDx-Melanoma and their test results were acted upon, we estimate the potential savings to the U.S. healthcare system could be up to \$250 million, after considering the cost of DecisionDx-Melanoma.

In addition, DecisionDx-Melanoma can be used to make more informed decisions on advanced imaging, frequency of clinical visits, referral to medical oncology, adjuvant therapy initiation and clinical trial enrollment. In some cases, a DecisionDx-Melanoma test result may guide an appropriate reduction in these decisions based upon a low risk of metastasis, while in others

it will guide an appropriate increase in medical or surgical intervention with the end result being improved use of healthcare resources.

The American Medical Association's ("the AMA's") Current Procedural Terminology Editorial Panel accepted Castle's application for a Category I MAAA, Current Procedural Terminology ("CPT") code for its DecisionDx-Melanoma test. The CPT Editorial Panel is an independent group of expert volunteers representing various sectors of the healthcare industry. Its role is to ensure that code changes undergo evidence-based review and meet specific criteria. The code became effective on January 1, 2021. With this acceptance, two of our proprietary MAAA tests, DecisionDx-Melanoma and DecisionDx-UM, have met the criteria required for a Category I MAAA CPT code.

DecisionDx-SCC

Decision Dx-SCC

The current treatment pathway (staging systems that rely on combination of clinical or pathology factors to stage or classify risk of metastasis) for patients identified as having high-risk cutaneous SCC suffers from a low PPV for risk of metastasis or recurrence. As a result, many patients categorized as high risk received adjuvant therapy and other unnecessary medical and surgical interventions even though they would not have gone on to metastasize. Conversely, the low predictive accuracy of current methods to identify high-risk patients can lead to undertreatment if patients with a truly high biologic risk are missed. Because these patients cannot currently be identified, they will miss the opportunity to receive the most aggressive of today's therapeutic options.

To address this clinical need in SCC, we developed DecisionDx-SCC, a proprietary 40-gene expression profile test that uses an individual patient's tumor biology to predict individual risk of SCC metastasis for patients with one or more risk factors. The test result, in which patients are stratified into a Class 1, 2A or 2B risk category, predicts individual metastatic risk to inform risk-appropriate management. The test is designed to provide a better PPV while maintaining similar NPV. We commercially launched DecisionDx-SCC on August 31, 2020. Nine peer-reviewed publications have demonstrated that DecisionDx-SCC is an independent predictor of metastatic risk and/or that integrating DecisionDx-SCC with current prognostic methods can add positive predictive value to clinician decisions regarding staging and management.

In 2020, development and validation data on DecisionDx-SCC was published in the Journal of the American Academy of Dermatology in an article titled "Validation of a 40-Gene Expression Profile Test to Predict Metastatic Risk in Localized High-Risk Cutaneous Squamous Cell Carcinoma." The study findings indicate that DecisionDx-SCC demonstrated strong independent prognostic value in multivariate analysis compared to the traditional BWH and AJCC staging systems. More recently, further validation results of a cohort of 420 patients with high-risk SCC from 33 U.S. centers were published in *Future Oncology*. The study titled, "Enhanced Metastatic Risk Assessment in Cutaneous Squamous Cell Carcinoma With the 40-Gene Expression Profile Test," upheld previous results demonstrating that DecisionDx-SCC demonstrated significant prognostic value, and that cases with a Class 1 result had metastasis rates near the general SCC population while Class 2B patients had rates greater than 50%. Additionally, a study focused on tumors of the head and neck region also showed strong stratification of risk by DecisionDx-SCC in that cohort, and independent value added to risk prognosis by the test in multivariable models that include other risk factors. We have ongoing multi-center studies involving more than 75 U.S. centers.

Comprehensive Diagnostic Offering



Of the two million suspicious pigmented lesions biopsied annually in the U.S., we estimate that approximately 300,000 of those cannot confidently be classified as either benign or malignant through traditional histopathology methods. A biopsy of a pigmented lesion may lead to an indeterminate diagnosis, in which case the treating physician generally leans towards making a conservative decision and assumes that the lesion is melanoma.

To address this clinical need, we developed DecisionDx DiffDx-Melanoma, a proprietary 35-GEP test designed to be used as an ancillary tool to histopathology when the distinction between a benign lesion and melanoma is uncertain. We commercially launched this product on November 2, 2020. DiffDx-Melanoma classifies these lesions as benign (gene expression profile suggestive of benign neoplasm); intermediate-risk (gene express profile cannot exclude malignancy); or malignant (gene expression profile suggestive of melanoma). Interpreted in the context of other clinical, laboratory and histopathologic information, DiffDx-Melanoma is designed to add diagnostic clarity and confidence for dermatopathologists while helping dermatologists deliver more informed patient management plans. Validation of this test included a variety of benign and malignant lesions. DecisionDx DiffDx-Melanoma, in tandem with myPath Melanoma, enables us to provide our CDO of molecular testing solutions for difficult-to-diagnose melanocytic lesions.

In 2020, two studies were published in SKIN: The Journal of Cutaneous Medicine. The development and validation study, “Development and Validation of a Diagnostic 35-Gene Expression Profile Test for Ambiguous or Difficult-To-Diagnose Suspicious Pigmented Skin Lesions,” showed that our DecisionDx DiffDx-Melanoma test had a technical success rate of 97%, meaning that a test result was successfully generated, and achieved accuracy metrics that could alleviate uncertainty in difficult-to-diagnose lesions leading to decreased unnecessary procedures while appropriately identifying at-risk patients. The clinical utility study, “A 35-Gene Expression Profile Test for Use in Suspicious Pigmented Lesions Impacts Clinical Management Decisions of Dermatopathologists and Dermatologists,” concluded that the diagnosis of challenging melanocytic neoplasms and subsequent clinical management decisions were influenced by DecisionDx DiffDx-Melanoma results in alignment with the test result. The utility of the test may provide the opportunity for clinicians to deliver more informed patient management plans.

Similar to DecisionDx DiffDx-Melanoma, myPath Melanoma is a proprietary GEP test that we acquired from Myriad Genetics, Inc. in May 2021, following rigorous validation in cutaneous melanocytic lesions to accurately differentiate between benign and malignant melanocytic lesions of unknown potential. myPath Melanoma has over 35,000 clinically resulted cases and 9 publications supporting the accurate diagnosis of benign or malignant lesions by the test. The test evaluates the expression of 23 genes using standard quantitative qRT-PCR and provides an accurate and objective classification suggestive of benign, intermediate, or malignant lesions.

We currently offer both myPath Melanoma and DecisionDx DiffDx-Melanoma in an integrated workflow to enhance both accuracy and technical reliability of diagnostic testing. This comprehensive diagnostic workflow leverages the strengths of both diagnostic GEP tests to provide improved diagnostic clarity. This offering is supported by 12 peer-reviewed publications.

DecisionDx-UM

Decision Dx-UM

Overview

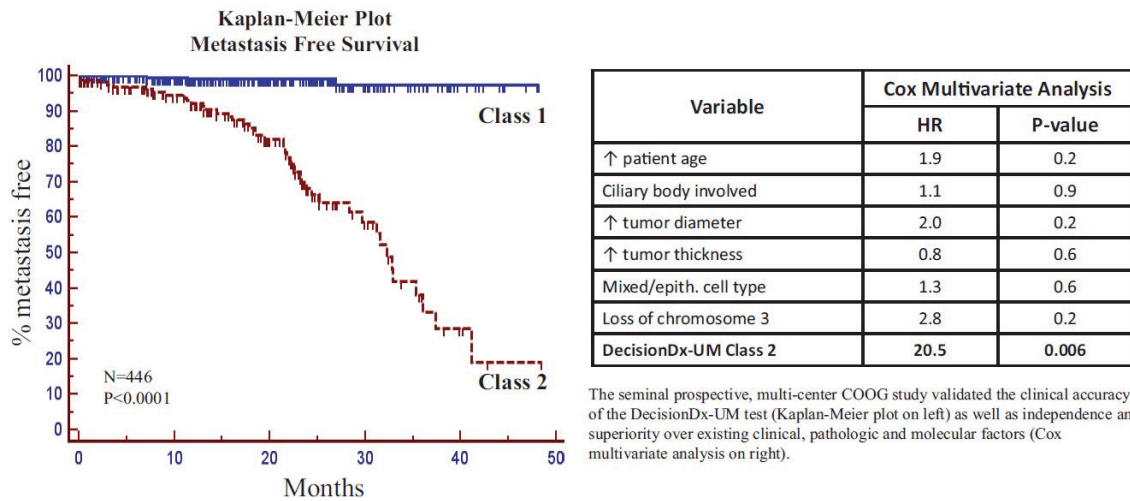
At the time of diagnosis nearly all patients with uveal melanoma have no evidence of metastasis yet, approximately 30% of uveal melanoma patients will metastasize within five years and nearly 50% of uveal melanoma patients will metastasize at some point. Traditional clinical staging and molecular diagnostic tests for uveal melanoma have been commercialized, but until recent years the lack of prospective studies of these tests, coupled with low accuracy, resulted in these tests primarily being used for research purposes rather than for clinical management of patients in the U.S. As a result, before commercial availability of DecisionDx-UM, nearly all U.S. centers grouped patients into a single, high-risk treatment plan that included frequent, high intensity surveillance using advanced imaging, frequent clinical visits and encouragement to enroll in clinical studies.

DecisionDx-UM is our proprietary GEP test that helps healthcare providers predict the risk of metastasis in patients with uveal melanoma. We licensed the intellectual property for DecisionDx-UM from The Washington University in St. Louis, Missouri (“WUSTL”), and completed analytical validation and began marketing DecisionDx-UM in late 2009 for use in patients diagnosed with uveal melanoma without evidence of metastatic disease. DecisionDx-UM identifies patients at low risk for progression of their uveal melanoma so that their physicians can appropriately de-escalate the level of care provided. DecisionDx-UM is delivered to approximately 1,600 patients annually, representing approximately 80% of the patients diagnosed in the United States.

Twenty-one peer-reviewed publications involving more than 3,000 patients support the clinical validity and utility of DecisionDx-UM.

The Kaplan-Meier plot from the initial prospective, multi-center Collaborative Ocular Oncology Group (“COOG”) study found that a DecisionDx-UM Class 2 result was more strongly associated with metastasis than any other clinical, pathological or molecular factor, and the negative predictive value for patients with a DecisionDx-UM Class 1 result was 99%. This study also

compared DecisionDx-UM to the traditional staging based on clinical and pathology factors, and chromosome 3 status (an alternative molecular test to predict the risk of metastasis in uveal melanoma), using Cox multivariate analysis, and found that the only statistically significant factor in predicting a likelihood of metastasis was DecisionDx-UM.



The data from the COOG study, as well as the consistency shown from the additional clinical validity studies, has supported widespread adoption of DecisionDx-UM with more than 90% of the ocular oncology institutions in the United States ordering this test. DecisionDx-UM has been used to guide treatment plan decisions regarding the intensity of a patient’s surveillance and management plan as well as clinical trial enrollment. The current NCCN Guidelines for Uveal Melanoma (last updated June 2021) incorporate DecisionDx-UM as the first risk of distant metastasis predictor and recommend that class result be used to guide frequency and intensity of systemic imaging.

TissueCypher

tissuecypher

BARRETT’S ESOPHAGUS ASSAY

Esophageal cancer is one of the fastest-growing cancers (by incidence) in the world. The incidence of this once rare cancer has increased by more than 500% since the 1970s. Esophageal cancer remains highly lethal, with a five-year survival rate of 19%.

Chronic reflux in the esophagus causes changes to the molecular and cellular features of the esophagus, which often results in a condition called BE. BE is a serious complication of GERD and a risk factor for the development of esophageal cancer.

There are approximately 4 million patients in the U.S. diagnosed with BE, and annually, approximately 400,000 endoscopies are performed on BE patients. The TissueCypher Barrett’s Esophagus Assay, which is supported by eight peer reviewed publications, addresses an unmet need in BE, as it is designed to objectively and accurately predict progression from non-dysplastic, indefinite for dysplasia and low-grade dysplasia BE to high-grade dysplasia or esophageal adenocarcinoma (“EAC”). This is critical, as EAC is highly lethal, and endoscopic eradication therapy in patients with BE has been proven to reduce progression to EAC. As of February 28, 2022, two abstracts for GI conferences (podium presentations at European Society of Gastrointestinal Endoscopy Days 2022 and Digestive Disease Week 2022) and one peer-reviewed publication have been accepted.

BE is the only known precursor to EAC, which is highly lethal and has a five-year survival rate of 19%, according to Cancer Facts and Figures, ACS 2020. Treatment options, particularly for advanced EAC, are limited, and early detection is critical for optimal patient management. As a result, an estimated 4 million patients with BE in the U.S. are in active surveillance programs, which involve periodic endoscopic surveillance of the esophagus with the goal of detecting malignant progression at a treatable stage. During the endoscopy, biopsies are obtained from the affected tissue, and BE is graded based upon pathology features (histologic assessment) of these biopsies into High-Grade Dysplasia (“HGD”), Low-Grade Dysplasia (“LGD”), Indefinite Dysplasia (“IND”) and Non-Dysplastic (“ND”). Generally, patients with HGD undergo esophageal eradication therapy, which may include ablation or surgical removal of the BE lesions. Patients with LGD generally undergo either endoscopic surveillance every three to six months or endoscopic eradication therapy, while patients with IND or ND generally undergo endoscopic surveillance every three months to five years. While treatment decisions, including surveillance timing, are

directed by pathology grading, this approach is limited by significant inter-observer variation (pathology discordance) in the grading of tissue biopsies. This discordance is found between community pathologists, as well as pathologists who specialize in BE in large academic centers. Furthermore, molecular and cellular changes associated with progression to cancer often precede the morphologic changes that pathologists can evaluate using histology.

Additionally, while patients with ND, IND and LGD do have a lower rate of progression to EAC than HGD, due to the higher incidence of ND, IND and LGD, these patients represent approximately 63% of patients who may progress to EAC. Since endoscopic eradication therapy is performed with the expectation that it will reduce or stop progression to EAC, the fact that the majority of patients who progress are not graded as having HGD represents a significant unmet clinical need. In addition, the recommendations for the frequency of endoscopic surveillance are based upon low to moderate quality evidence. Together, these limitations in the current standard of care for risk assessment of patients with BE leads to overuse of endoscopies and imprecise use of endoscopic eradication therapy procedures, adding unnecessary costs that fail to reduce the incidence and mortality associated with EAC.

The TissueCypher Barrett's Esophagus Assay is a protein-based MAAA test that was designed and developed to address these limitations in the current standard of care for risk stratification of patients with BE. TissueCypher guides clinical management of BE by:

1. Identifying patients who are at high risk of developing EAC but are currently missed due to reliance on traditional histopathology and clinical variables. This should enable early therapeutic intervention to prevent EAC, or increase surveillance for early detection of EAC at a treatable stage; and
2. Identifying patients who are at low risk of developing EAC, enabling extension of surveillance intervals and reduction in unnecessary procedures.

The TissueCypher Barrett's Esophagus Assay is a laboratory developed test ("LDT") provided as a testing service to healthcare providers across the United States, and provides automated, objective risk stratification for patients with ND, IND and LGD BE. It is the only commercially available test providing prognostic risk assessment from esophageal pinch biopsies.

Our Commercial Channel

Sales and Marketing

Our sales and marketing efforts are primarily focused on the United States skin cancer and gastroenterology markets. We employ a direct sales and marketing strategy to educate clinicians on the clinical and economic benefits of our products. Our sales approach is highly technical, and our team is trained to articulate the scientific and clinical evidence behind our products and how they influence the clinical care pathway and ultimately improve patient outcomes. Our sales force is focused on educating and informing the entire patient care team, which consists of treating clinicians, nurses, laboratory and pathology personnel, and finance administrators, on the appropriate use and value of our tests.

The principal focus of our current commercial efforts is to educate clinicians and pathologists on the value of our molecular diagnostic testing products through our direct sales force in the U.S. In dermatology, we began 2020 with 32 outside sales territories. In the third quarter of 2020, we expanded our dermatologic commercial team to create a dedicated sales force of ten territories to support the launch of our DecisionDx Diff-Dx Melanoma test to dermatopathologists. During the first half of 2021, we folded this dedicated team into our existing sales team and completed a further expansion, bringing our dermatologic sales force to the mid-60s. In connection with our acquisition of Cernostics in December 2021, we hired an initial commercial team of approximately 14 outside sales territories, along with commensurate internal sales associates and medical science liaisons, to support our launch of the TissueCypher Barrett's Esophagus Assay. This dedicated team focuses on gastroenterology specialists that diagnose and manage patients with BE. However, we will continue to evaluate our mix of outside sales territories, inside sales support, marketing and medical affairs in the context of our dermatologic tests and gastroenterology tests and adjust our investments based upon these evaluations.

In 2021, we entered into an agreement with Modernizing Medicine ("ModMed") that established an interface with ModMed's electronic health records system, EMA®. The interface is designed to enable dermatologic clinicians to order our DecisionDx skin cancer tests from directly within a patient's medical record in EMA. Our full suite of dermatologic tests is now available to order within EMA.

DecisionDx-UM addresses a small cancer market, and patients are managed by a small group of ocular oncology surgeons, generally ophthalmology or retina trained specialists. We serve these patients and their physicians by providing highly technical interactions that focus on optimizing the appropriate use of our proprietary and ancillary products.

Medical Affairs

We also deploy an experienced medical affairs group to assist education of treating physicians and key opinion leaders, to identify and engage sites for our sponsored clinical studies and to evaluate collaborative study opportunities. Our medical affairs strategy complements our sales, marketing and clinical research operations efforts.

Reimbursement

The primary source of revenue for our products is reimbursement from third-party payors, which includes government payors, such as Medicare and the U.S. General Services Administration (“GSA”), and commercial payors, such as insurance companies. Achieving broad coverage and reimbursement of our current products by third-party payors and continued Medicare coverage are key components of our financial success. De novo coverage by government and third-party payors for our pipeline tests will be important over time.

Government Payors

Medicare coverage is limited to items and services that are within the scope of a Medicare benefit category and that are reasonable and necessary for the diagnosis or treatment of an illness or injury. Local coverage determinations (“LCDs”) are made through an evidence-based process by Medicare Administrative Contractors (“MACs”) with opportunities for public participation.

Palmetto GBA MoIDX (“Palmetto”) the MAC responsible for administering MoIDX, the program that assesses molecular diagnostic technologies, issued a final LCD for DecisionDx-Melanoma, which became effective on December 3, 2018. Noridian Healthcare Solutions, LLC (“Noridian”), the MAC responsible for administering claims for laboratory services performed in Arizona, adopted the same coverage policy as Palmetto on that date, and subsequently issued a final LCD on February 10, 2019. This LCD provided for coverage for patients who are eligible for the SLNB surgery with cutaneous melanoma tumors of 2.0 mm in thickness or less, and patients with clinically negative SLN basins who are being considered for the SLNB surgery to determine eligibility for adjuvant therapy. Melanomas less than or equal to 2.0 mm thick represent 86% of all melanomas. The median age at diagnosis is 63 years old, therefore the Medicare eligible population represents close to 50% of the addressable market.

Palmetto issued a final expanded LCD for DecisionDx-Melanoma, effective November 22, 2020. With this expanded LCD and the accompanying billing and coding articles, in 2021 approximately 96% of the DecisionDx-Melanoma tests performed for Medicare patients have met the coverage criteria. Noridian has adopted the same coverage policy as Palmetto and also issued an expanded final LCD for DecisionDx-Melanoma, effective December 6, 2020.

Separately, Palmetto issued a final LCD for DecisionDx-UM, which became effective in July 2017, and Noridian issued a similar LCD that became effective in September 2017. The Noridian LCD provides for coverage to determine metastatic risk in connection with the management of a patient’s newly diagnosed uveal melanoma and to guide surveillance and referral to medical oncology for those patients. Similar to cutaneous melanoma, the median age at diagnosis for uveal melanoma is estimated at 58-62 years old, therefore the Medicare eligible population represents close to 45% of the addressable market.

On May 17, 2019, CMS determined that DecisionDx-UM meets the criteria for “existing advanced diagnostic laboratory test” status, also referred to as “existing ADLT” status. For 2020, our rate was set by Noridian, our local MAC, but effective in 2021 our rate is set annually based upon the median private payor rate for the first half of the second preceding calendar year. Our rate for 2021 was \$7,776 and will remain at \$7,776 for 2022, in each case based on the calculation of the median private payor rate.

Also, on May 17, 2019, CMS determined that DecisionDx-Melanoma meets the criteria for “new ADLT” status. Accordingly, from July 1, 2019 through March 31, 2020, the Medicare reimbursement rate was equal to the initial list price of \$7,193. From April 1, 2020 through December 31, 2021, the rate was also \$7,193, which was calculated based upon the median private payor rate for DecisionDx-Melanoma from July 1, 2019 to November 30, 2019. CMS has informed us that the rate for 2022 will continue to be \$7,193, based on the median private payor rate.

myPath Melanoma is currently covered under a MoIDX LCD policy through Noridian that oversees laboratories in both Utah and Arizona. Noridian issued an LCD that became effective in June 2019. On September 6, 2019, myPath Melanoma was approved as a new ADLT. The rate for 2022 will be \$1,950.

TissueCypher is performed in our Pittsburgh, Pennsylvania laboratory and falls under the Medicare jurisdiction that is managed by Novitas Solutions (“Novitas”). Novitas previously reviewed TissueCypher and we are receiving payments for claims according to the Clinical Lab Fee Schedule (“CLFS”). For 2022, CMS published in its CLFS a payment amount of \$2,513 for the test.

Beginning in 2023, the rates for the DecisionDx-Melanoma, DecisionDx-UM, and myPath Melanoma tests will be set annually based upon the median private payor rate for the first half of the second preceding calendar year. For example, the rate for 2023 will be set using median private payor rate data from January 1, 2021 to June 30, 2021.

In the second quarter of 2020, we submitted our technical assessment dossier for DecisionDx-SCC to Palmetto and Noridian. The dossier was accepted as complete in the third quarter of 2020. In early 2021, we submitted our technical assessment dossier for DecisionDx DiffDx-Melanoma. The dossier was accepted as complete in the first quarter of 2021. We expect that draft LCDs for DecisionDx-SCC and DecisionDx DiffDx-Melanoma could potentially be posted by the end of the second quarter of 2022 resulting in potentially final LCDs effective in 2023. However, there is no assurance that the timing of any draft or final LCD will match our expectations or our historical experience with LCDs for our other tests.

In the second quarter of 2021, Palmetto and the other MACs that participate in the MoIDX program posted a revised draft LCD for DecisionDx-Melanoma. The draft LCD includes commentary about two publications regarding the clinical utility of GEP tests and was posted to give providers an opportunity to comment. Each of the draft LCDs include an assessment stating that the MAC does not believe that the new data is sufficient to change the coverage criteria. We have submitted comments on the draft LCD. The comment period on the last of these draft LCDs closed on August 8, 2021. We are unable to predict when the final draft LCD will be posted.

The U.S. Federal Supply Schedule, also known as the GSA Schedule and the Multiple Award Schedule, is a long-term government-wide contract with commercial companies. In August 2021, we were awarded a five-year GSA contract from the Veterans Health Administration for our DecisionDx-Melanoma GEP test.

Commercial Third-Party Payors

We are actively engaged in efforts to achieve broad coverage and reimbursement for our products, followed by contracting with commercial payors. Achieving positive coverage reduces the need for appeals and reduces failures to collect from the patient's commercial payor. Even with positive coverage decisions, we still experience delays in time to payment. Achieving in-network contracts with third-party payors can shorten the time required to receive payments. Implementing our strategy includes our managed care and medical affairs teams educating third-party payors regarding our strong clinical utility and outcomes data, which we believe validates the value of our products and will persuade more third-party payors to provide value-based reimbursement.

We have broad positive policy coverage for our DecisionDx-UM test, have executed contracts with certain commercial payors and anticipate further increases in contracting. We also have positive policy recommendations from many third-party technical assessment review groups. In 2021, we received payment on approximately 93% of all claims for this test.

We began engaging commercial third-party payors for positive coverage for DecisionDx-Melanoma and have seen some positive coverage policies. With the continued evidence development, we anticipate additional positive coverage policies occurring.

Dependence on Third-Party Payors

We receive a substantial portion of our revenue from a small number of third-party payors, primarily Medicare, BlueCross BlueShield affiliates and Medicare Advantage plans. Our revenue from patients covered by Medicare, Medicare Advantage plans, and BlueCross BlueShield plans, as a percentage of total revenue, was 57%, 28% and 7%, respectively, for the year ended December 31, 2021. BlueCross BlueShield plans and Medicare Advantage plans represent an aggregation of multiple payors making independent reimbursement decisions; however, these plans often base reimbursement decisions on common guidelines which can influence multiple plans simultaneously.

Competition

We are focused on improving health through innovative tests that guide patient care. We believe, today, that there is limited existing competition for our products that provide evidence-based genomic and proteomic solutions to physicians and their patients.

We believe the principal competitive factors in our target markets include:

- Proprietary, disciplined approach to genomic and proteomic analysis including the use of proprietary deep learning, machine learning, artificial intelligence and other techniques to identify and optimize biomarker selection and algorithmic approaches to answer the clinically important questions with accurate tests. This involves the ability to design and efficiently conduct the right clinical studies at the right time;

- Research and development investments to document the quality, quantity, consistency and strength of the clinical validity data, the impact our products have on clinical use, and demonstration of net health outcome improvement that reduce health system costs;
- Maintaining a strong reputation with the treating physician by providing consistent, transparent, and clinically relevant information that will improve the appropriate management of their patients;
- Ease of use in accessing our products, reimbursement support for our patients and laboratory reports that clearly communicate the clinically relevant data points;
- Demonstrated ability to work with, and secure coverage and reimbursement from, governmental and commercial payors;
- Ability to efficiently commercialize pipeline products to the same customer base as our current products.

We believe we compete favorably on the factors described above.

Today, our principal competition for DecisionDx-Melanoma is existing traditional clinical and pathology staging criteria. While some clinical and pathology criteria have changed over time, this approach has been the standard of care in the United States for many years, and physicians may be unwilling to accept the validity of the published data and adopt our test until it has become incorporated into national guidelines. In addition, we may, in the near future, face competition from a limited number of companies who are working in this disease space, such as SkylineDx and Neracare.

We are unaware of late-stage work being performed to develop and validate a product that would compete with DecisionDx-SCC. We believe that the current primary competitor for DecisionDx-SCC is existing traditional clinical and pathology staging criteria.

DecisionDx-UM competes with a subsidiary of LabCorp and several academic laboratories all of which have had tests available for several years. To date, our data has demonstrated that DecisionDx-UM is clinically and statistically superior to these products.

Today, principal competition for the TissueCypher Barrett's Esophagus Assay is existing traditional clinical and pathology assessment. In the future this assessment may include the use of immunohistochemical evaluation of individual protein biomarkers as an aid to pathology. While some clinical and pathology criteria have changed over time, this approach has been the standard of care in the United States for many years, and physicians may be unwilling to accept the validity of the published data and adopt our test until this has become incorporated into clinical guideline recommendations from gastrointestinal clinical societies, or other national guidelines. In addition, we may in the near future, face competition from a limited number of companies who are working in this disease space, such as Interpace Diagnostics. Other companies actively engaged in GERD screening to diagnose BE may also look to develop prognostic assays for patients diagnosed with BE, and these could compete with TissueCypher in the future.

Laboratory Operations

Our LDTs, consisting of DecisionDx-Melanoma, DecisionDx-SCC, our CDO and DecisionDx-UM, are currently performed in our College of American Pathologists ("CAP") accredited, Clinical Laboratory Improvement Amendments of 1988 ("CLIA")-certified laboratory in Phoenix, Arizona, which went operational in April 2016. As of 2021, we have an approximately 29,700 square feet of facility space supporting our growth and providing certain operational redundancy. We currently perform all laboratory procedures involved in our tests from receiving a requisition form to issuance of the final test result in these facilities. We performed more than 28,000 proprietary GEP tests in 2021. We provide our proprietary DecisionDx-Melanoma, DecisionDx-SCC, myPath Melanoma, DecisionDx DiffDx-Melanoma and DecisionDx-UM products for patients in all fifty states including those that require specific, additional, out-of-state lab licenses or qualifications such as New York, California, Pennsylvania, Maryland, and Rhode Island. Upon receipt, orders and samples are processed through an automated laboratory information management system which, in addition to tracking sample chain of custody, initiates and tracks accessioning, sample eligibility, technical data generation, algorithmic analysis and results reporting. Most of samples are received as paraffin embedded sections from a formalin fixed tissue specimen.

We have a laboratory and associated facilities totaling approximately 8,100 square feet of space in Pittsburgh, Pennsylvania, for the purpose of producing TissueCypher, an LDT with utility in the BE disease space. While this lab is CLIA-certified and positioned to operate in all states except New York, we are working to achieve anticipated CAP accreditation and New York Permitted Lab status in 2022. Our expanded laboratory footprint should also enable us to use this facility to process our dermatology tests, as or if needed.

Our laboratory facilities house all functions related to quality control and assurance, licensing, accreditation and regulatory compliance. Our quality management program ensures the quality of our laboratory services and products through continuous monitoring of a broad range of key performance indicators including technical, customer service and cybersecurity metrics. Through this program, we promote a philosophy of continuous improvement based upon adherence to validated standards. Our Phoenix facilities houses our clinical research operations and local information technology support, with a similar focus of operation in our Pittsburgh facility.

Raw Materials and Suppliers

We procure certain reagents, equipment, chips/cards and other materials used to perform our tests from sole suppliers such as ThermoFisher Scientific, Inc. and Qiagen, Inc. Some of these items are unique to these suppliers and vendors. While we have developed alternate sourcing strategies for these materials and vendors, and while we have experienced no business interruption due to an inability to source these materials, we cannot be certain whether these strategies will be effective or whether alternative sources will be available when we need them. If these suppliers can no longer provide us with the materials we need to perform our test services, they do not meet our quality specifications, or we cannot obtain acceptable substitute materials, our business would be negatively affected.

License Agreement with The Washington University

In November 2009, we entered into a license agreement (“the License Agreement”) with WUSTL to license certain patent rights and technical information from WUSTL for the development of melanoma products (the “Products”), and services (the “Services”). The rights licensed under this agreement are used in DecisionDx-UM only.

Under the License Agreement, we obtain an exclusive, worldwide, royalty-bearing license to certain patent rights owned by WUSTL (“the Patent Rights”) and a non-exclusive, worldwide license to certain technical information and research property owned by WUSTL, with the right to grant sublicenses under certain conditions, in order to develop the Products and Services. WUSTL retains the right to use the Patent Rights for research purposes.

The Patent Rights that we license pursuant to the License Agreement have been generated through the use of U.S. government funding and are therefore subject to certain federal regulations. See “Risk Factors—Risks Related to Intellectual Property—Our in-licensed intellectual property has been discovered through government funded programs and thus may be subject to federal regulations such as “march-in” rights, certain reporting requirements and a preference for U.S.-based companies, and compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.”

Under the License Agreement, we are required to use best efforts to carry out the activities under an agreed-upon development plan (“the Development Plan”) and meet any and all milestones set forth in the Development Plan. We are required to make milestone payments to WUSTL upon successful completion of development and commercialization milestones as set forth in the Development Plan. For each Product or Service that receives FDA approval, premarket approval or premarket notification, we are obligated to make a milestone payment to WUSTL in the mid-four digits. For the issuance of the first U.S. patent and the first foreign patent, we are obligated to make aggregate milestone payments to WUSTL in the low-five digits.

Under the License Agreement, we were obligated to pay WUSTL an initial license issue fee in the low-five digits. We are also obligated to make royalty payments to WUSTL equal to (i) a percentage in the mid-single digits of our and any of our affiliates’ or sub-licensees’ net sales of Products and (ii) a percentage in the low-single digits of our and any of our affiliates’ or sub-licensees’ revenue from Services. We are also obligated to make royalty payments to WUSTL in the low-to-mid single digit percentage of net sales, with minimum royalty payments to WUSTL every six-month period following the first commercial sale.

The term of the License Agreement will continue for ten years following the last-to-expire valid claim relating to the Patent Rights, unless terminated earlier. WUSTL may terminate the License Agreement upon written notice in the event of (i) our material breach if such breach remains uncured for 90 days, (ii) the exercise of certain rights by us with respect to the Patent Rights and/or the licensed technical information outside the scope of the License Agreement, or (iii) for certain insolvency-related events. We may terminate the License Agreement without cause upon written notice to WUSTL and payment of any amount due to WUSTL under the License Agreement.

Intellectual Property

Our core technology for our products is related to methods and devices for analysis of genetic expression. Using this technology, we are able to provide a more accurate prediction of a patient’s metastatic risk as compared to other methods. We have secured and continue to pursue intellectual property rights globally, including through patent protection covering analysis of metastasis in cutaneous melanoma, as well as treatment of cutaneous SCC. We also rely on trademarks, trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. For more information, please see “Risk Factors—Risks Related to Intellectual Property.”

Patents and Patent Applications

We have developed a global patent portfolio that as of December 31, 2021, is comprised as follows:

Commercial Focus	Number of Applications and Patents		
	United States	International	Total
<i>Owned Patent Families</i>			
Methods for predicting risk of metastasis in cutaneous melanoma	2	15	17
Methods of diagnosing and treating patients with pigmented skin lesions	1	1	2
Methods of diagnosing and treating patients with cutaneous squamous cell carcinoma	2	10	12
Determining Prognosis and Treatment based on Clinical-Pathologic Factors and Continuous Multigene-Expression Profile Scores	1	—	1
Genes and gene signatures for diagnosis and treatment of melanoma	5	29	34
Method for automated tissue analysis	2	3	5
Systems and compositions for diagnosing BE and methods of using same	3	13	16
Methods of predicting progression of BE	2	16	18
<i>Licensed Portfolio from WUSTL</i>			
Method for predicting risk of metastasis	2	—	2
Compositions and methods for detecting cancer metastasis	2	2	4
Total	22	89	111

Included in the table above are 12 issued U.S. patents and 60 issued international patents. This global patent portfolio has filing dates ranging from 2009 to 2021, and therefore are projected to expire between 2029 and 2041, subject to any patent term extension or patent term adjustment that might be available in a particular jurisdiction. The owned and licensed families contain issued patents and pending applications that relate to devices, systems, and methods for macromolecular analysis, and reflect our active and ongoing research programs.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a period due to delay by the United States Patent and Trademark Office (“USPTO”) in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective non-provisional filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Trademarks and Trade Secrets

As of the date of this Annual Report on Form 10-K, our U.S. trademark portfolio contained 13 trademark registrations.

We rely upon trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our competitive position. We seek to protect our intellectual property and proprietary technology, in part, by entering into confidentiality agreements and intellectual property assignment agreements with our employees, consultants, corporate partners and, as applicable, our advisors. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with an employee or a third party. These agreements may be breached, and we may not have adequate remedies for any breach. We additionally seek to preserve the integrity and confidentiality of our data and trade secrets, such as our proprietary algorithms, by maintaining the physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners,

collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Government Regulation and Product Approval

Regulations

Clinical Laboratory Improvement Amendments of 1988 (“CLIA”)

As a clinical reference laboratory, we are required to hold certain federal, state and local licenses, certifications and permits to conduct our business. Under CLIA, we are required to hold a certificate applicable to the type of laboratory tests we perform and to comply with standards applicable to our operations, including test processes, personnel, facilities administration, equipment maintenance, recordkeeping, quality systems and proficiency testing. We must maintain CLIA compliance and certification to be eligible to bill for diagnostic services provided to Medicare beneficiaries.

To renew our CLIA certificate, we are subject to survey and inspection every two years to assess compliance with program standards. Because our Phoenix, Arizona laboratory is a CAP accredited laboratory, CMS may defer the survey and inspection to those conducted by CAP. We may also be subject to additional unannounced inspections. The regulatory and compliance standards applicable to the testing we perform change periodically, and any such changes are published by CAP. Our SOPs documents & records are updated accordingly and as needed. Any such changes may have a material effect on our business.

Penalties for non-compliance with CLIA requirements include suspension, limitation or revocation of the laboratory’s CLIA certificate, as well as directed plan of correction, state on-site monitoring, civil money penalties, civil injunctive suit or criminal penalties.

State Laboratory Licensing

In addition to federal certification requirements of laboratories under CLIA, CLIA provides that states may adopt laboratory regulations and licensure requirements that are more stringent than those under federal law. Such laws, among other things, establish standards for the day-to-day operation of a clinical reference laboratory, which includes ensuring personnel have the adequate knowledge of training to maintain quality control. We currently provide laboratory services in all 50 states. Additionally, we maintain licenses in New York, California, Maryland, Pennsylvania and Rhode Island which require specific licensure for out-of-state laboratories that accept specimens from those states.

Because we receive specimens from the state of New York, our clinical reference laboratory is required to be licensed by New York, have a lab director with a specific certificate of qualification and is subject to biennial New York state inspections to ensure the lab is compliant with New York licensing standards. New York regulations also mandate proficiency testing for laboratories licensed under New York state law, regardless of whether such laboratories are located in New York. If a laboratory is out of compliance with New York statutory or regulatory standards, the New York State Department of Health (“NYSDOH”) may suspend, limit, revoke or annul the laboratory’s New York license, censure the holder of the license, or assess civil money penalties. We have received formal approval from NYSDOH to offer the following of our proprietary assays to New York patients: DecisionDx-Melanoma, DecisionDx-CMSeq, DecisionDx-UM, DecisionDx-PRAME, DecisionDx-UMSeq, DecisionDx-SCC, DecisionDx DiffDx-Melanoma and myPath Melanoma. Additionally, we are working through the NYSDOH submission and approval process for our newly acquired laboratory and product, TissueCypher, which has utility in the BE disease space.

Federal Oversight of Laboratory Developed Tests

The laws and regulations governing the marketing of diagnostic products are evolving, extremely complex, and in many instances, there are no significant regulatory or judicial interpretations of these laws and regulations. Clinical laboratory tests are regulated under CLIA, as administered by CMS, as well as by applicable state laws. In addition, the Federal Food, Drug and Cosmetic Act (“FDCA”) defines a medical device to include any instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory, intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals. Our in vitro testing products are considered by the FDA to be subject to regulation as medical devices. Among other things, pursuant to the FDCA and its implementing regulations, the FDA regulates the research, testing, manufacturing, safety, labeling, storage, recordkeeping, pre-market clearance or approval, marketing and promotion, and sales and distribution of medical devices in the United States to ensure that medical products distributed domestically are safe and effective for their intended uses. In addition, the FDA regulates the export of medical devices manufactured in the United States to international markets.

Although the FDA has statutory authority to assure that medical devices are safe and effective for their intended uses, the FDA has generally exercised its enforcement discretion and not enforced applicable regulations with respect to in vitro diagnostics that are designed, manufactured, and used within a single laboratory for use only in that laboratory. These tests are referred to

as LDTs. As a result, we believe our diagnostic services are currently subject to the FDA's enforcement discretion and are not currently subject to the FDA's oversight. However, reagents, instruments, software or components provided by third parties and used to perform LDTs may be subject to regulation.

In recent years, the FDA has stated its intention to modify its enforcement discretion policy with respect to LDTs. For example, on July 31, 2014, the FDA notified Congress of its intent to modify, in a risk-based manner, its policy of enforcement discretion with respect to LDTs. On October 3, 2014, the FDA issued two draft guidance documents entitled "Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)," or the Framework Guidance, and "FDA Notification and Medical Device Reporting for Laboratory Developed Tests (LDTs)," or the Reporting Guidance. The Framework Guidance states that FDA intends to modify its policy of enforcement discretion with respect to LDTs in a risk-based manner consistent with the classification of medical devices generally in Classes I through III. The Reporting Guidance would further enable FDA to collect information regarding the LDTs currently being offered for clinical use through a notification process, as well as to enforce its regulations for reporting safety issues and collecting information on any known or suspected adverse events related to the use of an LDT.

Although the FDA halted finalization of the guidance in November 2016 to allow for further public discussion on an appropriate oversight approach to LDTs and to give congressional authorizing committees the opportunity to develop a legislative solution, the FDA could ultimately modify its current approach to LDTs in a way that would subject our products marketed as LDTs to the enforcement of regulatory requirements.

Medical Device Regulatory Framework

Although we currently market our proprietary testing products as LDTs, which are currently subject to enforcement discretion, we could be subject to more onerous FDA compliance obligations in the future. Specifically, if the FDA begins to actively regulate LDTs, then, unless an exemption applies, each new or significantly modified medical device we seek to commercially distribute in the United States will require either a premarket notification to the FDA requesting permission for commercial distribution under Section 510(k) of the FDCA, also referred to as a 510(k) clearance, or approval from the FDA of a premarket approval ("PMA"), application. Both the 510(k) clearance and PMA processes can be resource intensive, expensive, and lengthy, and require payment of significant user fees.

Device Classification

Under the FDCA, medical devices are classified into one of three classes—Class I, Class II or Class III depending on the degree of risk associated with each medical device and the extent of control needed to provide reasonable assurances with respect to safety and effectiveness.

Class I devices are those with the lowest risk to the patient and are those for which safety and effectiveness can be reasonably assured by adherence to a set of FDA regulations, referred to as the General Controls for Medical Devices, which require compliance with the applicable portions of the FDA's Quality System Regulation, facility registration and product listing, reporting of adverse events and malfunctions, and appropriate, truthful and non-misleading labeling and promotional materials. Some Class I devices also require premarket clearance by the FDA through the 510(k) premarket notification process described below. Most Class I products are exempt from the premarket notification requirements.

Class II devices are those that are subject to the General Controls, and Special Controls as deemed necessary by the FDA to ensure the safety and effectiveness of the device. These Special Controls can include performance standards, patient registries, FDA guidance documents and post-market surveillance. Most Class II devices are subject to premarket review and clearance by the FDA. Premarket review and clearance by the FDA for Class II devices is accomplished through the 510(k) premarket notification process.

Class III devices include devices deemed by the FDA to pose the greatest risk such as life-supporting or life-sustaining devices, or implantable devices, in addition to those deemed novel and not substantially equivalent following the 510(k) process. The safety and effectiveness of Class III devices cannot be reasonably assured solely by the General Controls and Special Controls described above. Therefore, these devices are subject to the PMA application process, which is generally more costly and time-consuming than the 510(k) process. Through the PMA application process, the applicant must submit data and information demonstrating reasonable assurance of the safety and effectiveness of the device for its intended use to the FDA's satisfaction. Accordingly, a PMA typically includes, but is not limited to, extensive technical information regarding device design and development, pre-clinical and clinical trial data, manufacturing information, labeling and financial disclosure information for the clinical investigators in device studies. The PMA application must provide valid scientific evidence that demonstrates to the FDA's satisfaction a reasonable assurance of the safety and effectiveness of the device for its intended use.

The Investigational Device Process

In the United States, absent certain limited exceptions, human clinical trials intended to support medical device clearance or approval require an investigational device exemption (“IDE”), application. Some types of studies deemed to present “non-significant risk” are deemed to have an approved IDE once certain requirements are addressed and IRB approval is obtained. If the device presents a “significant risk” to human health, as defined by the FDA, the sponsor must submit an IDE application to the FDA and obtain IDE approval prior to commencing the human clinical trials. The IDE application must be supported by appropriate data, such as animal and laboratory testing results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. Generally, clinical trials for a significant risk device may begin once the IDE application is approved by the FDA and the study protocol and informed consent are approved by appropriate IRBs at the clinical trial sites. Submission of an IDE will not necessarily result in the ability to commence clinical trials, and although the FDA’s approval of an IDE allows clinical testing to go forward for a specified number of subjects, it does not bind the FDA to accept the results of the trial as sufficient to prove the product’s safety and efficacy, even if the trial meets its intended success criteria.

All clinical trials must be conducted in accordance with the FDA’s IDE regulations that govern investigational device labeling, prohibit promotion and specify an array of recordkeeping, reporting and monitoring responsibilities of study sponsors and study investigators. Clinical trials must further comply with the FDA’s good clinical practice regulations for IRB approval and for informed consent and other human subject protections. Required records and reports are subject to inspection by the FDA. The results of clinical testing may be unfavorable, or, even if the intended safety and efficacy success criteria are achieved, may not be considered sufficient for the FDA to grant marketing approval or clearance of a product. The commencement or completion of any clinical trial may be delayed or halted, or be inadequate to support approval of a PMA application, for numerous reasons.

The 510(k) Clearance Process

Under the 510(k) clearance process, the manufacturer must submit to the FDA a premarket notification, demonstrating that the device is “substantially equivalent” to a legally marketed predicate device. A predicate device is a legally marketed device that is not subject to a PMA, i.e., a device that was legally marketed prior to May 28, 1976 (pre-amendments device) and for which a PMA is not required, a device that has been reclassified from Class III to Class II or I, or a device that was previously found substantially equivalent through the 510(k) process. To be “substantially equivalent,” the proposed device must have the same intended use as the predicate device, and either have the same technological characteristics as the predicate device or have different technological characteristics and not raise different questions of safety or effectiveness than the predicate device. Clinical data is sometimes required to support substantial equivalence.

After a 510(k) premarket notification is submitted, the FDA determines whether to accept it for substantive review. If it lacks necessary information for substantive review, the FDA will refuse to accept the 510(k) notification. If it is accepted for filing, the FDA begins a substantive review. By statute, the FDA is required to complete its review of a 510(k) notification within 90 days of receiving the 510(k) notification. As a practical matter, clearance often takes longer, and clearance is never assured. Although many 510(k) premarket notifications are cleared without clinical data, the FDA may require further information, including clinical data, to make a determination regarding substantial equivalence, which may significantly prolong the review process. If the FDA agrees that the device is substantially equivalent, it will grant clearance to commercially market the device.

If the FDA determines that the device is not “substantially equivalent” to a predicate device, or if the device is automatically classified into Class III, the device sponsor must then fulfill the much more rigorous premarketing requirements of the PMA approval process, or seek reclassification of the device through the de novo process. The de novo classification process is an alternate pathway to classify medical devices that are automatically classified into Class III, but which are low to moderate risk. A manufacturer can submit a petition for direct de novo review if the manufacturer is unable to identify an appropriate predicate device and the new device or new use of the device presents a moderate or low risk. De novo classification may also be available after receipt of a “not substantially equivalent” letter following submission of a 510(k) to FDA.

After a device receives 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a new or major change in its intended use, will require a new 510(k) clearance or, depending on the modification, could require a PMA application. The FDA requires each manufacturer to determine whether the proposed change requires a new submission in the first instance, but the FDA can review any such decision and disagree with a manufacturer’s determination. Many minor modifications are accomplished by a letter-to-file in which the manufacturer documents the change in an internal letter-to-file. The letter-to-file is in lieu of submitting a new 510(k) to obtain clearance for such change. The FDA can always review these letters to file in an inspection. If the FDA disagrees with a manufacturer’s determination regarding whether a new premarket submission is required for the modification of an existing 510(k)-cleared device, the FDA can require the manufacturer to cease marketing and/or recall the modified device until 510(k) clearance or approval of a PMA application is obtained. In addition, in these circumstances, the FDA can impose significant regulatory fines or penalties for failure to submit the requisite application(s).

The PMA Approval Process

Following receipt of a PMA application, the FDA conducts an administrative review to determine whether the application is sufficiently complete to permit a substantive review. If it is not, the agency will refuse to file the PMA. If it is, the FDA will accept the application for filing and begin the review. The FDA has 180 days to review a filed PMA application, however, in practice the application review process often exceeds this deadline. During this review period, the FDA may request additional information or clarification of information already provided, and the FDA may issue a major deficiency letter to the applicant, requesting the applicant's response to deficiencies communicated by the FDA.

Before approving or denying a PMA, an FDA advisory committee may review the PMA at a public meeting and provide the FDA with the committee's recommendation on whether the FDA should approve the submission, approve it with specific conditions, or not approve it. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Prior to approval of a PMA, the FDA may conduct inspections of the clinical trial data and clinical trial sites, as well as inspections of the manufacturing facility and processes. Overall, the FDA review of a PMA application generally takes between one and three years but may take significantly longer. The FDA can delay, limit or deny approval of a PMA application for many reasons, including:

- the device may not be shown safe or effective to the FDA's satisfaction;
- the data from pre-clinical studies and/or clinical trials may be found unreliable or insufficient to support approval;
- the manufacturing process or facilities may not meet applicable requirements; and
- changes in FDA approval policies or adoption of new regulations may require additional data.

If the FDA evaluation of a PMA is favorable, the FDA will issue either an approval letter, or an approvable letter, the latter of which usually contains a number of conditions that must be met in order to secure final approval of the PMA. When and if those conditions have been fulfilled to the satisfaction of the FDA, the agency will issue a PMA approval letter authorizing commercial marketing of the device, subject to the conditions of approval and the limitations established in the approval letter. If the FDA's evaluation of a PMA application or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. The FDA also may determine that additional tests or clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and data is submitted in an amendment to the PMA, or the PMA is withdrawn and resubmitted when the data are available. The PMA process can be expensive, uncertain and lengthy and a number of devices for which the FDA approval has been sought by other companies have never been approved by the FDA for marketing.

New PMA applications or PMA supplements are required for modification to the manufacturing process, equipment or facility, quality control procedures, sterilization, packaging, expiration date, labeling, device specifications, ingredients, materials or design of a device that has been approved through the PMA process. PMA supplements often require submission of the same type of information as an initial PMA application, except that the supplement is limited to information needed to support any changes from the device covered by the approved PMA application and may or may not require as extensive technical or clinical data or the convening of an advisory panel, depending on the nature of the proposed change.

In approving a PMA application, as a condition of approval, the FDA may also require some form of post-approval study or post-market surveillance, whereby the applicant conducts a follow-up study or follows certain patient groups for a number of years and makes periodic reports to the FDA on the clinical status of those patients when necessary to protect the public health or to provide additional or longer-term safety and effectiveness data for the device. The FDA may also approve a PMA application with other post-approval conditions intended to ensure the safety and effectiveness of the device, such as, among other things, restrictions on labeling, promotion, sale, distribution and use. New PMA applications or PMA supplements may also be required for modifications to any approved diagnostic tests, including modifications to our manufacturing processes, device labeling and device design, based on the findings of post-approval studies.

Federal and State Physician Self-Referral Prohibitions

We are subject to the federal physician self-referral prohibitions, commonly known as the Stark Law, and to comparable state laws. Together these restrictions generally prohibit us from billing a patient or any governmental or private payor for certain designated health services, including clinical laboratory services, when the physician ordering the service, or any member of such physician's immediate family, has a financial interest, such as an ownership or investment interest in or compensation arrangement with us, unless the arrangement meets an exception to the prohibition.

Sanctions for a Stark Law violation include the following:

- denial of payment for the services provided in violation of the prohibition;
- refunds of amounts collected by an entity in violation of the Stark Law;
- a civil penalty for each bill or claim for a service arising out of the prohibited referral;
- the imposition of up to three times the amounts for each item or service wrongfully claimed;
- possible exclusion from federal healthcare programs, including Medicare and Medicaid; and
- a civil penalty for each arrangement or scheme that the parties know (or should know) has the principal purpose of circumventing the Stark Law's prohibition.

These prohibitions apply regardless of any intent by the parties to induce or reward referrals or the reasons for the financial relationship and the referral. In addition, knowing violations of the Stark Law may also serve as the basis for liability under the federal False Claims Act ("the FCA"), which can result in additional civil and criminal penalties.

Federal and State Anti-Kickback Laws

The federal Anti-Kickback Statute ("the AKS") makes it a felony for a person or entity, including a clinical laboratory, to knowingly and willfully offer, pay, solicit or receive any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, in order to induce business that is reimbursable under any federal healthcare program. A violation of the AKS may result in imprisonment for up to ten years and fines for each violation and administrative civil money penalties, including an additional amount of up to three times the amount of the remuneration paid. Convictions under the AKS result in mandatory exclusion from federal healthcare programs for a minimum of five years. In addition, The U.S. Department of Health and Human Services ("HHS") has the authority to impose civil assessments and fines and to exclude healthcare providers and others engaged in prohibited activities from Medicare, Medicaid and other federal healthcare programs. In addition, the government may assert that a claim that includes items or services resulting from a violation of the AKS constitutes a false or fraudulent claim under the FCA, which is discussed in greater detail below. Additionally, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Although the AKS applies only to items and services reimbursable under any federal healthcare program, a number of states have passed statutes substantially similar to the AKS that apply to all payors. Penalties of such state laws include imprisonment and significant monetary fines.

Federal and state law enforcement authorities scrutinize arrangements between healthcare providers and potential referral sources to ensure that the arrangements are not designed as a mechanism to induce patient care referrals or induce the purchase or prescribing of particular products or services. Generally, courts have taken a broad interpretation of the scope of the AKS, holding that the statute may be violated if merely one purpose of a payment arrangement is to induce referrals or purchases.

In addition to statutory exceptions to the AKS, regulations provide for a number of safe harbors. If an arrangement meets the provisions of a safe harbor, it is deemed not to violate the AKS. An arrangement must fully comply with each element of an applicable safe harbor in order to qualify for protection.

Failure to meet the requirements of the safe harbor, however, does not render an arrangement illegal. Rather, the government may evaluate such arrangements on a case-by-case basis, taking into account all facts and circumstances.

The Eliminating Kickbacks in Recovery Act

The Eliminating Kickbacks in Recovery Act of 2018 ("EKRA") prohibits knowingly and willfully soliciting or receiving any remuneration (including any kickback, bribe or rebate) directly or indirectly, overtly or covertly, in cash or in kind, in return for referring a patient or patronage to a laboratory; or paying or offering any remuneration (including any kickback, bribe or rebate) directly or indirectly, overtly or covertly, in cash or in kind, to induce a referral of an individual to a laboratory or in exchange for an individual using the services of that laboratory. EKRA was enacted to help reduce opioid-related fraud and abuse. However, EKRA defines the term "laboratory" broadly and without reference to any connection to substance use disorder treatment. EKRA applies to all payors including commercial payors and government payors. The law includes a limited number of exceptions, some of which closely align with corresponding AKS exceptions and safe harbors, and others that materially differ. Currently, there is no regulation interpreting or implementing EKRA, nor any guidance released by a federal agency regarding the scope of EKRA.

Other Federal and State Healthcare Laws

In addition to the requirements discussed above, several other healthcare fraud and abuse laws could have an effect on our business. For example, provisions of the Social Security Act permit Medicare and Medicaid to exclude an entity that charges the federal healthcare programs substantially in excess of its usual charges for its services. The terms “usual charge” and “substantially in excess” are subject to varying interpretations.

The FCA prohibits, among other things, a person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval and from, making, using, or causing to be made or used, a false record or statement material to a false or fraudulent claim in order to secure payment or retaining an overpayment by the federal government. In addition to actions initiated by the government itself, the statute authorizes actions to be brought on behalf of the federal government by a private party having knowledge of the alleged fraud, through the FCA’s “qui tam” or whistleblower provision. Because the complaint is initially filed under seal, the action may be pending for some time before the defendant is even aware of the action. If the government intervenes and is ultimately successful in obtaining redress in the matter or if the plaintiff succeeds in obtaining redress without the government’s involvement, then the plaintiff will receive a percentage of the recovery. Finally, the Social Security Act includes its own provisions that prohibit the filing of false claims or submitting false statements in order to obtain payment. Several states have enacted comparable false claims laws which may be broader in scope and apply regardless of payor.

The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented, or caused to be presented, a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. A person who offers or provides to a Medicare or Medicaid beneficiary any remuneration, including waivers of co-payments and deductible amounts (or any part thereof), that the person knows or should know is likely to influence the beneficiary’s selection of a particular provider, practitioner or supplier of Medicare or Medicaid payable items or services may be liable under the civil monetary penalties statute. Moreover, in certain cases, providers who routinely waive copayments and deductibles for Medicare and Medicaid beneficiaries, for example, in connection with patient assistance programs, can also be held liable under the AKS and FCA. One of the statutory exceptions to the prohibition is non-routine, unadvertised waivers of copayments or deductible amounts based on individualized determinations of financial need or exhaustion of reasonable collection efforts. The Office of Inspector General of HHS (“the OIG”) emphasizes, however, that this exception should only be used occasionally to address special financial needs of a particular patient. Although this prohibition applies only to federal healthcare program beneficiaries, applicable state laws related to, among other things, unlawful schemes to defraud, excessive fees for services, tortious interference with patient contracts and statutory or common law fraud, may also be implicated for similar practices offered to patients covered by commercial payor.

The federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of, or payment for, healthcare benefits, items or services. Like the AKS, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the “ACA”) also imposed annual reporting requirements on manufacturers of certain devices, drugs and biologics for certain payments and transfers of value by them and in some cases their distributors to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. Any failure to comply with these reporting requirements could result in significant fines and penalties. Because we manufacture our own LDTs solely for use by or within our own laboratory, we believe that we are exempt from these reporting requirements. We cannot assure you, however, that the government will agree with our determination, and a determination that we have violated these laws and regulations, or a public announcement that we are being investigated for possible violations, could adversely affect our business, prospects, results of operations or financial condition.

State equivalents of each of the above federal laws, such as anti-kickback and false claims laws, may impose similar or more prohibitive restrictions, and may apply to items or services reimbursed by non-governmental third-party payors, including private insurers.

If our operations are found to be in violation of any of the fraud and abuse laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, contractual damages,

reputational harm, integrity oversight and reporting obligations, diminished profits and future earnings, and the curtailment or restructuring of our operations.

International Regulations

Many countries in which we may offer any of our testing products in the future have anti-kickback regulations prohibiting providers from offering, paying, soliciting or receiving remuneration, directly or indirectly, in order to induce business that is reimbursable under any national healthcare program. In situations involving physicians employed by state-funded institutions or national healthcare agencies, violation of the local anti-kickback law 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 to offer or provide, directly or through a third party, including any potential distributors we may 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 will also be 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.

The standard of intent and knowledge in the Anti-Bribery cases is minimal-intent and knowledge are usually inferred from that fact that bribery took place. The accounting provisions do not require intent. Violations of the FCPA’s anti-bribery provisions for corporations and other business entities are subject to a fine of up to \$2 million and officers, directors, stockholders, employees, and agents are subject to a fine of up to \$100,000 and imprisonment for up to five years. Other countries, including the United Kingdom and other OECD Anti-Bribery Convention members, have similar anti-corruption regulations, such as the United Kingdom Anti-Bribery Act.

When marketing our testing products outside of the United States, we may be subject to foreign regulatory requirements governing human clinical testing, prohibitions on the import of tissue necessary for us to perform our testing products or restrictions on the export of tissue imposed by countries outside of the United States or the import of tissue into the United States, and marketing approval. These requirements vary by jurisdiction, differ from those in the United States and may in some cases require us to perform additional pre-clinical or clinical testing. In many countries outside of the United States, coverage, pricing and reimbursement approvals are also required.

Privacy and Security Laws

Health Insurance Portability and Accountability Act

Under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (“HITECH”) HHS has issued regulations to protect the privacy and provide for the security of protected health information (“PHI”) used or disclosed by certain entities including healthcare providers, such as us. HIPAA also regulates standardization of data content, codes and formats used in certain healthcare transactions and standardization of identifiers for health plans and providers. Penalties for violations of HIPAA and HITECH laws and regulations include significant civil and criminal penalties.

Three standards have been promulgated under HIPAA’s and HITECH’s regulations: the Standards for Privacy of Individually Identifiable Health Information, which restrict the use and disclosure of certain individually identifiable health information, the Standards for Electronic Transactions, which establish standards for common healthcare transactions, such as claims information, plan eligibility, payment information and the use of electronic signatures, and the Security Standards for the Protection of Electronic Protected Health Information, which require covered entities and business associates to implement and maintain certain security measures to safeguard certain electronic health information, including the adoption of administrative, physical and technical safeguards to protect such information.

The HIPAA privacy regulations cover the use and disclosure of PHI by covered entities and business associates, which are defined to include subcontractors that create, receive, maintain, or transmit PHI on behalf of a covered entity, as well as their covered subcontractors. They also set forth certain rights that an individual has with respect to his or her PHI maintained by a covered entity, including the right to access or amend certain records containing PHI, or to request restrictions on the use or disclosure of PHI. The HIPAA security regulations establish requirements for safeguarding the confidentiality, integrity, and availability of PHI that is electronically transmitted or electronically stored. HITECH, among other things, established certain health information security breach notification requirements. A covered entity must notify any individual whose PHI is breached according to the specifications set forth in the breach notification rule. The HIPAA privacy and security regulations establish a uniform federal “floor” and do not preempt state laws that are more stringent or provide individuals with greater rights with respect to the privacy or security of, and access to, their records containing PHI or insofar as such state laws apply to personal information that is broader in scope than PHI.

Individuals (or their personal representatives, as applicable) have the right to access test reports directly from laboratories and to direct that copies of those reports be transmitted to persons or entities designated by the individual.

HIPAA authorizes state attorneys general to file suit on behalf of their residents for violations. Courts are able to award damages, costs and attorneys' fees related to violations of HIPAA in such cases. While HIPAA does not create a private right of action allowing individuals to file suit against us in civil court for violations of HIPAA, its standards have been used as the basis for duty of care cases in state civil suits such as those for negligence or recklessness in the misuse or breach of PHI. In addition, HIPAA mandates that the Secretary of HHS conduct periodic compliance audits of HIPAA covered entities, such as us, and their business associates for compliance with the HIPAA privacy and security standards. It also tasks HHS with establishing a methodology whereby harmed individuals who were the victims of breaches of unsecured PHI may receive a percentage of the civil monetary penalty paid by the violator.

As a covered entity with downstream vendors and subcontractors and, in certain instances, as a business associate of other covered entities with whom we have entered into a business associate agreement, we have certain obligations under HIPAA regarding the use and disclosure of any PHI that may be provided to us. HIPAA and HITECH impose civil and criminal penalties against covered entities and business associates for noncompliance with privacy and security requirements. Further, various states, such as California and Massachusetts, have implemented similar privacy laws and regulations that impose restrictive requirements regulating the use and disclosure of health information and other personally identifiable information ("PII").

Numerous other federal, state and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, use, access to, confidentiality and security of patient health information. We intend to continue to comprehensively protect all personal information and to comply with all applicable laws regarding the protection of such information.

Reimbursement for Clinical Laboratory Services

We generate revenue on our products from several sources, including third-party payors, laboratory services intermediaries, and self-paying individuals. Depending on the billing arrangement and applicable law, we must bill various third-party payors, such as insurance companies, Medicare, Medicaid, and patients, all of which have different billing requirements. Compliance with applicable laws and regulations as well as internal compliance policies and procedures adds further complexity to the billing process. CMS establishes new procedures and continuously evaluates and implements changes to the reimbursement process for billing the Medicare program.

To receive reimbursement from third-party payors, we bill our tests using a variety of CPT codes, as defined by the AMA. For those genetic tests we conduct that do not have a dedicated CPT code, tests may be billed under a miscellaneous code for an unlisted molecular pathology procedure. Because these miscellaneous codes do not describe a specific service, the third-party payor claim may need to be examined to determine the service that was provided, whether the service was appropriate and medically necessary and whether payment should be rendered. This process can require a letter of medical necessity from the ordering physician and it can result in a delay in processing the claim, a lower reimbursement amount, or denial of the claim.

With the evolution of genetic testing, we have seen individual third-party payors' medical coverage policies around the CPT codes we bill and their associated payment rates change over time, resulting in changes to our reimbursement revenues. We believe all of our products provide significant clinical value and reduction in downstream healthcare spend, as evidenced in research studies and clinical publications, which we believe will continue to support and drive third-party payor reimbursement.

Under Medicare, payment for products like ours is generally made under the CLFS with payment amounts assigned to specific procedure billing codes. In April 2014, Congress passed the Protecting Access to Medicare Act ("PAMA"), which included substantial changes to the way in which clinical laboratory services will be paid under Medicare. Under PAMA, certain laboratories were required to report to CMS private payor payment rates and volumes for their tests. CMS uses this data to calculate a weighted median payment rate for each test, which will be used to establish revised Medicare CLFS reimbursement rates for the test. Laboratories that fail to report the required payment information may be subject to substantial civil penalties. We bill Medicare for our products, and therefore we are subject to reporting requirements under PAMA. See "Reimbursement—Government Payors" above for additional information.

PAMA also authorizes the adoption of new, temporary billing codes and/or unique test identifiers for FDA-cleared or approved tests as well as ADLTs. The AMA's CPT Editorial Panel has approved a proposal to create a new section of billing codes to facilitate implementation of this section of PAMA. These proprietary laboratory analyses codes may be requested by a clinical laboratory or manufacturer to specifically identify their test. If approved, the codes are issued by the AMA on a quarterly basis. Our DecisionDx-UM test was granted a Category I MAAA CPT code and was effective January 1, 2020. Our DecisionDx-Melanoma test was granted a Category I MAAA CPT code and was effective January 1, 2021.

Healthcare Reform

In March 2010, the ACA became law. The ACA contains a number of provisions that are expected to impact our business and operations, some of which in ways we cannot currently predict, including those governing enrollment in state and federal healthcare programs, reimbursement changes and fraud and abuse, which impact existing state and federal healthcare programs and will result in the development of new programs. Among other things, the ACA required each medical device manufacturer to pay a sales tax equal to 2.3% of the price for which such manufacturer sells its medical devices, and began to apply to sales of taxable medical devices after December 31, 2012, but was suspended in 2016. Further, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the medical device tax and “Cadillac” tax on high-cost employer-sponsored health coverage and, effective January 1, 2021, also eliminates the health insurer tax. The ACA also contains a number of other provisions, including provisions governing enrollment in federal and state healthcare programs, reimbursement matters and fraud and abuse, which we expect will impact our industry and our operations in ways that we cannot currently predict.

Since 2016, there have been efforts to repeal all or part of the ACA, and the previous administration and the U.S. Congress have taken action to roll back certain provisions of the ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. Thus, the ACA will remain in effect in its current form. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is also unclear how such challenges and the healthcare reform measures of the Biden administration will impact the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, on August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, reduced Medicare payments to providers by 2% per fiscal year, effective on April 1, 2013 which, due to subsequent legislative amendments to the statute including the Infrastructure Investment and Jobs Act, will remain in effect through 2031, unless additional Congressional action is taken. The Coronavirus Aid, Relief and Economic Security Act enacted on March 27, 2020 (“the CARES Act”) and other COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2022. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. Further, Congress is considering additional health reform measures as part of other reform initiatives.

We anticipate there will continue to be proposals by legislators at both the federal and state levels, regulators and commercial third-party payors to reduce costs while expanding individual healthcare benefits. Certain of these changes could impose additional limitations on the prices we will be able to charge for our products and the coverage of or the amounts of reimbursement available for our products from third-party payors, including government and commercial payors. In addition, it is possible that additional governmental action will be taken in response to the COVID-19 crisis in the future.

Human Capital Resources

Overview

Our vision is to transform disease management by keeping people first: patients, clinicians, employees and investors. We understand the importance of maintaining a strong corporate culture with our employees at the center, based on the cornerstones we laid in 2008 at our inception: trust, excellence, collaboration, integrity, innovation and excitement. We strive to find members of our team who embody the values of our company. As of December 31, 2021, we had 345 employees, of whom 342 were full-time employees. During the year ended December 31, 2021, we added 144 employees to our team, a 71.6% increase from 2020. We face competition for experienced, qualified personnel in our industry, particularly for highly skilled scientists, laboratory technicians and salespeople versed in diagnostic and prognostic testing services.

The tables below provide information on the distribution of our employees by functional area and by location as of December 31, 2021:

	Number of Employees
Laboratory Testing Operations	76
Research & Development	65
Sales & Marketing	106
Administrative & General	98
Total as of December 31, 2021	<u>345</u>

	Number of Employees
Friendswood, Texas	76
Phoenix, Arizona	111
Pittsburgh, Pennsylvania	15
Home-based throughout the U.S.	143
Total as of December 31, 2021	<u>345</u>

Our employees are not represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Diversity, Equity and Inclusion

We recognize the importance of diversity, equity and inclusion in recruiting, developing and retaining the best available talent. We are committed to further understanding and building upon our existing diversity, equity and inclusion strengths and are in the process of identifying opportunities and developing related initiatives.

As of December 31, 2021, our employees were 64.6% female and 35.4% male. Our overall employee population as of December 31, 2021 was 64.3% White, 7.2% Hispanic or Latino, 4.6% Asian, 3.5% Black or African-American and 20.4% two or more races (not Hispanic or Latino) and other. In executive positions, which we define as Executive Director or Regional Business Director level and above, our employee population as of December 31, 2021 was 75.0% White, 3.6% Hispanic or Latino and 21.4% other (not Hispanic or Latino). Females represented 35.7% of employees in executive positions.

In December 2021, we adopted an affirmative action plan which includes annual compensation analyses and ongoing reviews of our selection and hiring practices alongside a continued focus on building and maintaining a diverse workforce. We are continuing to further assess and understand additional measures that can advance diversity, equity and inclusion at Castle.

Compensation, Benefits and Professional Development

We are committed to offering competitive benefits and compensation packages to our employees. In addition to competitive base pay, we offer the following benefits, among others, to our full-time employees:

- a defined contribution 401(k) plan with employer matching contributions;
- an annual bonus opportunity;
- equity compensation, including stock options and/or restricted stock units and an employee stock purchase plan;

- medical, dental and vision plans;
- paid maternity, paternity and adoption leave policies;
- paid holidays and paid time off; and
- an employee assistance program.

We survey all new hires 90 days after the start of their employment to solicit feedback on employee engagement. We provide performance reviews at least once per year, with pay raises commensurate with market and performance indicators. Our turnover remains low for the year ended December 31, 2021.

We prioritize and encourage internal growth and professional development of our employees. To encourage employee development, we offer a professional development reimbursement program to eligible employees who attend job-related professional development activities.

Corporate and Other Information

We were incorporated in Delaware in September 2007. Our principal executive offices are located at 505 S. Friendswood Drive, Suite 401, Friendswood, Texas 77456 and our telephone number is (866) 788-9007. Our corporate website address is www.CastleBiosciences.com. Information contained on, or accessible through, our website is not considered part of this Annual Report on Form 10-K or our other filings with the SEC. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to such reports filed or furnished pursuant to Section 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended (“the Exchange Act”) are available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

This Annual Report on Form 10-K contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report on Form 10-K, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies’ trade names or trademarks to imply a relationship with, endorsement of or sponsorship of us by, any other companies.

Item 1A. Risk Factors.

Risk Factors

You should consider carefully the risks described below, as well as the other information in this Annual Report on Form 10-K, before deciding whether to purchase, hold or sell shares of our common stock. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all of the factors described as well as the other information in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” when evaluating our business. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Financial Condition

Our reliance upon a small number of third-party payors for a significant portion of our revenue may materially adversely affect our financial condition and results of operations.

We receive a substantial portion of our revenue from a small number of third-party payors, primarily Medicare. Our revenue for our test reports provided for patients covered by Medicare and Medicare Advantage plans as a percentage of total revenue, was 57% and 28%, respectively, for the year ended December 31, 2021 and 58% and 29%, respectively, for the year ended December 31, 2020. If our largest current payors were to significantly reduce, or cease to pay, the amount they reimburse for our products, or if they do not reach favorable coverage and reimbursement decisions for our products, or attempt to recover amounts they had already paid, it could have a material adverse effect on our business, financial condition and results of operations and cause significant fluctuations in our results of operations.

Due to how we recognize revenue, our quarterly revenues may not reflect our underlying business.

We have concluded that our contracts include variable consideration because the amounts paid by Medicare or commercial health insurance carriers may be paid at less than our standard rates or not paid at all, with such differences considered implicit price concessions. Variable consideration attributable to these price concessions is measured at the expected value using the “most likely amount” method under Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* (“ASC 606”). The amounts are determined by historical average collection rates by test type and payor category taking into consideration the range of possible outcomes, the predictive value of our past experiences, the time period of when uncertainties expect to be resolved and the amount of consideration that is susceptible to factors outside of our influence, such as the judgment and actions of third parties. Determining variable consideration through a consideration of these factors involves a significant level of estimation uncertainty, and our estimations may turn out to be incorrect. Such variable consideration is included in the transaction price only to the extent it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainties with respect to the amount are resolved. Variable consideration may be constrained and excluded from the transaction price in situations where there is no contractually agreed upon reimbursement coverage or in the absence of a predictable pattern and history of collectability with a payor. Variable consideration for Medicare claims that are not covered by an LCD, including those claims subject to approval by an Administrative Law Judge (“ALJ”) at an appeal hearing, is deemed to be fully constrained due to factors outside our influence (i.e., judgment or actions of third parties) and the uncertainty of the amount to be received is not expected to be resolved for a long period of time. Variable consideration is evaluated each reporting period and adjustments are recorded as increases or decreases in revenues. As a result of the timing and amount of adjustments for variable consideration, our operating results and comparisons of such results on a period-to-period basis may be difficult to understand and may not be meaningful. In addition, these fluctuations in revenue may make it difficult for us, for research analysts and for investors to accurately forecast our revenue and operating results. If our revenue or operating results fall below expectations, the price of our common stock would likely decline.

We have incurred significant losses since inception, and we may never achieve profitability.

Since our inception, we have had a history of net losses. For the year ended December 31, 2021, we had a net loss of \$31.3 million and as of December 31, 2021 had an accumulated deficit of \$93.8 million. We cannot predict if we will achieve profitability in the near future or at all. We expect to incur losses in the future as we plan to invest significant additional funds toward the expansion of our commercial organization, the conduct of clinical utility and validity studies to support adoption of our products and the development or acquisition of additional products. We also expect significant increases in our stock-based compensation expense in future periods, reflecting higher stock option valuations as a public company and additional awards outstanding due to increased headcount. Additionally, our performance could be affected by the ongoing impacts of COVID-19. Due to the requirements associated with being a public company, including those associated with no longer qualifying as an

emerging growth company and a smaller reporting company and becoming a large accelerated filer, we expect to continue incur significant additional legal, accounting and other expenses. We also expect that any acquisitions of businesses, assets, products or technologies will increase our expenses. These increased expenses will make it harder for us to achieve future profitability. We may also incur significant losses in the future for a number of reasons, many of which are beyond our control, including the other risks described in this Annual Report on Form 10-K, adoption of our products, coverage of and reimbursement rates for our products from third-party payors, and future research and development activities. Our failure to achieve profitability in the future could cause the market price of our common stock to decline and make it more difficult or costly for us to raise additional capital.

We are an early, commercial-stage company and have a limited operating history, which may make it difficult to evaluate our current business and predict our future performance.

We are an early commercial-stage company and have a limited operating history. Our limited operating history may make it difficult to evaluate our current business and this makes predictions about our future success or viability subject to significant uncertainty. In particular, we intend to use a portion of our working capital to increase our headcount, including through the expansion of our sales and marketing and research and development teams, which will increase our operating costs in a manner not historically reflected in our consolidated financial statements. In combination with our other anticipated increased operating expenses in connection with the ongoing demands of a public company, these anticipated changes in our operating expenses may make it difficult to evaluate our current business, assess our future performance relative to prior performance and accurately predict our future performance.

We will continue to encounter risks and difficulties frequently experienced by early commercial-stage companies, including those associated with increasing the size of our organization and the prioritization of our commercial, research and business development activities. If we do not address these risks successfully, our business could suffer.

Changes in financial accounting standards or practices may cause adverse, unexpected financial reporting fluctuations and affect our reported operating results.

Accounting principles generally accepted in the United States of America are subject to interpretation by the Financial Accounting Standards Board, the SEC, and various bodies formed to promulgate and interpret appropriate accounting principles. A change in accounting standards or practices can have a significant effect on our reported results and may even affect our reporting of transactions completed before the change is effective. New accounting pronouncements and varying interpretations of accounting pronouncements have occurred and may occur in the future. Changes to existing rules or the questioning of current practices may adversely affect our reported financial results or the way we conduct our business. As of December 31, 2021, we are no longer an emerging growth company and now apply public company adoption dates for new or revised accounting standards.

Our quarterly and annual operating results and cash flows may fluctuate in the future, which could cause the market price of our stock to decline substantially.

Numerous factors, many of which are outside our control may cause or contribute to significant fluctuations in our quarterly and annual operating results. For example, following the onset of the COVID-19 pandemic in 2020 we experienced decreases in revenue and test report volumes. These fluctuations may make financial planning and forecasting uncertain. In addition, these fluctuations may result in unanticipated decreases in our available cash, which could negatively affect our business and prospects. In addition, one or more of such factors may cause our revenue or operating expenses in one period to be disproportionately higher or lower relative to the others. As a result, comparing our operating results on a period-to-period basis may be difficult to understand and may not be meaningful. You should not rely on our past results as indicative of our future performance.

In addition, a significant portion of our operating expense is relatively fixed in nature, and planned expenditures are based in part on expectations regarding future revenue. Accordingly, unexpected revenue shortfalls could decrease our gross margins and cause significant changes in our operating results from quarter to quarter. If this occurs, the trading price of our stock could fall substantially.

This variability and unpredictability caused by factors such as those described above could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any guidance we may provide, or if the guidance we provide is below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

If our internal control over financial reporting is not effective, we may not be able to accurately report our financial results or file our periodic reports in a timely manner, which may cause adverse effects on our business and may cause investors to lose confidence in our reported financial information and may lead to a decline in our stock price.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports in a timely manner. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim consolidated financial statements will not be prevented or detected on a timely basis. If we fail to adequately staff our accounting and finance function, or fail to maintain adequate internal control over financial reporting, any new or recurring material weaknesses could prevent our management from concluding our internal control over financial reporting is effective and could result in our auditor issuing an adverse opinion on our internal control over financial reporting. If we identify any future significant deficiencies or material weaknesses, the accuracy and timeliness of our financial reporting may be adversely affected, our ability to prevent material misstatements in our consolidated financial statements could be impaired, a material misstatement in our consolidated financial statements could occur and we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports, which could cause our business to suffer and our stock price to decline.

Since becoming a publicly traded company in 2019, we have increased the headcount of our accounting and finance functions to further support the demands placed upon us as a public company, including the requirements of the Sarbanes-Oxley Act of 2002 (“Sarbanes-Oxley”). We expect to continue expending significant time and resources related to our internal control over financial reporting, including by further expanding our finance and accounting staff over time, but there can be no assurance our efforts will be effective.

We may need to raise additional capital to fund our existing operations, commercialize new products or expand our operations.

We believe our existing cash and cash equivalents and anticipated cash generated from sales of our products will be sufficient to fund our operations for the foreseeable future. If our available cash and cash equivalents and anticipated cash generated from sales of our products are insufficient to satisfy our liquidity requirements including because of lower demand for our products, lower than currently expected rates of reimbursement from third-party payors or other risks described in this Annual Report on Form 10-K, we may finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not currently have any committed external source of funds. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

We may consider raising additional capital in the future to expand our business, to pursue strategic investments, to take advantage of financing opportunities or for other reasons, including to:

- increase our sales and marketing efforts for DecisionDx-Melanoma, DecisionDx-SCC, DecisionDx DiffDx-Melanoma, myPath Melanoma, DecisionDx-UM and TissueCypher Barrett’s Esophagus Assay and address competitive developments among these or future commercial products;
- fund ongoing evidence development for our existing products as well as additional pipeline programs;
- expand our laboratory testing facility and related testing capacity;
- expand our technologies into other types of skin cancer, ocular cancer or GI management and detection products;
- acquire, license or invest in technologies;
- acquire or invest in complementary businesses or assets; and
- finance capital expenditures and general and administrative expenses.

Our present and future funding requirements will depend on many factors, including:

- our ability to achieve revenue growth;
- our rate of progress in establishing payor coverage and reimbursement arrangements with third-party payors;
- our rate of progress in, and cost of the sales, marketing, coverage and reimbursement activities associated with, establishing adoption of our lead product, DecisionDx-Melanoma, among our other products;
- the cost of expanding our laboratory operations and offerings, including our sales, marketing, coverage and reimbursement efforts;
- our rate of progress in, and cost of research and development activities associated with, diagnostic products in research and early development;

- the potential cost of, and delays in, the development of new products as a result of changes in regulatory oversight applicable to our products;
- acquisitions of businesses, assets, products or technologies;
- the effects of the COVID-19 pandemic; and
- the effect of competing technological and market developments.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or products, or grant licenses on terms that may not be favorable to us.

Any disruptions to, or volatility in, the credit and financial markets or any deterioration in overall economic conditions may make any necessary debt or equity financing more difficult to obtain, more costly and/or more dilutive. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our commercialization, research and development efforts or grant rights to third parties to market and/or develop products that we would otherwise prefer to market and develop ourselves.

Risks Related to Our Business

The COVID-19 pandemic has adversely impacted and could continue to adversely impact our business, including the demand for our test reports, as well as the business or operations of physicians and other healthcare providers who order our test reports and the third-party payors responsible for reimbursement for our tests, customers and other third parties with whom we conduct business.

Public health crises such as pandemics or similar outbreaks have adversely impacted and could continue to adversely impact our business. As a result of the ongoing COVID-19 pandemic, or public health crises, and federal, state and local government responses to these events, we have and/or may in the future experience disruptions that could adversely impact our business, including, but not limited to:

- decreased test report volume due to a decline in orders of DecisionDx-Melanoma and DecisionDx-UM tests as patient visits for routine examinations and biopsies have been, and may continue to be, delayed and/or canceled;
- disruption of our sales and commercialization activities due to limitations on our ability to communicate with physicians as a result of travel restrictions and hindered means of communicating with physicians;
- delays or disruptions by third parties in the collection, preparation or delivery of the tumor samples that we test;
- delays or difficulties in delivering test reports, interruptions in research and development and other limitations of key business activities due to members of our workforce becoming ill, compliance with applicable vaccination mandates and/or stay-at-home or other similar orders imposed by or that may be imposed by state and local governments, including at our Phoenix, Arizona, Pittsburgh, Pennsylvania and Friendswood, Texas locations;
- delayed reimbursement from third party payors, disruption in our supply channel and other adverse impacts on our business resulting from the negative effects of the COVID-19 pandemic on our suppliers, service providers and other third parties on whom we rely; and
- delayed or postponed interactions with regulators and other important agencies and contractors, due to limitations in employee resources, travel restrictions or forced furlough of government employees.

Following the onset of the COVID-19 pandemic, we experienced declines in orders and test report volume. For example, in the second quarter of 2020, test reports delivered for our lead product, DecisionDx-Melanoma, decreased 18.5% compared to the second quarter of 2019. For the year ended December 31, 2020, our growth in DecisionDx-Melanoma test report volume was 4.5%, compared to year-over-year growth of 29.1% for the year ended December 31, 2019. Our analysis of third-party data indicates that cutaneous melanoma diagnoses for the year ended December 31, 2020 were down approximately 20% compared to the year ended December 31, 2019. In the first quarter of 2021, test reports delivered for DecisionDx-Melanoma decreased by 11.2% compared to the first quarter of 2020. We believe the adverse impacts on our test report volume growth were linked to delays in the diagnoses as well as the cumulative impact on promotional responsiveness as a result of reduced sales calls per day and in-person sales calls during the COVID-19 pandemic.

Our future results will be dependent upon the extent and duration of the COVID-19 crisis, including the emergence and spread of variants of the virus, such as the Omicron variant, and government restrictions, which are beyond our control. Although state and local government restrictions put in place to slow the spread of the virus have been eased in certain locations, restrictions may be reinstated from time to time in various regions depending on the circumstances, potentially impacting the flow of future patient visits as well as access to current and future clinician customers. Even with the easing of state and local restrictions and the availability of vaccinations, patient visits and diagnosis of cutaneous melanoma, and other diseases covered by our diagnostic and prognostic tests, may be impacted by continued apprehension regarding possible exposure to the virus as well as shifting from in-person clinical visits to telehealth approaches which may result in missed or delayed diagnoses of skin cancer and other diseases. For example, our analysis of third-party data indicates that cutaneous melanoma diagnoses during the year ended December 31, 2021 remain approximately 11% below historical 2019 levels. As conditions are continuously evolving, we are unable to predict how our future test report volume will be impacted or the extent to which our results of operations, financial condition or cash flows will be impacted by the COVID-19 pandemic, or other future public health crises. Accordingly, the test report data presented above and elsewhere in this Annual Report on Form 10-K is not necessarily indicative of our results of operations that can be expected in future periods.

Under legislation enacted (or that may be enacted) by the United States federal government to respond to COVID-19, we have received and may receive in the future, cash payments or other forms of assistance allocated to healthcare and other companies. The eligibility requirements for any such payments or other assistance may be subject to restrictive terms and conditions, which may be ambiguous or subject to further modification, interpretation and guidance issued by government agencies on an ongoing basis. In the event we fail to comply with any of the terms or conditions associated with a payment we receive or if the terms and conditions or related interpretations change, we may be required to return it. The receipt of government payments or other assistance during the COVID-19 crisis has generated negative publicity for some companies and may continue to generate negative publicity for companies in the future. If we receive any negative publicity as a result of receiving or accepting a government payment or other assistance, such as the \$1.9 million in provider relief funds we received from HHS on April 16, 2020, it could harm our reputation, trigger a review or audit by applicable government agencies and/or adversely impact our stock price.

The COVID-19 crisis continues to rapidly evolve. The extent to which COVID-19 will further impact our business will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the crisis, resurgences of the virus, the emergence and spread of variants of the virus, vaccination rates, vaccination mandates, vaccination effectiveness, therapeutic treatments, the use of telemedicine, travel restrictions, stay-at-home or other similar orders and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the virus. Any of these factors, individually or in combination, could materially and adversely affect our business, results of operations, financial condition or cash flows. In addition, the current and potential adverse impacts of the COVID-19 crisis on our business, financial condition, results of operations and growth prospects, may also have the effect of heightening many of the other risks and uncertainties described elsewhere in this “Risk Factors” section.

Our revenue currently depends primarily on sales of DecisionDx-Melanoma, and we will need to generate sufficient revenue from this and other products to grow our business.

Most of our revenue in 2021 and 2020 was derived from the sale of our lead product, DecisionDx-Melanoma. While we also derive revenue from DecisionDx-UM, DecisionDx-SCC, our CDO (which consists of myPath Melanoma and DecisionDx DiffDx-Melanoma) and TissueCypher Barrett’s Esophagus Assay, we expect that the majority of our revenue for the foreseeable future will be derived from sales of DecisionDx-Melanoma. Further, we believe that our long-term commercial success will depend on our ability to develop and market additional products. Our ability to derive revenue from DecisionDx-Melanoma, DecisionDx-UM, DecisionDx-SCC, our CDO and TissueCypher Barrett’s Esophagus Assay and any future products that we commercialize or acquire is uncertain and depends on favorable coverage and reimbursement policies from government payors, such as Medicare, and from private payors, such as insurance companies. Without positive coverage policies, our products may not be reimbursed and we may not be able to recognize revenue. If we are unable to increase sales and expand coverage and reimbursement for DecisionDx-Melanoma, develop and commercialize other products, and successfully obtain coverage and adequate reimbursement for such products, our revenue and our ability to achieve profitability would be impaired, and the market price of our stock could decline substantially.

Billing for our products is complex and requires substantial time and resources to collect payment.

Billing for clinical laboratory testing services is complex, time-consuming and expensive. Depending on the billing arrangement and applicable law, we bill various payors, including Medicare, Medicaid, private insurance companies, private healthcare institutions, and patients, all of which have different billing requirements. We generally bill third-party payors for products and pursue reimbursement on a case-by-case basis where pricing contracts are not in place. To the extent laws or contracts require us to bill patient co-payments or co-insurance, we must also comply with these requirements. We may also

face increased risk in our collection efforts, including potential write-offs of accounts receivable and long collection cycles, which could adversely affect our business, results of operations and financial condition.

Several factors make the billing process complex, including:

- differences between the billing rates and reimbursement rates for our products;
- compliance with complex federal and state regulations related to billing government healthcare programs, including Medicare, Medicaid, Veterans Administration and TRICARE;
- risk of government audits related to billing;
- disputes among payors as to which party is responsible for payment;
- differences in coverage and information and billing requirements among payors, including the need for prior authorization and/or advanced notification;
- the effect of patient co-payments or co-insurance and our ability to collect such payments from patients;
- changes to billing codes used for our products;
- changes to requirements related to our current or future clinical studies, including our registry studies, which can affect eligibility for payment;
- ongoing monitoring provisions of LCDs for our products, which can affect the circumstances under which a claim would be considered medically necessary;
- incorrect or missing billing information; and
- the resources required to manage the billing and claims appeals process.

We use standard industry billing codes, known as CPT codes, to bill for our products. If these codes were to change, there is a risk of an error being made in the claim adjudication process. Such errors can occur with claims submission, third-party transmission or in the processing of the claim by the payor. Claim adjudication errors may result in a delay in payment processing or a reduction in the amount of the payment we receive.

As we introduce new products, we may need to add new codes to our billing process as well as our financial reporting systems. Failure or delays in effecting these changes in external billing and internal systems and processes could negatively affect our collection rates, revenue and cost of collecting.

Additionally, our billing activities require us to implement compliance procedures and oversight, train and monitor our employees, and undertake internal audits to evaluate compliance with applicable laws and regulations as well as internal compliance policies and procedures. When payors deny our claims, we may challenge the reason, low payment amount or payment denials. Payors also conduct external audits to evaluate payments, which add further complexity to the billing process. If the payor makes an overpayment determination, there is a risk that we may be required to return all or some portion of prior payments we have received.

Additionally, the ACA requires providers and suppliers to report and return any overpayments received from government payors under the Medicare and Medicaid programs within 60 days of identification. Failure to identify and return such overpayments exposes the provider or supplier to liability under federal false claims laws. These billing complexities, and the related uncertainty in obtaining payment for our products, could negatively affect our revenue and cash flow, our ability to achieve profitability, and the consistency and comparability of our results of operations.

In addition to the complexities noted above, we rely upon a third-party software application in the administration of our billing and collection process. We transitioned from a third-party billing service provider and added additional headcount to move our billing process in-house using a third-party software application starting January 1, 2021. Any significant disruption or deficiency in the design of our billing process could adversely impact our ability to generate and send invoices, calculate revenues, track payments and collect our accounts receivable. Although to date we have not experienced any disruptions or identified any deficiencies with our new billing system, there can be no assurances that any disruptions or deficiencies will not occur in the future. Additionally, any failure in the design or operation of our internal controls related to our billing and collection processes could adversely impact our ability to conclude on the effectiveness of our internal control over financial reporting and could cause our auditor to issue an adverse opinion on our internal control over financial reporting.

We rely on third parties for tissue sample collection, preparation and delivery. Any defects in sample collection or preparation by such third parties and any delays in delivery of such samples could cause errors in our test reports and delay our ability to deliver test reports in a timely manner, which could significantly harm our business.

The tissue samples that we test are biopsied, preserved, prepared and delivered to us by third parties, including dermatopathologists and laboratory facilities. As such, we rely on these third parties to prepare, label and deliver the tissue samples that we test in compliance with applicable laws and guidelines, and in a timely manner. Therefore, the accuracy and correctness of the test reports that we deliver are dependent on proper chain of custody and appropriate methods of sample collection or preparation utilized by these third parties, and our ability to timely deliver reports is dependent upon the ability of these third parties to provide these samples to us in a timely manner. The ability of these third parties to provide these samples to us in a timely manner could be delayed by events beyond our control, including but not limited to natural disasters and public health epidemics, such as the COVID-19 crisis. Any errors in any part of the sample collection or preparation process could cause us to deliver incorrect test reports, potentially resulting in harm to patients whose physicians implement a change in treatment decisions based upon our test report. If we are unable to timely deliver test reports, physicians may be less likely to recommend and order our products. The occurrence of any of the foregoing could significantly harm our reputation and our results of operations, causing significant harm to our business.

We rely on our database of samples for the development and improvement of our products. Depletion or loss of our samples could significantly harm our business.

The development and validation of accurate products is a complex process that requires access to tissue specimens and long-term outcomes data. Our research and development efforts to improve our existing commercial products and develop new pipeline products may require the depletion of our existing database of samples. If our samples are lost or destroyed, or substantially depleted before we are able to generate meaningful data, we may be unable to improve our existing products, continue the development of pipeline products or validate product candidates. While we have historically been able to create and maintain a large sample bank to expand the clinical use of our products and develop new products, we may be unable to do so in the future. If we were unable to maintain or replenish our sample bank, we may be unable to improve our products or develop new products.

If our primary clinical laboratory facility becomes damaged or inoperable or we are required to vacate our existing facility, our ability to conduct our laboratory analysis and pursue our research and development efforts may be jeopardized.

We currently perform most of our testing and store our database of tumor samples at our primary clinical laboratory facility in Phoenix, Arizona. Our facility and equipment could be harmed or rendered inoperable by natural or man-made disasters, including war, fire, earthquake, power loss, communications failure, terrorism, burglary, public health crises (including restrictions that may be imposed on businesses by state and local governments under stay-at-home or similar orders and mandates) or other events, which may make it difficult or impossible for us to perform our testing services for some period of time or to receive and store samples. The inability to perform tests or to reduce the backlog of sample analysis that could develop if our facility becomes inoperable, for even a short period of time, may result in the loss of revenue, loss of customers or harm to our reputation, and we may be unable to regain that revenue, those customers or repair our reputation in the future. Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters and man-made disasters or other sudden, unforeseen and severe adverse events.

In addition, the loss of our tissue samples due to such events could limit or prevent our ability to conduct research and development analysis on existing tests as well as tests in active pipeline development.

While we have a business continuity plan in place, and have completed the build out of an additional laboratory facility in close proximity to our primary facility to support our growth and provide certain operational redundancy, our facilities and the equipment we use to perform our testing and research and development could be unavailable or costly and time-consuming to repair or replace. It would be difficult, time-consuming and expensive to rebuild our facilities, to locate and qualify a new facility, replace certain pieces of equipment or license or transfer our proprietary technology to a third-party, particularly in light of licensure and accreditation requirements. Even in the unlikely event that we are able to find a third party with such qualifications to enable us to resume our operations, we may be unable to negotiate commercially reasonable terms.

We carry insurance for damage to our property and the disruption of our business, but this insurance may not cover all of the risks associated with damage or disruption to our business, may not provide coverage in amounts sufficient to cover our potential losses and may not continue to be available to us on acceptable terms, if at all.

Our current or future products may not achieve or maintain significant commercial market acceptance.

We believe our commercial success is dependent upon our ability to continue to successfully market and sell our products, to continue to expand our current relationships and develop new relationships with healthcare providers, to expand and maintain

coverage for our products, and to develop and commercialize new products. Our ability to achieve and maintain commercial market acceptance of our existing and future products will depend on a number of factors, including:

- our ability to increase awareness of our products through successful clinical utility and validity studies;
- the rate of adoption of our products by physicians and other healthcare providers;
- our ability to achieve guideline inclusion for our products;
- the timeliness with which we can provide our clinical reports to the ordering physician;
- the timing and scope of any regulatory approval for our products, if such approvals become required, and maintaining ongoing compliance with regulatory requirements;
- our ability to obtain and maintain positive coverage decisions for our products from government and commercial payors;
- our ability to obtain and maintain adequate reimbursement from third-party payors, including Medicare, Medicare Advantage plans and BlueCross BlueShield plans, which accounted for an aggregate of approximately 92% and 93% of our total revenue for the years ended December 31, 2021 and 2020, respectively;
- the impact of our investments in research and development and commercial growth;
- negative publicity regarding our or our competitors' products resulting from scientific publications, or defects or errors in the products; and
- our ability to further validate our products through clinical research and accompanying publications.

We cannot assure you that we will be successful in addressing each of these factors or other factors that might affect the market acceptance of our products. If we are unsuccessful in achieving and maintaining market acceptance of our products, our business and results of operations will suffer.

New product development involves a lengthy and complex process, and we may be unable to develop and commercialize, or receive reimbursement for, on a timely basis, or at all, new products.

We continually seek to develop new product offerings, which requires us to devote considerable resources to research and development. Before we can commercialize a new pipeline product, we will need to expend significant resources in order to conduct substantial research and development, including clinical utility and validity studies, and further develop and scale our laboratory processes and infrastructure to accommodate additional products. For example, in 2021, we launched our innovative pipeline to develop a genomic test aimed at predicting response to systemic therapy in patients with moderate to severe psoriasis, atopic dermatitis and related inflammatory skin conditions. We have initiated a 4,800 patient, prospective, multi-center clinical study to develop and validate this inflammatory skin disease pipeline test with the expectation of launching this pipeline test by the end of 2025.

Our product development process takes time and involves a high degree of risk, and such development efforts may fail for many reasons, including failure of the product to perform as expected, failure to successfully complete analytic and clinical validation, or failure to demonstrate the clinical utility of the product.

As we develop new products, we will have to make significant investments in research and development, marketing, selling, coverage and reimbursement activities. Typically, few research and development projects result in a commercialized product, and there can be no assurance that we will be able to successfully develop new products that can be commercialized. At any point, we may abandon development of a product or we may be required to expend considerable resources conducting research, which would adversely affect the timing for generating potential revenue from a new product and our ability to invest in other products in our pipeline. If a clinical validation study fails to demonstrate the prospectively defined endpoints of the study or if we fail to sufficiently demonstrate analytical validity or clinical utility, we might choose to abandon the development of the product, which could harm our business. In addition, competitors may develop and commercialize competing products or technologies faster than us or at a lower cost.

We may experience limits on our revenue if we are unable to increase and support adoption of our products by physicians and other healthcare providers.

Physicians and other healthcare providers may be unwilling to adopt our products due to their reliance on existing traditional clinical and pathology staging criteria and our ability to generate revenue from our products would be significantly impaired if we were unable to educate physicians, healthcare providers, patients and third-party payors about the benefits and advantages of our products. The COVID-19 crisis has impacted our in-person healthcare interactions, such as field-based sales and medical affairs, and we have had to convert visits, programs and projects to be performed online and by telephone. Although our in-person healthcare interactions have recently increased, they may become subject to restrictions or cancellations from time to

time, due to the uncertainties surrounding the duration, extent and ongoing impacts of the COVID-19 crisis, possibly impacting the effectiveness of our efforts. We will need to continue to educate physicians and pathologists about the benefits and cost-effectiveness of our products through published papers, presentations at scientific conferences, one-on-one marketing efforts by our sales force and one-on-one education by our medical affairs team. However, physicians and other healthcare providers may be reluctant to adopt our products in circumstances where our products are not incorporated into the current standard of care or practice guidelines. For example, while clinical utility of DecisionDx-Melanoma has been demonstrated in peer-reviewed publications, the SLNB surgery is the most widely used staging tool for determining a cutaneous melanoma patient's metastatic risk. Whether healthcare providers adopt DecisionDx-Melanoma as a complementary or triage diagnostic method relative to the SLNB surgery will depend on our ability to increase awareness of DecisionDx-Melanoma and its clinical validation.

In addition, all of our testing services are performed by our certified laboratory located in Phoenix, Arizona, under CLIA, rather than by local laboratory or pathology practices. Accordingly, it may be difficult for us to collect samples from pathologists, and pathologists may be reluctant to support our testing services.

We rely on limited or sole suppliers for some of the reagents, equipment, chips and other materials used by our products, and we may not be able to find replacements or transition to alternative suppliers.

We rely on limited or sole suppliers for certain reagents and other materials and components that we use for our products. Some of these items are unique to these suppliers and vendors. While we have developed alternate sourcing strategies for these materials and vendors, we cannot be certain whether these strategies will be effective or the alternative sources will be available when we need them. If these suppliers can no longer provide us with the materials we need, if the materials do not meet our quality specifications or are otherwise unusable, if we cannot obtain acceptable substitute materials, or if we elect to change suppliers, an interruption in laboratory operations could occur, we may not be able to deliver patient reports on a timely basis, or at all, and we may incur higher one-time switching costs. Any such interruption may significantly affect our future revenue, cause us to incur higher costs, and harm our customer relationships and reputation. In addition, in order to mitigate these risks, we maintain inventories of these supplies at higher levels than would be the case if multiple sources of supply were available. If our testing volume decreases or we switch suppliers, we may hold excess supplies with expiration dates that occur before use which would adversely affect our losses and cash flow position. As we introduce any new products, we may experience supply issues as we ramp test volume. If we should encounter delays or difficulties in securing, reconfiguring or revalidating the equipment, reagents or other materials we require for our products, our business, financial condition, results of operations and reputation could be adversely affected.

If our products do not meet the expectations of physicians and patients, our operating results, reputation and business could suffer.

Our success depends on physician and patient confidence that we can provide reliable, high-quality information that will improve treatment outcomes, lower healthcare costs and enable better patient care. We believe that patients, physicians and other healthcare providers are likely to be particularly sensitive to defects and errors in our products, including if our products fail to accurately predict risk of metastasis with high accuracy from samples, and there can be no guarantee that our products will meet their expectations. As a result, the failure of our products to perform as expected could significantly impair our operating results and our reputation, including if we become subject to legal claims arising from any defects or errors in our products or reports.

If we are unable to compete successfully, our business will suffer and we may be unable to increase or sustain our revenue or achieve profitability.

We face competition from companies and academic institutions that have either developed or may seek to develop products intended to compete with our products.

In addition, competitors may develop their own versions of our solutions in countries where we do not have patents or where our intellectual property rights are not recognized and compete with us in those countries, including encouraging the use of their solutions by physicians in other countries.

Some potential competitors may have longer operating histories, larger customer bases, greater brand recognition and market penetration, substantially greater financial, technological and research and development resources and selling and marketing capabilities, and more experience dealing with third-party payors. As a result, they may be able to respond more quickly to changes in customer requirements, devote greater resources to the development, promotion and sale of their products than we do or sell their products at prices designed to win significant levels of market share. We may not be able to compete effectively against these organizations. Increased competition and cost-saving initiatives on the part of governmental entities and other third-party payors are likely to result in pricing pressures, which could harm our sales, profitability or ability to gain market share. In addition, competitors may be acquired by, receive investments from or enter into other commercial relationships with larger, well-established and well-financed companies. Certain potential competitors may be able to secure key inputs from vendors on more favorable terms, devote greater resources to marketing and promotional campaigns, adopt more aggressive

pricing policies and devote substantially more resources to test development than we can. In addition, companies or governments that control access to testing through umbrella contracts or regional preferences could promote our competitors or prevent us from performing certain services. If we are unable to compete successfully against current and future competitors, our business will suffer and we may be unable to increase market acceptance and sales of our products, which could prevent us from increasing our revenue or achieving profitability and could cause our stock price to decline. As we add new tests and services, we will face many of these same competitive risks for these new tests.

The sizes of the markets for our current and future products have not been established with precision and may be smaller than we estimate.

Our estimates of the total addressable markets for DecisionDx-Melanoma, DecisionDx-UM, DecisionDx-SCC, myPath Melanoma, DecisionDx DiffDx-Melanoma and TissueCypher for BE are based on a number of internal and third-party estimates, including, without limitation, the annual rate of patients with the applicable form of skin cancer, the list price of our products relative to the reimbursement we expect to receive from third-party payors and the assumed prices at which we can sell our products in markets that have not been established. For example, we estimate that the total addressable market for DecisionDx-Melanoma is approximately \$540 million, which is based, in part, on our review of multiple publications which show that diagnosis of melanoma is underreported by 30% to 72%. While we believe our assumptions and the data underlying our estimates are reasonable, these assumptions and estimates may not be correct and the conditions supporting our assumptions or estimates may change at any time, thereby reducing the predictive accuracy of these underlying factors. As a result, our estimates of the annual total addressable market for our current or future products may prove to be incorrect. If the actual number of patients who would benefit from our products, the price at which we can sell future products, or the annual total addressable market for our products is smaller than we have estimated, it may impair our sales growth and have an adverse impact on our business.

The diagnostic testing industry is subject to rapid change, which could make our current or future products obsolete.

Our industry is characterized by rapid changes, including technological and scientific breakthroughs, frequent new product introductions and enhancements and evolving industry standards, all of which could make our current products and the other products we are developing obsolete. Our future success will depend on our ability to keep pace with the evolving needs of physicians and patients on a timely and cost-effective basis and to pursue new market opportunities that develop as a result of scientific and technological advances. In recent years, there have been numerous advances in technologies relating to the diagnosis and treatment of cancer. There have also been advances in methods used to analyze very large amounts of molecular information. We must continuously enhance our existing products and develop new products to keep pace with evolving standards of care. If we do not update our products to reflect new scientific knowledge about cancer biology, information about new cancer therapies or relevant clinical studies, our products could become obsolete and sales of our current products and any new products we develop could decline or fail to grow as expected.

Risks Related to Reimbursement and Government Regulation

We currently have limited reimbursement coverage for our lead product, DecisionDx-Melanoma, and if third-party payors, including government and commercial payors, do not provide sufficient coverage of, or adequate reimbursement for, our products, our commercial success, including revenue, will be negatively affected.

Our revenue depends on achieving broad coverage and adequate reimbursement for our products from third-party payors, including both government and commercial third-party payors. If third-party payors do not provide coverage of, or do not provide adequate reimbursement for, a substantial portion of the list price of our products, we may need to seek additional payment from the patient beyond any co-payments and deductibles, which may adversely affect demand for our products. Coverage determinations by a third-party payor may depend on a number of factors, including, but not limited to, a third-party payor's determination of whether our products are appropriate, medically necessary or cost-effective. If we are unable to provide third-party payors with sufficient evidence of the clinical utility and validity of our products, they may not provide coverage, or may provide limited coverage, which will adversely affect our revenues and our ability to succeed. To the extent that more competitors enter our markets, the availability of coverage and the reimbursement rate for our products may decrease as we encounter pricing pressure from these competitors.

Since each third-party payor makes its own decision as to whether to establish a policy to cover our products, enter into a contract with us and set the amount it will reimburse for a product, these negotiations are a time-consuming and costly process, and they do not guarantee that the third-party payor will provide coverage or adequate reimbursement for our products. In addition, the determinations by a third-party payor whether to cover our products and the amount it will reimburse for them are often made on an indication-by-indication basis.

In cases where there is no coverage policy or we do not have a contracted rate for reimbursement as a participating provider, the patient is typically responsible for a greater share of the cost of the product, which may result in further delay of our revenue, increase our collection costs or decrease the likelihood of collection.

Our claims for reimbursement from third-party payors may be denied upon submission, and we may need to take additional steps to receive payment, such as appealing the denials. Such appeals and other processes are time-consuming and expensive, and may not result in payment. Third-party payors may perform audits of historically paid claims and attempt to recoup funds years after the funds were initially distributed if the third-party payors believe the funds were paid in error or determine that our products were medically unnecessary. If a third-party payor audits our claims and issues a negative audit finding, and we are not able to overturn the audit findings through appeal, the recoupment may result in a material adverse effect on our revenue. Additionally, in some cases commercial third-party payors for whom we are not a participating provider may elect at any time to review claims previously paid and determine the amount they paid was too much. In these situations, the third-party payor will typically notify us of their decision and then offset whatever amount they determine they overpaid against amounts they owe us on current claims. We cannot predict when, or how often, a third-party payor might engage in these reviews and we may not be able to dispute these retroactive adjustments.

Under ASC 606, we recognize revenue at the amount we expect to be entitled, subject to a constraint for variable consideration, in the period in which our tests are delivered to the treating physician. We have determined that our contracts contain variable consideration under ASC 606 because the amounts paid by third-party payors may be paid at less than our standard rates or not paid at all, with such differences considered implicit price concessions. Variable consideration is recognized only to the extent it is probable that a significant reversal of revenue will not occur in future periods when the uncertainties are resolved.

Variable consideration is evaluated each reporting period and adjustments are recorded as increases or decreases in revenues. Variable consideration for Medicare claims that are not covered by an LCD, including those claims subject to approval by an ALJ at an appeal hearing, is deemed to be fully constrained due to factors outside our influence (i.e., judgment or actions of third parties) and the uncertainty of the amount to be received is not expected to be resolved for a long period of time. For these fully constrained claims, we generally recognize revenue in the period the uncertainties are resolved, if favorable. In June 2017 we submitted to the Office of Medicare Hearings and Appeals (“OMHA”) a request to participate in an appeal program developed with the intent of providing appellants a means to have large volumes of claim disputes adjudicated at an accelerated rate. We submitted 2,698 DecisionDx-Melanoma claims dating from 2013 through spring 2017 for adjudication on a consolidated basis. In March 2020, OMHA issued a decision denying payment on all of these claims. In accordance with ASC 606 and consistent with prior periods, we have not recognized (fully constrained the variable consideration) any revenues attributable to these claims in our consolidated financial statements pending the outcome of this matter. We have appealed this decision, but there can be no assurances regarding the timing or the outcome of this or any other appeal decision. Due to potential future changes in Medicare coverage policies and appeal cycles, insurance coverage policies, contractual rates and other trends in the reimbursement of our tests, our revenues may fluctuate significantly from period to period.

Although we are an in-network participating provider with some commercial third-party payors, including several Blue Cross Blue Shield plans, and certain large, national commercial third-party payors, including Aetna, other commercial third-party payors have issued non-coverage policies that currently categorize our tests as experimental or investigational. If we are not successful in obtaining coverage from third-party payors, in reversing existing non-coverage policies, or if other third-party payors issue similar non-coverage policies, this could have a material adverse effect on our business and operations.

Palmetto, the MAC responsible for administering MoIDX, the program that assesses molecular diagnostic technologies, issued a final LCD for DecisionDx-Melanoma, which became effective on December 3, 2018 and issued a final expanded LCD effective November 22, 2020. This LCD provides for coverage of DecisionDx-Melanoma for certain SLNB-eligible patients with cutaneous melanoma tumors with clinically negative sentinel node basins who are being considered for SLNB to determine eligibility for adjuvant therapy. The final expanded LCD also covers use of DecisionDx-Melanoma by physicians for assessment of appropriate treatment plans, regardless of the decision to undergo or avoid the SLNB surgery. Similarly, Palmetto issued a final LCD for DecisionDx-UM effective July 10, 2017. This LCD provides for coverage of DecisionDx-UM to determine metastatic risk in connection with the management of a patient’s newly diagnosed uveal melanoma and to guide surveillance and referral to medical oncology for those patients. We worked with Palmetto to obtain these positive coverage decisions through the submission of a detailed dossier of analytical and clinical data to substantiate that the tests meet Medicare’s medical necessity requirements. Per their joint operating agreement, Noridian, the MAC responsible for administering claims for laboratory services performed in Arizona, has adopted the same coverage policy as Palmetto for DecisionDx-UM and DecisionDx-Melanoma. This coverage process is lengthy, time-consuming, has changed over time, may change in the future and requires significant dedication of resources, and as we develop new products, we may be unsuccessful in receiving LCD determinations for those products or in maintaining our current LCDs. On a periodic basis, CMS requests bids for its MAC services, and MAC jurisdictions have changed in the past. A change in our MAC, or future changes in the MoIDX program, the elimination of the program, or a change in the administrator of that program, may affect our ability to obtain Medicare coverage and reimbursement for products for which we have coverage, for products for which we do not yet have coverage, or for any products we may launch in the future, or delay payments for our tests.

Under Medicare, payment for products like ours is generally made under the CLFS, with payment amounts assigned to specific procedure billing codes. In April 2014, Congress passed PAMA, which included substantial changes to the way in which

clinical laboratory services are paid under Medicare. Under PAMA, certain laboratories are required to report to CMS commercial third-party payor payment rates and volumes for each test they perform. CMS uses this data to calculate a weighted median payment rate for each test, which will be used to establish revised Medicare CLFS reimbursement rates for the test. Laboratories that fail to report the required payment information may be subject to substantial civil monetary penalties. We bill Medicare for our products, and therefore we are subject to reporting requirements under PAMA.

In the second quarter of 2020, we submitted our technical assessment dossier for DecisionDx-SCC to Palmetto and Noridian. The dossier was accepted as complete in the third quarter of 2020. In early 2021, we submitted our technical assessment dossier for DecisionDx DiffDx-Melanoma. The dossier was accepted as complete in the first quarter of 2021. We expect that draft LCDs for DecisionDx-SCC and DecisionDx DiffDx-Melanoma could potentially be posted by the end of the second quarter of 2022 resulting in potentially final LCDs effective in 2023. However, there is no assurance that the timing of any draft or final LCD will match our expectations or our historical experience with LCDs for our other tests.

In the second quarter of 2021, Palmetto and the other MACs that participate in the MoIDX program posted a draft revised LCD for DecisionDx-Melanoma. The draft LCD includes commentary about two publications regarding the clinical utility of GEP tests and was posted to give providers an opportunity to comment. Each of the draft LCDs include an assessment stating that the MAC does not believe that the new data is sufficient to change the coverage criteria. We have submitted comments on the draft LCD. The comment period on the last of these draft LCDs closed on August 8, 2021. We are unable to predict when the final draft LCD will be posted.

If we are unable to obtain and maintain adequate reimbursement rates from commercial third-party payors, this may adversely affect our Medicare rate. It is unclear what impact new pricing structures, such as those adopted under PAMA, may have on our business, financial condition, results of operations or cash flows.

The U.S. federal government continues to show significant interest in pursuing healthcare reform and reducing healthcare costs. Similarly, commercial third-party payors may seek to reduce costs by limiting coverage or reducing reimbursement for our products. Any government-adopted reform measures or changes to commercial third-party payor coverage and reimbursement policies could cause significant pressure on the pricing of, and reimbursement for, healthcare products and services, including our products, which could decrease demand for our products, and adversely affect our sales and revenue.

In addition, some third-party payors have implemented, or are in the process of implementing, laboratory benefit management programs, often using third-party benefit managers to manage these programs. The stated goals of these programs are to help improve the quality of outpatient laboratory services, support evidence-based guidelines for patient care and lower costs. The impact on laboratories, such as ours, of active laboratory benefit management by third parties is unclear, and we expect that it could have a negative impact on our revenue in the short term. It is possible that third-party payors will resist reimbursement for the products that we offer, in favor of less expensive products, may require pre-approval for our products or may impose additional pricing pressure on and substantial administrative burden for reimbursement for our products.

We expect to continue to focus substantial resources on increasing coverage and reimbursement for our current products and any future products we may develop. We believe it may take several years to achieve broad coverage and adequate contracted reimbursement with a majority of third-party payors for our products.

However, we cannot predict whether, under what circumstances, or at what payment levels third-party payors will cover and reimburse our products. If we fail to establish and maintain broad adoption of, and coverage and reimbursement for, our products, our ability to generate revenue could be harmed and our future prospects and our business could suffer.

Our products are currently marketed as laboratory developed tests, and any changes in regulations or the FDA's enforcement discretion for laboratory developed tests, or violations of regulations by us, could adversely affect our business, prospects, results of operations or financial condition.

The diagnostics industry is highly regulated, and we cannot assure you that the regulatory environment in which we operate will not change significantly and adversely in the future. In many instances, there are no significant regulatory or judicial interpretations of these laws and regulations. Although the FDA has statutory authority to assure that medical devices are safe and effective for their intended uses, the FDA has generally exercised its enforcement discretion and not enforced applicable regulations with respect to in vitro diagnostics that are designed, manufactured and used within a single laboratory. These tests are referred to as LDTs. We currently market our products as LDTs.

The FDA has adopted a policy of enforcement discretion with respect to LDTs whereby the FDA does not actively require premarket review of LDTs or otherwise impose its requirements applicable to other medical devices on LDTs. However, the FDA has stated its intention to modify its enforcement discretion policy with respect to LDTs. The FDA could ultimately modify its current approach to LDTs in a way that would subject our products marketed as LDTs to the enforcement of additional regulatory requirements. Moreover, legislative measures have recently been proposed in Congress that, if ultimately enacted, could provide the FDA with additional authority to require premarket review of and regulate LDTs. If and when such

changes to the regulatory framework occur, we could for the first time be subject to enforcement of regulatory requirements as a device manufacturer such as registration and listing requirements, medical device reporting requirements and the requirements of the FDA's Quality System Regulation. We may be required to conduct clinical trials prior to continuing to sell our existing products or launching any other products we may develop. This may increase the cost of conducting, or otherwise harm, our business.

Moreover, even if the FDA does not modify its policy of enforcement discretion, the FDA may disagree that we are marketing our LDTs within the scope of its policy of enforcement discretion and may impose significant regulatory requirements. While we believe that we are currently in material compliance with applicable laws and regulations as historically enforced by the FDA, we cannot assure you that the FDA will agree with our determination. A determination that we have violated these laws and regulations, or a public announcement that we are being investigated for possible violations, could adversely affect our business, prospects, results of operations or financial condition.

If the FDA begins to actively regulate our diagnostic products, we may be required to obtain premarket clearance under Section 510(k) of FDCA or a PMA. The process for submitting a 510(k) premarket notification and receiving FDA clearance usually takes from three to 12 months, but it can take significantly longer and clearance is never guaranteed. The process for submitting and obtaining FDA approval of a PMA is much more costly, lengthy and uncertain. It generally takes from one to three years or even longer, and approval is not guaranteed. PMA approval typically requires extensive clinical data and can be significantly longer, more expensive and more uncertain than the 510(k) clearance process. Despite the time, effort and expense expended, there can be no assurance that a particular device ultimately will be cleared or approved by the FDA through either the 510(k) clearance process or the PMA process on a timely basis, or at all. Moreover, there can be no assurance that any cleared or approved labeling claims will be consistent with our current claims or adequate to support continued adoption of and reimbursement for our products. If premarket review is required for some or all of our products, the FDA may require that we stop selling our products pending clearance or approval, which would negatively impact our business. Even if our products are allowed to remain on the market prior to clearance or approval, demand or reimbursement for our products may decline if there is uncertainty about our products, if we are required to label our products as investigational by the FDA, or if the FDA limits the labeling claims we are permitted to make for our products. As a result, we could experience significantly increased development costs and a delay in generating additional revenue from our products, or from other pipeline products.

If the FDA imposes significant changes to the regulation of LDTs it could reduce our revenues or increase our costs and adversely affect our business, prospects, results of operations or financial condition.

We conduct business in a heavily regulated industry, and failure to comply with federal, state and foreign laboratory licensing requirements and the applicable requirements of the FDA or any other regulatory authority, could cause us to lose the ability to perform our tests, experience disruptions to our business, or become subject to administrative or judicial sanctions.

The diagnostics industry is highly regulated, and the laws and regulations governing the marketing of diagnostic tests are extremely complex. Areas of the regulatory environment that may affect our ability to conduct business include, without limitation:

- federal and state laws applicable to test ordering, documentation of tests ordered, billing practices and claims payment and/or regulatory agencies enforcing those laws and regulations;
- federal and state fraud and abuse laws;
- federal and state laboratory anti-mark-up laws;
- coverage and reimbursement levels by Medicare, Medicaid, other governmental payors and private insurers;
- restrictions on coverage of and reimbursement for tests;
- federal and state laws governing laboratory testing, including CLIA, and state licensing laws and accreditation requirements;
- federal and state laws and enforcement policies governing the development, use and distribution of diagnostic medical devices, including LDTs;
- federal, state and local laws governing the handling and disposal of medical and hazardous waste;
- federal and state Occupational Safety and Health Administration rules and regulations; and
- HIPAA and similar state data privacy laws.

In particular, the FDCA defines a medical device to include any instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component, part, or accessory, intended for use in the

diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals. Our products are considered by the FDA to be subject to regulation as medical devices, and marketed under FDA's policy of enforcement discretion for LDTs. Among other things, pursuant to the FDCA and its implementing regulations, the FDA regulates the research, testing, manufacturing, safety, labeling, storage, recordkeeping, premarket clearance or approval, marketing and promotion, and sales and distribution of medical devices in the United States to ensure that medical products distributed domestically are safe and effective for their intended uses. In addition, the FDA regulates the import and export of medical devices manufactured between the United States and international markets.

We are also subject to CLIA, a federal law that regulates clinical laboratories that perform testing on specimens derived from humans for the purpose of providing information for the diagnosis, prevention or treatment of disease. CLIA regulations establish specific standards with respect to personnel qualifications, facility administration, proficiency testing, quality control, quality assurance and inspections. Any testing subject to CLIA regulation must be performed in a CLIA certified or accredited lab. CLIA certification or accreditation is also required in order for us to be eligible to bill state and federal healthcare programs, as well as commercial third-party payors, for our products.

We have a current CLIA accreditation under the College of American Pathologists ("CAP") program to conduct our tests at our clinical reference laboratory in Phoenix, Arizona. CAP maintains a clinical laboratory accreditation program. While not required for the operation of a CLIA-certified laboratory, many private insurers require CAP accreditation as a condition to contracting with clinical laboratories to cover their tests. In addition, some countries outside the United States require CAP accreditation as a condition to permitting clinical laboratories to test samples taken from their citizens. CAP accredited laboratories are surveyed for compliance with CAP standards every two years in order to maintain accreditation. Failure to maintain CAP accreditation could have a material adverse effect on the sales of our products and the results of our operations.

Therefore, to maintain our CLIA accreditation, we have elected to be subject to survey and inspection every two years by CAP. Moreover, CLIA inspectors may make random inspections of our laboratory from time to time.

Our most recent CAP inspection occurred in the fourth quarter of 2020 and our CLIA accreditation certificate expires on December 20, 2022.

In addition, certain states require our laboratory to be licensed in such states in order to test specimens from those states. Accordingly, our laboratory is also licensed by California, Maryland, New York, Pennsylvania and Rhode Island. Other states may have similar requirements or may adopt similar requirements in the future.

Although we have obtained licenses from states where we believe we are required to be licensed, we may become aware of other states that require out-of-state laboratories to obtain licensure in order to accept specimens from the state, and it is possible that other states currently have such requirements or will have such requirements in the future.

In order to test specimens from New York, LDTs must be approved by NYSDOH on a test-by-test basis before they are offered. Our laboratory director must also be separately qualified to be a laboratory director in New York. DecisionDx-Melanoma, DecisionDx-UM, DecisionDx-PRAME, DecisionDx-SCC and DecisionDx DiffDx-Melanoma have each been formally approved. Our laboratory director has been qualified by NYSDOH. We are subject to periodic inspection by the NYSDOH and are required to demonstrate ongoing compliance with NYSDOH regulations and standards. To the extent NYSDOH identified any non-compliance and we are unable to remedy such non-compliance, the State of New York could withdraw approval for our products. We will need to seek NYSDOH approval of any future LDTs we develop and want to offer for clinical testing to New York residents, and there can be no assurance that we will be able to obtain such approval.

We may also be subject to regulation in foreign jurisdictions as we seek to expand international utilization of our products or such jurisdictions adopt new licensure requirements, which may require review of our products in order to offer them or may have other limitations such as restrictions on the transport of human tissue samples necessary for us to perform our tests that may limit our ability to make our products available outside of the United States. Complying with licensure requirements in new jurisdictions may be expensive, time-consuming and subject us to significant and unanticipated delays.

Failure to comply with applicable clinical laboratory licensure requirements may result in a range of enforcement actions, including suspension, limitation or revocation of our CLIA accreditation and/or state licenses, imposition of a directed plan of action, onsite monitoring, civil monetary penalties, criminal sanctions and revocation of the laboratory's approval to receive Medicare and Medicaid payment for its services, as well as significant adverse publicity. Any sanction imposed under CLIA, its implementing regulations, or state or foreign laws or regulations governing clinical laboratory licensure or our failure to renew our CLIA accreditation, or a state or foreign license, could have a material adverse effect on our business, financial condition and results of operations. Even if we were able to bring our laboratory back into compliance, we could incur significant expenses and potentially lose revenue in doing so.

Doing business with the public sector, including the U.S. government, subjects us to risk of audits, investigations, sanctions and penalties.

We have and may enter into contracts in the future with the U.S. government or other governmental entities, and this subjects us to statutes and regulations applicable to companies doing business with the government. Government contracts normally contain additional requirements that may increase our costs of doing business, reduce our profits and expose us to liability for failure to comply with these terms and conditions. Such requirements may include mandatory socioeconomic compliance requirements, including labor requirements, non-discrimination and affirmative action programs and environmental compliance requirements. Being a government contractor also subjects us to reviews, audits and investigations regarding our compliance. If we fail to comply with our obligations associated with being a government contractor, our contracts may be subject to termination, and we may be subject to financial and/or other liability under our contracts, which could adversely affect our results of operations.

The FDA may modify its enforcement discretion policy with respect to LDTs in a risk-based manner, and we may become subject to extensive regulatory requirements and may be required to conduct additional clinical trials prior to continuing to sell our existing tests or launching any other tests we may develop, which may increase the cost of conducting, or otherwise harm, our business.

If the FDA changes or ends its policy of enforcement discretion with respect to LDTs, and our products become subject to the FDA's requirements for premarket review of medical devices, we may be required to cease commercial sales of our products and conduct clinical trials prior to making submissions to the FDA to obtain premarket clearance or approval. If we are required to conduct such clinical trials, delays in the commencement or completion of clinical trials could significantly increase our product development costs and delay commercialization of any currently marketed testing that we may be required to cease selling or the commercialization of any future tests that we may develop. Many of the factors that may cause or lead to a delay in the commencement or completion of clinical trials may also ultimately lead to delay or denial of regulatory clearance or approval. The commencement of clinical trials may be delayed due to insufficient patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites and the eligibility criteria for the clinical trial.

The FDA requires medical device manufacturers to comply with, among other things, current good manufacturing practices for medical devices, known as the Quality System Regulation, which requires manufacturers to follow elaborate design, testing, control, documentation and other quality assurance procedures during the manufacturing process; the medical device reporting regulation, which requires that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if it were to recur; labeling regulations, including the FDA's general prohibition against promoting products for unapproved or "off-label" uses; and the reports of corrections and removals regulation, which requires manufacturers to report to the FDA if a device correction or removal was initiated to reduce a risk to health posed by the device or to remedy a violation of the FDCA caused by the device which may present a risk to health.

Even if we were able to obtain FDA clearance or approval for one or more of our products, if required, a diagnostic test may be subject to limitations on the indications for which it may be marketed or to other regulatory conditions. In addition, such clearance or approval may contain requirements for costly post-market testing and surveillance to monitor the safety or efficacy of the test.

In addition, the FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approvals. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing authorization that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

Interim, topline and preliminary data from our clinical studies that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are

available. From time to time, we may also disclose interim data from our clinical studies. Interim data from clinical studies that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our reputation and marketing efforts.

Further, others, including healthcare providers or payors, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding our business. If the topline or interim data that we report differ from actual results, or if others, including healthcare providers or payors, disagree with the conclusions reached, our ability to commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Changes in healthcare policy could increase our costs, decrease our revenues and impact sales of and reimbursement for our products.

In March 2010, the ACA became law. This law substantially changed the way healthcare is financed by both government and commercial third-party payors, and significantly impacted our industry. The ACA contains a number of provisions that are expected to impact our business and operations, some of which in ways we cannot currently predict, including those governing enrollment in state and federal healthcare programs, reimbursement changes and fraud and abuse, which impact existing state and federal healthcare programs and will result in the development of new programs. Among other things, the ACA required medical device manufacturers to pay a sales tax equal to 2.3% of the price for which such manufacturer sells its medical devices, and began to apply to sales of taxable medical devices after December 31, 2012, but was suspended in 2016. Further, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the medical device tax and “Cadillac” tax on high-cost employer-sponsored health coverage and, effective January 1, 2021, also eliminated the health insurer tax.

Since 2016, there have been efforts to repeal all or part of the ACA, and the previous administration and the U.S. Congress have taken action to roll back certain provisions of the ACA.

For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the ACA and our business.

On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, reduced Medicare payments to providers by 2% per fiscal year, effective on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the Infrastructure Investment and Jobs Act, will remain in effect through 2031, unless additional Congressional action is taken. The CARES Act and other COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2022. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. Further, Congress is considering additional health reform measures as part of other reform initiatives.

We anticipate there will continue to be proposals by legislators at both the federal and state levels, regulators and commercial third-party payors to reduce costs while expanding individual healthcare benefits. For example, it is possible that additional governmental action is taken in response to the COVID-19 crisis. Certain of these changes could impose additional limitations on the prices we will be able to charge for our products, the coverage of or the amounts of reimbursement available for our products from third-party payors, including government and commercial payors.

We are subject to numerous federal and state healthcare statutes and regulations, and complying with laws pertaining to our business is an expensive and time-consuming process. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties and a material adverse effect to our business and operations.

Physicians, other healthcare providers and third-party payors play a primary role in the recommendation of our products. Our arrangements with healthcare providers, third-party payors and customers may expose us to broadly applicable fraud and abuse

and other healthcare laws and regulations that affect the business and financial arrangements and relationships through which we market and sell our products. The laws that affect our ability to operate include, but are not limited to:

- the AKS, which prohibits, among other things, any person or entity from knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of an item or service reimbursable, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term “remuneration” has been broadly interpreted to include anything of value, such as specimen collection materials or test kits. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, however these are drawn narrowly. Additionally, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and monetary penalties of up to \$100,000 for each violation, plus up to three times the remuneration involved, imprisonment of up to ten years and exclusion from government healthcare programs. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the FCA;
- the Stark Law, which prohibits a physician from making a referral for certain designated health services covered by the Medicare or Medicaid program, including laboratory and pathology services, if the physician or an immediate family member of the physician has a financial relationship with the entity providing the designated health services and prohibits that entity from billing, presenting or causing to be presented a claim for the designated health services furnished pursuant to the prohibited referral, unless an exception applies. Sanctions for violating the Stark Law include denial of payment, civil monetary penalties and exclusion from the federal healthcare programs. Failure to refund amounts received as a result of a prohibited referral on a timely basis may constitute a false or fraudulent claim and may result in civil penalties and additional penalties under the FCA;
- federal civil and criminal false claims laws, such as the FCA, which can be enforced by private citizens through civil qui tam action, and civil monetary penalty laws prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented through distribution of template medical necessity language or other coverage and reimbursement information, false, fictitious or fraudulent claims for payment or approval by the federal government, including federal healthcare programs, such as Medicare and Medicaid, and knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. In addition, a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the FCA. Private individuals can bring False Claims Act “qui tam” actions, on behalf of the government and such individuals, commonly known as “whistleblowers,” may share in amounts paid by the entity to the government in fines or settlement. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;
- EKRA, prohibits payments for referrals to recovery homes, clinical treatment facilities, and laboratories. EKRA’s reach extends beyond federal healthcare programs to include private insurance (i.e., it is an “all payor” statute). For purposes of EKRA, the term “laboratory” is defined broadly and without reference to any connection to substance use disorder treatment. The law includes a limited number of exceptions, some of which closely align with corresponding federal Anti-Kickback Statute exceptions and safe harbors, and others that materially differ;
- HIPAA, which, among other things, imposes criminal liability for executing or attempting to execute a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, in connection with the delivery of or payment for healthcare benefits, items or services. Like the AKS, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by HITECH, and their implementing regulations, which imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon entities subject to the law, such as health plans, healthcare clearinghouses and certain healthcare providers, known as covered entities, and their respective business associates, individuals or entities that perform services for them that involve individually identifiable health information as well as their covered subcontractors. Failure to comply with the HIPAA’s obligations can result in civil monetary penalties, and, in certain circumstances, criminal penalties. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable

to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions;

- state laws that prohibit other specified practices, such as billing physicians for tests that they order or providing tests at no or discounted cost to induce physician or patient adoption; insurance fraud laws; waiving coinsurance, copayments, deductibles, and other amounts owed by patients; billing a state Medicaid program at a price that is higher than what is charged to one or more other third-party payors employing, exercising control over or splitting professional fees with licensed professionals in violation of state laws prohibiting fee splitting or the corporate practice of medicine and other professions;
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the federal transparency requirements under the Physician Payments Sunshine Act, created under the ACA, which requires, among other things, certain manufacturers of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid, or the Children's Health Insurance Program to annually report to CMS information related to payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals and information regarding physician ownership and investment interests, including such ownership and investment interests held by a physician's immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission, and may result in liability under other federal laws or regulations. We believe that we are exempt from these reporting requirements. We cannot assure you, however, that our regulators, principally the federal government, will agree with our determination, and a determination that we have violated these laws and regulations, or a public announcement that we are being investigated for possible violations, could adversely affect our business;
- the prohibition on reassignment of Medicare claims, which, subject to certain exceptions, precludes the reassignment of Medicare claims to any other part;
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, that may impose similar or more prohibitive restrictions, and may apply to items or services reimbursed by any non-governmental third-party payors, including private insurers; and
- federal, state and foreign laws that govern the privacy and security of health information in certain circumstances, including state health information privacy and data breach notification laws which govern the collection, use, disclosure, and protection of health-related and other personal information, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

As a clinical laboratory, our business practices may face additional scrutiny from government regulatory agencies such as the Department of Justice, the OIG and CMS. Certain arrangements between clinical laboratories and referring physicians have been identified in fraud alerts issued by the OIG as implicating the AKS. The OIG has stated that it is particularly concerned about these types of arrangements because the choice of laboratory, as well as the decision to order laboratory tests, typically are made or strongly influenced by the physician, with little or no input from patients. Moreover, the provision of payments or other items of value by a clinical laboratory to a referral source could be prohibited under the Stark Law unless the arrangement meets all criteria of an applicable exception. The government has been active in enforcement of these laws as they apply to clinical laboratories.

We have entered into consulting and scientific advisory board arrangements, speaking arrangements and clinical research agreements with physicians and other healthcare providers, including some who could influence the use of our products. Because of the complex and far-reaching nature of these laws, regulatory agencies may view these transactions as prohibited arrangements that must be restructured, or discontinued, or for which we could be subject to other significant penalties. We could be adversely affected if regulatory agencies interpret our financial relationships with providers who may influence the ordering of and use of our products to be in violation of applicable laws.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies, healthcare providers and other third parties, including charitable foundations, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities may conclude that our business practices, including our consulting arrangements with physicians, as well as our financial assistance programs, do not comply with current or future statutes, regulations, agency guidance or case law involving applicable healthcare laws. Responding to investigations can be time and resource-consuming and can divert management's

attention from the business. Any such investigation or settlement could increase our costs or otherwise have an adverse effect on our business.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations is costly. If our operations are found to be in violation of any of these laws or any other current or future governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could substantially disrupt our operations. If any of the physicians or other healthcare providers or entities with whom we do business is found to be not in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

We are subject to certain U.S. anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations and may become subject to their similar foreign equivalents. We can face serious consequences for violations.

U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations prohibit, among other things, companies and their employees, agents, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving, directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of these trade laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect that we may engage in non-U.S. activities over time. We expect to rely on third-party suppliers and/or third parties to obtain necessary permits, licenses, and patent registrations. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

We are subject to stringent and changing state, federal, local, foreign, and other privacy and security obligations, and our failure to comply or perceived failure to comply with those obligations could result in regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; loss of customers or sales; and other adverse business consequences.

In the ordinary course of our business, we collect, store, use, transmit, disclose, or otherwise process (“Process”) confidential, proprietary, and sensitive data, including PHI, personal information, credit card and other financial information, intellectual property and proprietary business information owned or controlled by ourselves or our customers, payors and other parties. Our data processing activities subject us to numerous data privacy and security obligations, such as laws, regulations, guidance, industry standards, external and internal privacy and security policies, contracts and other obligations that govern the Processing of personal information by us and on our behalf.

In the United States, numerous federal, state, and local governments have enacted data privacy and security laws, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act). For example, HIPAA, as amended by HITECH, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. Additionally, California has enacted several laws governing the Processing of personal information, such as the California Consumer Privacy Act of 2018 (“CCPA”), which provides California residents certain rights relate to their personal information, and the California Confidentiality of Medical Information Act, which restricts the use and disclosure of health information and other personal information. Although the CCPA exempts some personal information processed in the context of clinical trials, the CCPA, to the extent applicable to our business and operations, may increase compliance costs and potential liability with respect to other personal information we maintain about California residents. In addition, other states have enacted or proposed privacy laws, further complicating compliance efforts. Outside the United States, there are also an increasing number of laws, regulations, industry standards and other obligations concerning privacy and security, including for example the European Union’s (“EU”) General Data Protection Regulation (EU) 2016/679 (“GDPR”).

In addition, privacy advocates and industry groups have proposed, and may in the future propose, standards with which we are legally or contractually bound to comply. Moreover, certain jurisdictions have enacted data localization laws and cross-border personal information transfer laws, which could make it more difficult to transfer personal information across jurisdictions

(such as transferring or receiving personal information that originates in the EU). Existing mechanisms that may facilitate cross-border personal information transfers may change or be invalidated.

Our obligations related to data privacy and security are quickly changing in an increasingly stringent fashion, creating some uncertainty as to the effective future legal framework. These laws may be subject to varying interpretations by courts and government stakeholders, creating complex compliance issues for us and our clients. Preparing for and complying with these obligations requires us to devote significant resources (including, without limitation, financial and time-related resources).

These obligations may necessitate changes to our information technologies, systems, and practices and to those of any third parties that process personal information on our behalf. In addition, these obligations may require us to change our business model or to take on more onerous obligations in our contracts. Although we endeavor to comply with all applicable obligations, we may, at times, fail or be perceived to have failed to do so. Moreover, despite our efforts, our personnel or third parties upon whom we rely may fail to comply with such obligations, which could negatively impact our business operations and compliance posture. Failure or perceived failure to comply with these obligations could result in significant consequences, including but not limited to government enforcement actions (which could include civil, criminal, and administrative penalties), private litigation, additional reporting requirements and/or oversight, bans on processing personal information, and orders to destroy or not use personal information. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: increase our cost of providing our services, decrease demand for our services, reduce our revenue, interrupt our business operations, limit our ability to develop our services, expenditure of time and resources to defend any claim or inquiry, and adverse publicity.

Ethical, legal and social concerns related to the use of genetic information could reduce demand for our products.

Genetic testing has raised ethical, legal, and social issues regarding privacy and the appropriate uses of the resulting information. Governmental authorities have, through the Genetic Information Nondisclosure Act of 2008, and could further, for social or other purposes, limit or regulate the use of genetic information or genetic testing or prohibit testing for genetic predisposition to certain conditions, particularly for those that have no known cure. Ethical and social concerns may also influence governmental authorities to deny or delay the issuance of patents for technology relevant to our business. While we do not currently perform genetic tests for genetic predisposition to certain conditions, these concerns may lead patients to refuse to use, or clinicians to be reluctant to order, our genomic tests or genetic tests for somatic mutations even if permissible. These and other ethical, legal and social concerns may limit market acceptance of our products or reduce the potential markets for our products, either of which could have an adverse effect on our business, financial condition, or results of operations.

Risks Related to Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our technology, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize diagnostic tests similar or identical to ours, and our ability to successfully commercialize our products may be impaired.

We rely on patent protection as well as trademark, copyright, trade secret and other intellectual property rights protection as well as nondisclosure, confidentiality and other contractual restrictions to protect our brands and proprietary tests and technologies, 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. In addition, we may incur substantial litigation costs in our attempts to recover or restrict use of our intellectual property.

As is the case with other life science companies, our success depends in large part on our ability to obtain and maintain protection of the intellectual property we may own solely or jointly with others or in-license from others, particularly patents, in the United States and other countries with respect to our products and technologies. We apply for patents covering our products and technologies and uses thereof, as we deem appropriate. However, obtaining and enforcing life sciences patents is costly, time-consuming and complex, and we may fail to apply for patents on important tests, services and technologies in a timely fashion or at all, or we may fail to apply for patents in potentially relevant jurisdictions. We may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed from or to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Our patent portfolio includes 12 issued U.S. patents and ten pending U.S. patent applications, with foreign counterparts. It is possible that none of our pending patent applications will result in issued patents in a timely fashion or at all, and even if patents

are granted, they may not provide a basis for intellectual property protection of commercially viable tests or services, may not provide us with any competitive advantages, or may be challenged and invalidated by third parties. It is possible that others will design around our future patented technologies. We may not be successful in defending any such challenges made against our patents or patent applications. Any successful third-party challenge to our patents could result in the unenforceability or invalidity of such patents and increased competition to our business. Even if our patents are held valid and enforceable, they may still be found insufficient to provide protection against competing products and services sufficient to achieve our business objectives. We may have to challenge the patents or patent applications of third parties, such as to counter infringement or unauthorized use. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, or may refuse to enjoin the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. Even if we prevail against an infringer in a U.S. district court or foreign trial-level court, there is always the risk that the infringer will file an appeal and the initial court judgment will be overturned at the appeals court and/or that an adverse decision will be issued by the appeals court relating to the validity or enforceability of our patents. The outcome of patent litigation or other proceeding can be uncertain, and any attempt by us to enforce our patent rights against others or to challenge the patent rights of others may not be successful, or, if successful, may take substantial time and result in substantial cost, and may divert our efforts and attention from other aspects of our business.

The patent positions of life sciences companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in such companies' patents has emerged to date in the United States or elsewhere. Courts frequently render opinions in the life sciences field that may affect the patentability of certain inventions or discoveries, including opinions that may affect the patentability of methods for analyzing or comparing DNA sequences.

In particular, the patent positions of companies engaged in the development and commercialization of genomic diagnostic tests are particularly uncertain. Various courts, including the U.S. Supreme Court, have rendered decisions that affect the scope of patentability of certain inventions or discoveries relating to certain diagnostic tests and related methods. These decisions state, among other things, that a patent claim that recites an abstract idea, natural phenomenon or law of nature (for example, the relationship between particular genetic variants and cancer) are not themselves patentable. Precisely what constitutes a law of nature is uncertain, and it is possible that certain aspects of genetic diagnostics tests would be considered natural laws. Accordingly, the evolving case law in the United States may adversely affect our ability to obtain patents and may facilitate third-party challenges to any owned or licensed patents. The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and we may encounter difficulties in protecting and defending such rights in foreign jurisdictions. The legal systems of many other countries do not favor the enforcement of patents and other intellectual property protection, particularly those relating to life science technologies, which could make it difficult for us to stop the infringement of our patents in such countries. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

To the extent our intellectual property offers inadequate protection, or is found to be invalid or unenforceable, we would be exposed to a greater risk of direct competition, and our competitive position could be adversely affected, as could our business. Both the patent application process and the process of managing patent disputes can be time-consuming and expensive. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology, but that are not covered by the claims of the patents that we own or control, assuming such patents have issued or do issue;
- we or our licensors or any future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive tests for sale in our major commercial markets;

- third parties performing manufacturing or testing for us using our products or technologies could use the intellectual property of others without obtaining a proper license;
- parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights over that intellectual property;
- we may not develop or in-license additional proprietary technologies that are patentable;
- we may not be able to obtain and maintain necessary licenses on commercially reasonable terms, or at all; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business and results of operations.

Changes in patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other life sciences companies, our success is heavily dependent on intellectual property, particularly patents relating to our research programs and products. Obtaining and enforcing patents in the life sciences industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States or the USPTO rules and regulations could increase these uncertainties and costs. Patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act (“AIA”), signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The AIA includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent in USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. For applications filed after March 15, 2013 that do not claim the benefit of applications filed before that date, the AIA transitioned the United States from a first to invent system to a first-inventor-to-file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications, our ability to obtain future patents, and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations.

Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Our in-licensed intellectual property has been discovered through government funded programs and thus may be subject to federal regulations such as “march-in” rights, certain reporting requirements and a preference for U.S.-based companies, and compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

Intellectual property rights that have been in-licensed pursuant to the License Agreement with WUSTL have been generated through the use of U.S. government funding, and are therefore subject to certain federal regulations. As a result, the United States federal government may retain certain rights to intellectual property embodied in our current or future product candidates under the Bayh-Dole Act. These federal government rights include a “nonexclusive, nontransferable, irrevocable, paid-up license” to use inventions for any governmental purpose. The Bayh-Dole Act also provides federal agencies with “march-in rights.” March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants” if it determines that (1) adequate steps have not been taken to commercialize the invention, (2) government action is necessary to meet public health or safety needs or (3) government action is necessary to meet requirements for public use under federal regulations. If the patent owner refuses to do so, the government may grant the license itself.

The U.S. government also has the right to take title to these inventions if the licensor fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States, and the

License Agreement requires that we comply with this requirement. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our owned or future in-licensed intellectual property is also generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

Issued patents covering our products and related technologies could be found invalid or unenforceable if challenged.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability. Some of our patents or patent applications (including licensed patents) have been, are being or may be challenged at a future point in time in an opposition, nullification, derivation, reexamination, *inter partes* review, post-grant review or interference action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether. Any successful third-party challenge to our patents in this or any other proceeding could result in the unenforceability or invalidity of such patents, which may lead to increased competition to our business, which could harm our business. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future diagnostic tests.

We may not be aware of all third-party intellectual property rights potentially relating to our products. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until approximately 18 months after filing or, in some cases (*e.g.*, U.S. applications for which a request not to publish has been filed), not until such patent applications issue as patents. We might not have been the first to make the inventions covered by each of our pending patent applications and we might not have been the first to file patent applications for these inventions. To determine the priority of these inventions, we have and may have to participate in interference proceedings, derivation proceedings or other post-grant proceedings declared by the USPTO that could result in substantial cost to us. The outcome of such proceedings is uncertain. We can give no assurance that all of the potentially relevant art relating to our patents and patent applications has been found; overlooked prior art could be used by a third party to challenge the validity, enforceability and scope of our patents or prevent a patent from issuing from a pending patent application. As a result, we may not be able to obtain or maintain protection for certain inventions. No assurance can be given that other patent applications will not have priority over our patent applications. In addition, changes to the patent laws of the United States allow for various post-grant opposition proceedings that have not been extensively tested, and their outcome is therefore uncertain. Therefore, the validity, enforceability and scope of our patents in the United States and other countries cannot be predicted with certainty and, as a result, any patents that we own or license may not provide sufficient protection against our competitors. Furthermore, if third parties bring these proceedings against our patents, we could experience significant costs and management distraction.

Our commercial success depends significantly on our ability to operate without infringing upon the intellectual property rights of third parties.

The life sciences industry is subject to rapid technological change and substantial litigation regarding patent and other intellectual property rights. Our potential competitors in both the United States and abroad, may have substantially greater resources and are likely to make substantial investments in patent portfolios and competing technologies, and may apply for or obtain patents that could prevent, limit or otherwise interfere with our ability to make, use and sell our products. Numerous third-party patents exist in fields relating to our products and technologies, and it is difficult for industry participants, including us, to identify all third-party patent rights relevant to our products and technologies. Moreover, because some patent applications are maintained as confidential for a certain period of time, we cannot be certain that third parties have not filed patent applications that cover our products and technologies.

Patents could be issued to third parties that we may ultimately be found to infringe. Third parties may have or obtain valid and enforceable patents or proprietary rights that could block us from using our technology. Our failure to obtain or maintain a license to any technology that we require may materially harm our business, financial condition and results of operations. Furthermore, we would be exposed to a threat of litigation.

From time to time, we may be party to, or threatened with, litigation or other proceedings with third parties, including non-practicing entities, who allege that our products, components of our products, and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. The types of situations in which we may become a party to such litigation or proceedings include:

- we may initiate litigation or other proceedings against third parties seeking to invalidate the patents held by those third parties or to obtain a judgment that our products or technologies do not infringe those third parties' patents;
- we may participate at substantial cost in International Trade Commission proceedings to abate importation of products that would compete unfairly with our products or technologies;
- if a competitor files patent applications that claim technology also claimed by us or our licensors, we or our licensors may be required to participate in interference, derivation or opposition proceedings to determine the priority of invention, which could jeopardize our patent rights and potentially provide a third party with a dominant patent position;
- if third parties initiate litigation claiming that our products or technologies infringe their patent or other intellectual property rights, we will need to defend against such proceedings;
- if third parties initiate litigation or other proceedings seeking to invalidate patents owned by or licensed to us or to obtain a declaratory judgment that their products, services, or technologies do not infringe our patents or patents licensed to us, we will need to defend against such proceedings;
- we may be subject to ownership disputes relating to intellectual property, including disputes arising from conflicting obligations of consultants or others who are involved in developing our products and technologies; and
- if a license to necessary technology is terminated, the licensor may initiate litigation claiming that our products or technologies infringe or misappropriate its patent or other intellectual property rights and/or that we breached our obligations under the license agreement, and we would need to defend against such proceedings.

These lawsuits and proceedings, regardless of merit, are time-consuming and expensive to initiate, maintain, defend or settle, and could divert the time and attention of managerial and technical personnel, which could materially adversely affect our business. Any such claim could also force us to do one or more of the following:

- incur substantial monetary liability for infringement or other violations of intellectual property rights, which we may have to pay if a court decides that the diagnostic test or technology at issue infringes or violates the third party's rights, and if the court finds that the infringement was willful, we could be ordered to pay treble damages and the third party's attorneys' fees;
- stop manufacturing, offering for sale, selling, using, importing, exporting or licensing the diagnostic test or technology incorporating the allegedly infringing technology or stop incorporating the allegedly infringing technology into such test or technology;
- obtain from the owner of the infringed intellectual property right a license, which may require us to pay substantial upfront fees or royalties to sell or use the relevant technology and which may not be available on commercially reasonable terms, or at all;
- redesign our products and technologies so they do not infringe or violate the third party's intellectual property rights, which may not be possible or may require substantial monetary expenditures and time;
- enter into cross-licenses with applicable third party, which could weaken our overall intellectual property position;
- lose the opportunity to license our technology to others or to collect royalty payments based upon successful protection and assertion of our intellectual property against others;
- find alternative suppliers for non-infringing technologies, which could be costly and create significant delay; or
- relinquish rights associated with one or more of our patent claims, if our claims are held invalid or otherwise unenforceable.

Third parties may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity, adversely impact our business, cause delays, or prohibit us from marketing or otherwise commercializing our products and technologies. Any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operation, financial condition or cash flows.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a material adverse effect on the price of our common stock. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. The occurrence of any of these events may have a material adverse effect on our business, results of operation, financial condition or cash flows.

We depend on information technology systems that we license from third parties. Any failure of such systems or loss of licenses to the software that comprises an essential element of such systems could significantly harm our business.

We depend on information technology systems for significant elements of our operations, such as our laboratory information management systems, including test validation, specimen tracking and quality control, our bioinformatics analytical software systems, our test report generating systems and billing systems. For example, although we transitioned our billing and collection process in-house starting January 1, 2021, we continue to rely upon a third-party software application in the administration of these functions. Essential elements of these systems depend on software that we license from third parties. If we are unable to maintain the licenses to this software or our software providers discontinue or alter the programs on which we rely, it could render our test reports unreliable or hinder our ability to generate accurate test reports, among other things. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

We rely on licenses from third parties, and if we lose these licenses or are not able to obtain licenses to third-party technology on reasonable grounds or at all, then we may not be able to continue to commercialize existing diagnostic tests, be subjected to future litigation and may not be able to commercialize new diagnostic tests in the future.

We are party to certain royalty-bearing license agreements that grant us rights to use certain intellectual property, including patents and patent applications, in certain specified fields of use. Although we intend to develop products and technologies through our own internal research, we may need to obtain additional licenses from others to advance our research, development and commercialization activities. Our license agreements impose, and we expect that future license agreements will impose, various development, diligence, commercialization and other obligations on us.

In the future, we may identify third-party technology we may need, including to develop or commercialize new diagnostic tests or services. In return for the use of a third party's technology, we may agree to pay the licensor royalties based on sales of our solutions. Royalties are a component of the cost of our products or services and affect our margins. We may also need to negotiate licenses to patents or patent applications before or after introducing a commercialized test. The in-licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to in-license or acquire third-party intellectual property rights for technologies that we may consider attractive or necessary.

These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. Furthermore, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. In addition, we expect that competition for the in-licensing or acquisition of third-party intellectual property rights for technologies that are attractive to us may increase in the future, which may mean fewer suitable opportunities for us as well as higher acquisition or licensing costs. We may not be able to obtain necessary or strategic licenses to patents or patent applications, and our business may suffer if we are unable to enter into these licenses on acceptable terms or at all, if any necessary licenses are subsequently terminated, if the licensors fail to abide by the terms of the licenses or fail to prevent infringement by third parties, or if the licensed patents or other rights are found to be invalid or unenforceable.

In spite of our efforts, our licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize tests and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties might have the freedom to seek regulatory approval of, and to market, tests identical to ours and we may be required to cease our development and commercialization activities. For example, we license certain intellectual property from WUSTL that is incorporated into DecisionDx-UM. In 2021, we provided over 1,600 test reports for DecisionDx-UM. If this license agreement were terminated, we would be unable to continue to issue test reports and thus sales of DecisionDx-UM. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Moreover, disputes may arise with respect to any one of our licensing agreements, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;

- the extent to which our products, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If we do not prevail in such disputes, we may lose any of such license agreements.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations.

The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected diagnostic tests, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

Our failure to maintain such licenses could have a material adverse effect on our business, financial condition and results of operations. Any of these licenses could be terminated, such as if either party fails to abide by the terms of the license, or if the licensor fails to prevent infringement by third parties or if the licensed patents or other rights are found to be invalid or unenforceable. Absent the license agreements, we may infringe patents subject to those agreements, and if the license agreements are terminated, we may be subject to litigation by the licensor. Litigation could result in substantial costs and be a distraction to management. If we do not prevail, we may be required to pay damages, including treble damages, attorneys' fees, costs and expenses, royalties or, be enjoined from selling our products or services, including DecisionDx-Melanoma and DecisionDx-UM, which could adversely affect our ability to offer our products or services, our ability to continue operations and our financial condition.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our products in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly developing countries, and the breadth of patent claims allowed can be inconsistent. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and we may encounter difficulties in protecting and defending such rights in foreign jurisdictions. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own tests or products and may also export infringing tests or products to territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our products. Our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many other countries do not favor the enforcement of patents and other intellectual property protection, particularly those relating to life science technologies, which could make it difficult for us to stop the infringement of our patents in such countries. We do not have patent rights in certain foreign countries in which a market may exist. Moreover, in foreign jurisdictions where we do have patent rights, proceedings to enforce our patent rights could result in substantial cost and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. We may not be able to stop a competitor from marketing and selling in foreign countries tests, products and services that are the same as or similar to our products and technologies, in which case our competitive position in the international market would be harmed.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business could be harmed.

In addition to pursuing patents on our technology, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We take steps to protect our trade secrets, in part, by entering into agreements, including confidentiality agreements, non-disclosure agreements and intellectual property assignment agreements, with our employees, consultants, academic institutions, corporate partners and, when needed, our advisers. However, we cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and, once disclosed, we are likely to lose trade secret protection and may not be able to obtain adequate remedies for such breaches. Such agreements may not be enforceable or may not provide meaningful protection for our trade secrets or other proprietary information in the event of unauthorized use or disclosure or other breaches of the agreements, and we may not be able to prevent such unauthorized disclosure. If we are required to assert our rights against such party, it could result in significant cost and distraction.

Monitoring unauthorized disclosure is difficult, and we do not know whether the steps we have taken to prevent such disclosure are, or will be, adequate. If we were to enforce a claim that a third party had illegally obtained and was using our trade secrets, it would be expensive and time-consuming, and the outcome would be unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets.

We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, absent patent protection, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We do and may employ individuals who previously worked with universities or other companies, including potential competitors. We could in the future be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of current or former employers or competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an individual to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a current or former employer or competitor. Although, we are currently not subject to any such claims.

While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management and other employees. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our products, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the current or former employers. Therefore, we could be required to obtain a license from such third-party employer to commercialize our products or technology. Such a license may not be available on commercially reasonable terms or at all.

Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We have not yet registered certain of our trademarks in all of our potential markets, although we have registrations for, among others, DecisionDx DiffDx-Melanoma, DecisionDx-UM, DecisionDx-Melanoma, DecisionDx-SCC, myPath Melanoma and TissueCypher Barrett's Esophagus Assay in the United States. Our current or future registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or descriptive determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign

jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. In addition, third parties have used trademarks similar and identical to our trademarks in foreign jurisdictions, and have filed or may in the future file for registration of such trademarks. If they succeed in registering or developing common law rights in such trademarks, and if we are not successful in challenging such third-party rights, we may not be able to use these trademarks to market our products in those countries. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Although these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our products. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, right to use, or right to exclude others from using, intellectual property that is important to our products. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

Obtaining and maintaining our patent protection depends on compliance with various required procedures, document submissions, fee payments and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications must be paid to the USPTO and various governmental patent agencies outside of the United States at several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction, such as failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we, or our licensors, fail to maintain the patents and patent applications covering our products and technologies, potential competitors may be able to enter the market without infringing our patents and this circumstance would have a material adverse effect on our business.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.

Patents have a limited lifespan, and the protection patents afford is limited. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the term of a patent, and the protection it affords, is limited. Even if patents covering our products are obtained, once the patent term has expired, we may be open to competition from competitive tests or products. Given the amount of time required for the development, testing and regulatory review of potential new tests or products, patents protecting such tests or products might expire before or shortly after such tests or products are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing tests or other products similar or identical to ours.

Risks Related to Employee Matters and Managing Growth and Other Risks Related to Our Business

We are highly dependent on the services of our key personnel.

We are highly dependent on the services of our key personnel, including Derek J. Maetzold, our President and Chief Executive Officer. Although we have entered into agreements with our key personnel regarding their employment, they are not for a specific term and each of them may terminate their employment with us at any time, though we are not aware of any present intention of any of these individuals to leave us.

Our research and development programs and laboratory operations depend on our ability to attract and retain highly skilled scientists and technicians. We may not be able to attract or retain qualified scientists and technicians in the future due to the competition for qualified personnel among life science businesses, particularly near our laboratory facilities and office spaces located in Phoenix, Arizona and Pittsburgh, Pennsylvania and our corporate headquarters in Friendswood, Texas. We also face competition from universities and public and private research institutions in recruiting and retaining highly qualified scientific personnel. We may have difficulties locating, recruiting or retaining qualified salespeople. Recruiting and retention difficulties can limit our ability to support our research and development and sales programs. All of our employees are at-will, which means that either we or the employee may terminate their employment at any time.

Our employees, clinical investigators, consultants, speakers, vendors and any current or potential commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, clinical study investigators, consultants, speakers, vendors and any potential commercial partners. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: federal laws and regulations or those of comparable foreign regulatory authorities, including those laws that require the reporting of true, complete and accurate information; manufacturing standards; federal and state health and data privacy, security, fraud and abuse, government price reporting, transparency reporting requirements, and other healthcare laws and regulations in the United States and abroad; sexual harassment and other workplace misconduct; or laws that require the true, complete and accurate reporting of financial information or data. Such misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, as well as a disclosure program and other applicable policies and procedures, but it is not always possible to identify and deter employee misconduct, 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 comply with these laws or regulations. 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 civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government funded healthcare programs, such as Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional integrity reporting and oversight obligations, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We may be unable to manage our future growth effectively, which could make it difficult to execute our business strategy.

We have experienced significant revenue growth in a short period of time. We may not achieve similar growth rates in future periods. You should not rely on our operating results for any prior periods as an indication of our future operating performance. To effectively manage our anticipated future growth, we must continue to maintain and enhance our financial, accounting, laboratory operations, customer support and sales administration systems, processes and controls. Failure to effectively manage our anticipated growth could lead us to over-invest or under-invest in development, operational and administrative infrastructure, result in weaknesses in our infrastructure, systems, or internal controls, give rise to operational mistakes, losses, loss of customers, productivity or business opportunities, and result in loss of employees and reduced productivity of remaining employees.

We also anticipate further growth in our business operations. This future growth could create strain on our organizational, administrative and operational infrastructure, including laboratory operations, quality control, customer service and sales organization management. We expect to continue increasing our headcount and hire more specialized personnel in the future as we grow our business and expand our product offerings. We will need to continue to hire, train and manage additional qualified scientists, laboratory personnel, client and account services personnel, and sales and marketing staff and improve and maintain our technology to properly manage our growth. If our new hires perform poorly, if we are unsuccessful in hiring, training, managing and integrating these new employees or if we are not successful in retaining our existing employees, our business may be harmed.

In addition, our anticipated growth could require significant capital expenditures and might divert financial resources from other projects such as the development of new diagnostic tests and services. As we commercialize additional diagnostic and prognostic tests, we may need to incorporate new equipment, implement new technology systems, or hire new personnel with different qualifications. Failure to manage this growth or transition could result in turnaround time delays, higher costs, declining quality, deteriorating customer service, and slower responses to competitive challenges. A failure in any one of these areas could make it difficult for us to meet market expectations for our products, and could damage our reputation and the prospects for our business.

We may not be able to maintain the quality or expected turnaround times of our products, or satisfy customer demand as it grows. Our ability to manage our growth properly will require us to continue to improve our operational, financial and management controls, as well as our reporting systems and procedures. The time and resources required to implement these new systems and procedures is uncertain, and failure to complete this in a timely and efficient manner could adversely affect our operations. If our management is unable to effectively manage our anticipated growth, our expenses may increase more than expected, our revenue could decline or grow more slowly than expected and we may be unable to implement our business strategy. The quality of our products and services may suffer, which could negatively affect our reputation and harm our ability to retain and attract customers.

We may engage in strategic transactions, such as the acquisition of businesses, assets, products or technologies, which could be disruptive to our existing operations, divert the attention of our management team and adversely impact our liquidity, cash flows, financial condition and results of operations.

From time to time, we may consider strategic opportunities and engage in transactions such as acquisitions of businesses, assets, products or technologies, as well as technology licenses or investments in complementary businesses. For example, in May 2021, we completed the acquisition of Myriad myPath Laboratory and in December 2021, we completed the acquisition of Cernostics. Any such transactions may entail numerous operational and financial risks, including:

- delays, difficulties and higher than expected costs associated with integration activities, such as those involving operational processes, regulatory and licensure compliance, personnel and information technology systems;
- disruption of our existing business operations and diversion of management’s time, focus and attention;
- decreases in our liquidity and operating cash flows, increases in our overall operating costs, substantial amounts of amortization expense, increased capital expenditure requirements and non-recurring charges, including possible impairments of acquired assets;
- incurrence of substantial debt or dilutive issuances of equity securities, the assumption of additional liabilities and exposure to unknown liabilities;
- inability to retain key personnel of any acquired businesses; and
- failure to realize any of the anticipated revenues, synergies, efficiencies or other benefits of a transaction within our estimated time frame or at all.

With regard to our acquisitions of the Myriad myPath Laboratory in May 2021 and Cernostics in December 2021, respectively, actual results may differ materially from our plans and expectations. For example, there can be no assurances regarding our ability to successfully scale and integrate the myPath Melanoma or TissueCypher Barrett’s Esophagus Assay into our commercial offerings and the ability of the combined strengths of Castle and Myriad myPath, LLC or Cernostics to position us for continued growth and success as a leader in the diagnostics space.

We are unable to predict the timing, size or nature of any future transactions, whether they will be completed or financed on favorable terms, if at all, or what the impact of those transactions might be on our financial results, including if such transactions are not effectively and profitably integrated into our business. Our failure to successfully complete the integration of any business that we acquire could have an adverse effect on our prospects, business activities, cash flows, financial condition, results of operations and stock price. Additionally, our ability to successfully integrate, manage and derive financial and other benefits from any acquired business, asset, product or technology is unproven.

Our ability to use net operating loss carryforwards and certain other tax attributes to offset future taxable income may be subject to limitations.

As of December 31, 2021, we had federal net operating loss (“NOL”) carryforwards of approximately \$99.4 million, of which \$43.5 million will begin to expire in 2030 if not utilized to offset taxable income, and \$55.9 million may be carried forward indefinitely. Also, as of December 31, 2021, we had state net operating loss carryforwards of \$67.5 million, which begin to expire in 2028 if not utilized to offset state taxable income.

Under the legislation known as the Tax Cuts and Jobs Act of 2017 (“TCJA”), as modified by the CARES Act, federal NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such NOL carryforwards in taxable years beginning after December 31, 2020 is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to the TCJA or the CARES Act.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an “ownership change” (which is generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period), the corporation’s ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We have experienced ownership changes in the past and we may also experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our NOL carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. In addition, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

If our information technology systems or data, or those of third parties upon which we rely, are or were compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; loss of customers or sales; and other adverse consequences

In the ordinary course of business, we process proprietary, confidential, and sensitive information (including but not limited to intellectual property, proprietary business information and personal information). We manage and maintain our applications and information utilizing a combination of on-site systems, managed data centers, and cloud-based data centers, and we are increasingly dependent upon information technology systems, infrastructure and information to operate our business.

It is critical that we do so in a secure manner to maintain the confidentiality, availability and integrity of such information. We also have outsourced elements of our operations to third parties, including third-party service providers and technologies to help operate critical business systems to Process proprietary, confidential and sensitive information, and as a result we manage a number of third-party contractors who have access to our proprietary, confidential and sensitive information. Our ability to monitor these third parties’ cybersecurity information security practices is limited, and these third parties may not have adequate information security measures in place.

Cyberattacks, malicious internet-based activity, and online and offline fraud are prevalent, continue to increase, and are becoming increasingly difficult to detect. Threat actors, personnel (such as through theft or misuse), sophisticated nation-states, and nation-state-supported actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including cyber-attacks that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. Despite the implementation of security measures designed to protect against a security incident, we and our contractors and consultants are vulnerable to a variety of evolving threats including but not limited to service interruptions, system malfunction, natural disasters, terrorism, war, public health crises, telecommunication and electrical failures, malware (including as a result of advanced persistent threat intrusions), malicious code, ransomware, supply chain attacks, denial-of-service attacks (such as credential stuffing), social engineering and other attempts to affect service reliability and threaten the confidentiality, integrity and availability of information. Ransomware attacks have become increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. Supply-chain attacks have also increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain or our third-party partners’ supply chains have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems (including our services) or the third-party information technology systems that support us and our services. Any of the previously identified or similar threats could cause a disruption or security incident, which could result in unauthorized, unlawful, or accidental loss of, damage to, modification of, destruction of, alteration of, encryption of, disclosure of, access to, or acquisition of our information and could interrupt our ability to provide our services.

While we have not experienced any such system failure, accident or material security incident to date, we cannot assure you that our data protection efforts and our investment in information technology have or will prevent security incidents, and we may be unable in the future to detect vulnerabilities in our information technology systems because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after a security incident has occurred. Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents, including

affected individuals, the Secretary of the HHS, states Attorneys General and others. Such disclosures are costly, and the disclosures or failure to comply could lead to adverse consequences.

If we or a third party upon whom we rely experience a security incident or are perceived to have experienced a security incident, we may experience government enforcement actions, additional reporting requirements and/or oversight, restrictions on processing data (including personal information), litigation, indemnification obligations, negative publicity, reputational harm, monetary fund diversions, interruptions in our operations, and other harms. Such consequences may disrupt our operations (including our ability to conduct our analyses, provide test results, bill payors or patients, process claims and appeals, provide customer assistance, conduct research and development activities, collect, process, and prepare company financial information, provide information about our products and other patient and physician education and outreach efforts through our website, and manage the administrative aspects of our business), damage our reputation, negatively impact our ability to grow our business, and others. For example, we maintain a tumor specimen database comprised of over 60,000 samples. Some of these samples were used to develop and validate DecisionDx-Melanoma, and, of those, some are currently being used to improve on the test and some will be used in the future. If we were to lose this database, our ability to further validate, improve and therefore maintain and grow sales of DecisionDx-Melanoma could be significantly impaired.

Our contracts may not contain limitations of liability, and there can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages if we fail to comply with applicable privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or adequately mitigate liabilities or damages with respect to claims, costs, expenses, litigation, fines, penalties, business loss, information loss, regulatory actions or material adverse impacts arising out of our privacy and security practices, Processing or security incidents we may experience, or that such coverage will continue to be available on commercially reasonable terms or at all.

Product or professional liability lawsuits against us could cause us to incur substantial liabilities and could limit our commercialization of our products.

We face an inherent risk of product and professional liability exposure related to our products. The marketing, sale and use of our products could lead to the filing of product liability claims were someone to allege that our products identified or reported inaccurate or incomplete information, or otherwise failed to perform as designed. We may also be subject to liability for errors in, a misunderstanding of or inappropriate reliance upon, the information we provide in the ordinary course of our business activities.

If we cannot successfully defend ourselves against claims that our products caused injury or otherwise failed to function properly, we could incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for our current tests any tests that we may develop, and the inability to commercialize such tests;
- injury to our reputation and significant negative media attention;
- reluctance of experts willing to conduct our clinical studies;
- initiation of investigations by regulators;
- significant costs to defend the related litigation and diversion of management's time and our resources;
- substantial monetary awards to study subjects or patients;
- product recalls, withdrawals or labeling, or marketing or promotional restrictions; and
- loss of revenue.

We currently carry product liability insurance. However, the amount of this insurance may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

International expansion of our business exposes us to business, regulatory, political, operational, financial, and economic risks associated with doing business outside of the United States.

While we currently accept orders from customers outside of the United States, our historical business strategy has been directed toward customers within the United States. Our long-term business strategy contemplates potential international expansion. Doing business internationally involves a number of risks, including:

- multiple, conflicting and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, economic sanctions and embargoes, employment laws, regulatory requirements and other governmental approvals, permits and licenses;

- limits in our ability to penetrate international markets if we are not able to perform tests locally;
- logistics and regulations associated with shipping tissue samples, including infrastructure conditions and transportation delays;
- difficulties in staffing and managing foreign operations;
- failure to obtain regulatory approvals for the commercialization of our products in various countries;
- complexities and difficulties in obtaining intellectual property protection and enforcing our intellectual property;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- 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 products 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; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and distributors' activities that may fall within the purview of the FCPA, its books and records provisions, or its anti-bribery provisions.

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

Requirements associated with being a public company will continue to increase our costs, as well as divert significant company resources and management attention.

We are subject to the reporting requirements of the Exchange Act or the other rules and regulations of the SEC and any securities exchange relating to public companies. Sarbanes-Oxley, as well as rules subsequently adopted by the SEC and The Nasdaq Stock Market LLC (“Nasdaq”) to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted additional rules and regulations in these areas, such as mandatory “say on pay” voting requirements that now apply to us since we are no longer an emerging growth company effective December 31, 2021. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Compliance with the various reporting and other requirements applicable to public companies requires considerable time and attention of management. We cannot assure you that we will satisfy our obligations as a public company on a timely basis.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. We were previously afforded exemptions from certain public company reporting requirements and were permitted to apply scaled disclosure requirements as a result of our status as an emerging growth company and a smaller reporting company, respectively. However, effective December 31, 2021, we ceased to be an emerging growth company and are no longer be permitted to apply the related exemptions. For example, in connection with this change, beginning with this Annual Report on Form 10-K for the year ended December 31, 2021 we were required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting and were required to apply public company adoption dates to new and revised accounting standards. Further, we are now subject to the reporting deadlines of a large accelerated filer. Beginning with our first Quarterly Report on Form 10-Q for the fiscal year ending December 31, 2022, we will no longer be permitted to take advantage of scaled disclosure requirements for smaller reporting companies. If we are unable to comply with these requirements on a timely basis or if the attention of our management and personnel is diverted from other business concerns, it could have a material adverse effect on our business, financial condition and results of operations. The increased costs will increase our net loss or decrease our net income, and may require us to reduce costs in other areas of our business or increase the prices of our products. In addition, as we expand, it may be more difficult or more costly for us to obtain certain types of insurance, including directors’ and officers’ liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified personnel to serve on our board of directors, our board committees or as executive officers.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We, and the third parties with whom we share our facilities, are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Each of our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. We could be held liable for any resulting damages in the event of contamination or injury resulting from the use of hazardous materials by us or the third parties with whom we share our facilities, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research and development. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our business could be adversely impacted by inflation.

Recently, the rate of inflation in the U.S. has risen to levels not experienced in decades. We have begun to see some inflationary pressures, primarily in personnel and related costs. The extent of any future impacts from inflation on our business and our results of operations will be dependent upon how long the elevated inflation levels persist and if the rate of inflation were to further increase, neither of which we are able to predict. If elevated levels of inflation were to persist or if the rate of inflation were to accelerate, the purchasing power of our cash and cash equivalents may be eroded, our expenses could increase faster than anticipated and we may utilize our capital resources sooner than expected. Further, given the complexities of the reimbursement landscape in which we operate, our payors may be unwilling or unable to increase reimbursement rates to compensate for inflationary impacts.

Our business could be adversely affected by natural disasters, public health epidemics and other events beyond our control.

Although we maintain crisis management plans, our business operations are subject to interruption by natural disasters and other events and catastrophes beyond our control, including, but not limited to, earthquakes, floods, fires, tornadoes, hurricanes, power or other utility outages, telecommunications failures and public health crises. Further, outbreaks of epidemic diseases, such as the COVID-19 pandemic discussed above, or the fear of such events, could provoke responses, including government-imposed travel restrictions that could impede the mobility and effectiveness of our sales force, disrupt our operations or those of our suppliers and service providers. The ultimate impact of any of these or similar events is highly uncertain and could have a material adverse impact on our operations.

Risks Related to Ownership of Our Common Stock

The stock price of our common stock may be volatile or may decline regardless of our operating performance, and you may lose all or part of your investment.

The market price of our common stock may fluctuate significantly in response to numerous factors, many of which are beyond our control, including:

- our operating performance and the performance of other similar companies;
- our success in marketing and selling our products;
- reimbursement determinations by third-party payors and reimbursement rates for our products;
- changes in our projected operating results that we provide to the public, our failure to meet these projections or changes in recommendations by securities analysts that elect to follow our common stock;
- regulatory or legal developments in the United States and other countries;
- the level of expenses related to product development and clinical studies for our products;
- our ability to achieve product development goals in the timeframes we announce;
- announcements of clinical study results, regulatory developments, acquisitions, strategic alliances or significant agreements by us or by our competitors;

- the success or failure of our efforts to acquire, license or develop additional tests;
- recruitment or departure of key personnel;
- general economic conditions and market conditions specific to our industry;
- interest rates and the rate of inflation;
- the extent and duration of the impacts from the COVID-19 pandemic;
- trading activity by a limited number of stockholders who together beneficially own a significant percentage of our outstanding common stock;
- the size of our market float; and
- any other factors discussed in this Annual Report on Form 10-K.

In addition, the stock market in general, and diagnostic and life sciences companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our securities, regardless of our actual operating performance. In the past, stockholders have filed securities class action litigation following periods of market volatility. If we were to become involved in securities litigation, it could subject us to substantial costs, divert resources and the attention of management from our business and adversely affect our business.

If there are substantial sales of shares of our common stock, the price of our common stock could decline.

The price of our common stock could decline if there are substantial sales of our common stock, particularly sales by our directors, executive officers and significant stockholders, or if there is a large number of shares of our common stock available for sale and the market perceives that sales will occur. Shares held by directors, executive officers and other affiliates are subject to volume limitations under Rule 144 under the Securities Act of 1933.

Certain of our stockholders have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or our stockholders. We filed such a registration statement in January 2022 to register the resale of shares of our common stock issuable in connection with our acquisition of Cernostics in December 2021. We have registered shares of common stock that we have issued and may issue under our employee equity incentive plans. As a result, these shares will be able to be sold freely in the public market upon issuance.

The market price of the shares of our common stock could decline as a result of the sale of a substantial number of our shares of common stock in the public market or the perception in the market that the holders of a large number of shares intend to sell their shares.

We have broad discretion in the use of working capital and may not use it effectively or in ways that increase our share price.

We cannot specify with any certainty the particular uses of working capital, but we currently expect such uses will include: funding selling and marketing activities, including expansion of our sales force to support the ongoing commercialization of current and future products; research and development related to the continued support of our current products as well as the development of our product pipeline; and other general corporate purposes, including the additional costs associated with being a public company. The failure by our management to apply our working capital effectively could adversely affect our business and financial condition. Pending its use, we may invest working capital in a manner that does not produce income or that loses value. These investments may not yield a favorable return to our investors.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our common stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause our common stock price and trading volume to decline.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules

and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make any related party transaction disclosures. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected. In addition, we do not have a risk management program or processes or procedures for identifying and addressing risks to our business in other areas.

We have and may continue to enter into related party transactions that create conflicts of interest, or the appearances of conflicts of interest, which may harm our business and cause our stock price to decline.

We have entered into related party transactions that create conflicts of interest between our interests and the interests of our directors and executive officers. For example, we employ three children and a brother-in-law of Derek J. Maetzold, our President and Chief Executive Officer, three children and a son-in-law of Kristen M. Oelschlager, our Chief Operating Officer, and the son of Tobin W. Juvenal, our Chief Commercial Officer, in each case in non-officer positions. These arrangements are required to be disclosed in our annual proxy statement and/or in the notes to our consolidated financial statements based on certain criteria. We may engage in other transactions in the future involving our executive officers, directors and their family members and/or entities which they control or are affiliated, which could cause individuals in our management to seek to advance their economic interests or the economic interests of certain related parties above ours. Although we have a written policy on related party transactions that involves independent review and oversight by the audit committee of our board of directors, there can be no assurances that conflicts of interest will not exist, or that we will be able to adequately address or mitigate any actual or perceived conflicts of interest, and stockholders, analysts, proxy advisory firms, the news media and other parties may view these transactions as representing conflicts of interest or as otherwise inappropriate, which may result in negative public perception and reputational harm, and could impair our ability to enter into new customer relationships or attract and retain employees. Potential, perceived and actual conflicts of interest could cause investors to question the independence of our management, the adequacy and effectiveness of our disclosure controls and procedures or the integrity of our corporate governance procedures and compensation practices, which could have a material adverse effect on the trading price of our common stock and our business, financial condition and results of operations.

We do not intend to pay dividends for the foreseeable future.

We have never declared nor paid cash dividends on our capital stock. We currently intend to retain any future earnings to finance the operation and expansion of our business, and we do not expect to declare or pay any dividends in the foreseeable future. Consequently, stockholders must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investment.

The concentration of our stock ownership will likely limit your ability to influence corporate matters, including the ability to influence the outcome of director elections and other matters requiring stockholder approval.

Based upon shares outstanding as of December 31, 2021, our executive officers, directors and the known holders of more than 5% of our outstanding common stock, in the aggregate, beneficially owned approximately 27% of our common stock. As a result, these stockholders, acting together, will have significant influence over all matters that require approval by our stockholders, including the election of directors and approval of significant corporate transactions. Corporate actions might be taken even if other stockholders oppose them. This concentration of ownership might also have the effect of delaying or preventing a change of control of our company that other stockholders may view as beneficial.

Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock.

Provisions of our amended and restated certificate of incorporation and amended and restated bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our amended and restated certificate of incorporation and amended and restated bylaws:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (including the right to approve an acquisition or other change in our control);
- provide that the authorized number of directors may be changed only by resolution of the board of directors;

- provide that the board of directors or any individual director may only be removed with cause and the affirmative vote of the holders of at least 66-2/3% of the voting power of all of our then outstanding common stock;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide our board of directors into three classes;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner and also specify requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by the chairman of the board, our Chief Executive Officer or by the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors;
- provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if and only if the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, any state court located within the State of Delaware or, if and only if all such state courts lack subject matter jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws; (iv) any action or proceeding to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws; (v) any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and (vi) any action asserting a claim against us or any of our directors, officers or other employees governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants; provided these provisions of our amended and restated certificate of incorporation and amended and restated bylaws will not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and
- provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act, subject to and contingent upon a final adjudication in the State of Delaware of the enforceability of such exclusive forum provision.

The amendment of any of these provisions, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require approval by the holders of at least 66-2/3% of our then-outstanding common stock.

In addition, as a Delaware corporation, we are subject to Section 203 of the Delaware General Corporation Law. These provisions may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a certain period of time. A Delaware corporation may opt out of this provision by express provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out of this provision.

These and other provisions in our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, including delay or impede a merger, tender offer or proxy contest involving our company. The existence of these provisions could negatively affect the price of our common stock and limit opportunities for you to realize value in a corporate transaction.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if and only if the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, any state court located within the State of Delaware or, if and only if all such state courts lack subject matter jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees arising out of or pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or amended and restated bylaws; (iv) any action or proceeding to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; (v) any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and (vi) any action asserting a claim against us or any of our directors, officers or other employees that is governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants; provided these provisions would not apply to suits brought to enforce a duty or liability created by the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation and amended and restated bylaws provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act, subject to and contingent upon a final adjudication in the State of Delaware of the enforceability of such exclusive forum provision. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees and may discourage these types of lawsuits. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. If a court were to find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We have a lease agreement for approximately 23,700 square feet of office space in Friendswood, Texas that is used as our corporate headquarters. This lease commenced in late 2020 and has a 60-month term, with an option to renew for one additional five-year period. We also lease approximately 29,700 square feet of laboratory and office space in Phoenix, Arizona under two agreements, both of which expire on April 30, 2033. For both leases, there are options to renew for two additional five-year terms. In connection with our recent acquisition of Cernostics in December 2021, we have approximately 8,100 square feet of office and laboratory space in Pittsburgh, Pennsylvania under a lease which expires on November 30, 2022, with the option to renew for one additional year. In support of our growth strategy, we anticipate acquiring additional office and laboratory space in the near future.

Item 3. Legal Proceedings.

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. We believe there is no threatened litigation or litigation pending that could have, individually or in the aggregate, a material adverse effect on our financial position, results of operations or cash flows.

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.

Market Information

Our Common Stock, \$0.001 par value per share, began trading on the Nasdaq Global Market under the symbol “CSTL” on July 25, 2019. Prior to that date, there was no public trading market for our common stock.

Holders of Record

As of February 21, 2022, there were approximately 30 stockholders of record of our common stock, which does not include stockholders who hold shares in street name.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on, among other factors, our financial condition, operating results, capital requirements, contractual restrictions, general business conditions and other factors that our board of directors may deem relevant.

Securities Authorized for Issuance Under Our Equity Compensation Plans

Information regarding securities authorized for issuance under our equity compensation plans is incorporated herein by reference to Item 12, “Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters” of Part III of this Annual Report on Form 10-K.

Performance Graph

Not required for smaller reporting companies.

Recent Sales of Unregistered Equity Securities

None.

Use of Proceeds from IPO of Common Stock

On July 29, 2019, we completed the initial public offering of our common stock (our “IPO”), pursuant to which we issued and sold 4,600,000 shares of our common stock, including 600,000 shares associated with the full exercise of the underwriters’ option to purchase additional shares, at a price to the public of \$16.00 per share.

The offer and sale of all of the shares of our common stock in the IPO were registered under the Securities Act pursuant to our Registration Statements on Form S-1, as amended (File Nos. 333-232369 and 333-232796), which were declared or became effective on July 24, 2019.

There has been no material change in our planned use of the net proceeds from the IPO as described in the final prospectus filed with the SEC on July 26, 2019 relating to our Registration Statements on Form S-1 (File Nos. 333-232369 and 333-232796).

Since the effective date of our registration statement through December 31, 2021, we have not used any of the net proceeds from the IPO. Pending such uses, we have invested, and plan to continue to invest, the balance of the net proceeds from the IPO in cash and cash equivalent securities or highly liquid investment securities.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. Reserved.

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

You should read the following discussion and analysis of financial condition and results of operations together with our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results, performance or achievements could differ materially from any future results, performance or achievements discussed in these forward-looking statements. Factors

that could cause or contribute to such differences include, but are not limited to, those discussed in the section titled “Risk Factors.”

Overview

Castle Biosciences is improving health through innovative tests that guide patient care. For the diseases that our portfolio of tests cover, we believe the traditional approach to developing a treatment plan for cancers and other diseases using clinical and pathology factors alone is inadequate and can be improved by incorporating the personalized information our diagnostic and prognostic tests provide.

We currently market five proprietary MAAAs, designed to answer clinical questions in dermatologic cancers, UM and BE. Our revenue is primarily generated by our DecisionDx®-Melanoma risk stratification test for cutaneous melanoma and our DecisionDx®-UM risk stratification test for UM.

The foundation of our business is our dermatologic cancer franchise, and our lead product is DecisionDx-Melanoma, a proprietary risk stratification GEP test that predicts the risk of metastasis, or recurrence for patients diagnosed with invasive cutaneous melanoma, a deadly skin cancer. In the management of melanoma, as with nearly all diseases, treatment plans are directed by patient risk-stratification. This test has two distinct, complementary clinically actionable uses. The first revolves around predicting the likelihood of having a SLN negative biopsy result so that physicians and patients can discuss the risk and benefit of undergoing the SLNB surgical procedure. The second use is to inform the appropriate treatment plan during the initial five years post-diagnosis, regardless of the decision to undergo or avoid invasive SLNB surgery. In a typical year, we estimate approximately 130,000 patients are diagnosed with invasive cutaneous melanoma in the United States. We launched DecisionDx-Melanoma in May 2013. Based on the substantial clinical evidence that we have developed, we have received Medicare coverage for DecisionDx-Melanoma, which represents approximately 50% of the addressable patient population for this test.

On August 31, 2020, we commercially launched our SCC proprietary GEP test, DecisionDx®-SCC, for use in patients with one or more risk factors (also referred to as “high-risk” SCC). On November 2, 2020, we commercially launched our proprietary GEP test for difficult-to-diagnose melanocytic lesions, DecisionDx® DiffDx™-Melanoma for use in patients with a melanocytic lesion and uncertainty related to the malignancy of the lesion. We believe that these two additional skin cancer tests address areas of high clinical need in dermatological cancer and, together, represent an estimated addressable population of approximately 500,000 patients in the United States.

We further expanded our commercially available dermatologic portfolio in May 2021 when we acquired the myPath Laboratory from Myriad Genetics, Inc. for a cash purchase price of \$32.5 million. myPath Melanoma is a clinically validated GEP test that addresses the same unmet clinical need as our DecisionDx DiffDx-Melanoma test. Today, we offer both our myPath Melanoma test and our DecisionDx DiffDx-Melanoma test under an offering that we refer to as our CDO of molecular testing solutions. By offering both of these tests in a single offering, we believe we have demonstrated the ability to improve the test result performance for patients with difficult-to-diagnose melanocytic lesions.

In 2021, we announced the launch of our innovative pipeline initiative to develop a genomic test aimed at predicting response to systemic therapy in patients with moderate to severe psoriasis, atopic dermatitis and related inflammatory skin conditions. In the U.S. alone, there are approximately 18 million patients diagnosed with psoriasis and atopic dermatitis. Approximately 450,000 of these patients annually are eligible for systemic therapies. If successful, this inflammatory skin disease pipeline test has the potential to add approximately \$1.9 billion to our current estimated U.S. TAM. In 2021, we initiated a 4,800 patient, prospective, multi-center clinical study to develop and validate this pipeline test and have 50 committed centers, out of the initial target of 50. Based upon our current development and validation timelines, we expect to commercialize this pipeline test by the end of 2025.

In addition to our dermatologic franchise, we also market a test for patients diagnosed with UM, a rare cancer of the eye. DecisionDx®-UM is a proprietary, risk stratification GEP test that predicts the risk of metastasis for patients with UM. We believe DecisionDx-UM is the standard of care in the management of newly diagnosed UM in the majority of ocular oncology practices in the United States. We launched DecisionDx-UM in January 2010. Based on the substantial clinical evidence that we have developed, we received Medicare coverage for DecisionDx-UM, which represents approximately 50% of the addressable patient population.

In December 2021, we extended our commercial portfolio of proprietary tests into the gastroenterology market through our acquisition of Cernostics and the TissueCypher® platform. The TissueCypher platform focuses on unlocking, in the case of the initial test for use in patients with BE, the importance of the location of the expression of proteins or lack thereof within the morphology of the disease (also known as spatialomics). This “spatialomic” information is then interpreted using artificial intelligence approaches to predict the likelihood of progression to high-grade dysplasia and/or esophageal cancer in patients with non-dysplastic, indefinite or low-grade dysplasia BE. We believe the addition of expertise in the spatialomics area

positions us for continued growth and success in the diagnostics space, complementing our first-to-market dermatologic franchise and our proprietary test for UM.

The number of test reports we generate is a key indicator that we use to assess our business. A test report is generated when we receive a sample in our laboratory, and then the relevant test information is entered into our Laboratory Information Management System, the expression of the biomarkers is measured, then a proprietary algorithmic analysis of the combined biomarkers is performed to generate a report providing the results of that analysis, which is sent to the clinician who ordered the test. The numbers of GEP test reports delivered by us during the years ended December 31, 2021 and 2020 are presented in the table below:

	Proprietary Dermatologic GEP Tests					Grand Total
	DecisionDx-Melanoma	DecisionDx-SCC ⁽¹⁾	CDO ⁽²⁾	Dermatologic Total	DecisionDx-UM	
Q1 2021	4,060	527	218	4,805	337	5,142
Q2 2021	5,128	784	627	6,539	468	7,007
Q3 2021	5,505	934	913	7,352	375	7,727
Q4 2021	5,635	1,265	904	7,804	438	8,242
For the year ended December 31, 2021	<u>20,328</u>	<u>3,510</u>	<u>2,662</u>	<u>26,500</u>	<u>1,618</u>	<u>28,118</u>
Q1 2020	4,574	—	—	4,574	361	4,935
Q2 2020	3,008	—	—	3,008	306	3,314
Q3 2020	4,404	57	—	4,461	318	4,779
Q4 2020	4,246	428	73	4,747	410	5,157
For the year ended December 31, 2020	<u>16,232</u>	<u>485</u>	<u>73</u>	<u>16,790</u>	<u>1,395</u>	<u>18,185</u>

(1) We commercially launched DecisionDx-SCC on August 31, 2020.

(2) Includes DecisionDx DiffDx-Melanoma, which we commercially launched on November 2, 2020, and myPath Melanoma, which we began offering following our acquisition of Myriad myPath Laboratory on May 28, 2021. We offer both our myPath Melanoma and DecisionDx DiffDx-Melanoma under our CDO.

For the year ended December 31, 2021, our dermatologic test report volume increased by 57.8%, reflecting growth in DecisionDx-Melanoma as well as the full year availability of DecisionDx-SCC and DecisionDx DiffDx-Melanoma (now offered as part of CDO). For a discussion of how we recognize revenue derived from our GEP tests, refer to “Net Revenues” under “Components of Results of Operations” below.

The principal focus of our current commercial efforts is to educate clinicians and pathologists on the value of our molecular diagnostic testing products through our direct sales force in the U.S. In dermatology, we began 2020 with 32 outside sales territories. In the third quarter of 2020, we expanded our dermatologic commercial team to create a dedicated sales force of ten territories to support the launch of our DecisionDx Diff-Dx Melanoma test to dermatopathologists. During the first half of 2021, we folded this dedicated team into our existing sales team and completed a further expansion, bringing our dermatologic sales force to the mid-60s. In connection with our acquisition of Cernotics in December 2021, we hired an initial commercial team of approximately 14 outside sales territories, along with commensurate internal sales associates and medical science liaisons, to support our launch of the TissueCypher Barrett’s Esophagus Assay. This dedicated team focuses on gastroenterology specialists that diagnose and manage patients with BE. However, we will continue to evaluate our mix of outside sales territories, inside sales support, marketing and medical affairs in the context of our dermatologic tests and gastroenterology tests and adjust our investments based upon these evaluations.

We continue to see new clinicians order our dermatologic tests for the first time. For the year ended December 31, 2021, we saw approximately 1,938 new ordering clinicians for our dermatologic tests compared to 1,396 during the same period of 2020. Total ordering clinicians for our dermatologic tests were approximately 5,900 for the year ended December 31, 2021.

For additional information on the metrics we disclose, refer to “Information about certain metrics” below.

In developing our DecisionDx-SCC and DecisionDx DiffDx-Melanoma tests, we believed that in addition to addressing significant unmet clinical needs, we would see strategic opportunities for leverage, as many of the clinicians currently ordering DecisionDx-Melanoma would likely be the same clinicians who would find value in these other skin cancer tests. For example,

we found that for the year ended December 31, 2021, approximately 78% of all clinicians ordering DecisionDx-SCC had also ordered our DecisionDx-Melanoma test during that same period.

We bill third-party payors and patients for the tests we perform. The majority of our revenue collections is paid by third-party insurers, including Medicare. We have received LCDs, which provide coverage for our DecisionDx-Melanoma, myPath Melanoma and DecisionDx-UM tests that meet certain criteria for Medicare and Medicare Advantage beneficiaries, representing approximately 60 million covered lives. In 2022, DecisionDx-UM has received coverage from United Healthcare that will represent approximately 43 million covered lives. A “covered life” means a subscriber, or a dependent of a subscriber, who is insured under an insurance carrier’s policy.

Palmetto, the MAC responsible for administering MoIDX, the program that assesses molecular diagnostic technologies, issued a final expanded LCD for DecisionDx-Melanoma, effective November 22, 2020. With this expanded LCD and the accompanying billing and coding articles, we estimate that a significant majority of the DecisionDx-Melanoma tests performed for Medicare patients will meet the coverage criteria. Noridian, the MAC responsible for administering claims for laboratory services performed in Arizona, has adopted the same coverage policy as Palmetto and also issued an expanded final LCD for DecisionDx-Melanoma, effective December 6, 2020.

Separately, Palmetto issued a final LCD for DecisionDx-UM, which became effective in July 2017, and Noridian issued a similar LCD that became effective in September 2017. The Noridian LCD provides for coverage to determine metastatic risk in connection with the management of a patient’s newly diagnosed uveal melanoma and to guide surveillance and referral to medical oncology for those patients. Similar to cutaneous melanoma, the median age at diagnosis for uveal melanoma is estimated at 58-62 years old, therefore the Medicare eligible population represents close to 45% of the addressable market.

On May 17, 2019, CMS determined that DecisionDx-UM meets the criteria for “existing advanced diagnostic laboratory test” status, also referred to as “existing ADLT” status. For 2020, our rate was set by Noridian, our local MAC, but effective in 2021 our rate is set annually based upon the median private payor rate for the first half of the second preceding calendar year. Our rate for 2021 was \$7,776 and will remain at \$7,776 for 2022, in each case based on the calculation of the median private payor rate.

Also, on May 17, 2019, CMS determined that DecisionDx-Melanoma meets the criteria for “new ADLT” status. Accordingly, from July 1, 2019 through March 31, 2020, the Medicare reimbursement rate was equal to the initial list price of \$7,193. From April 1, 2020 through December 31, 2021, the rate was also \$7,193, which was calculated based upon the median private payor rate for DecisionDx-Melanoma from July 1, 2019 to November 30, 2019. CMS has informed us that the rate for 2022 will continue to be \$7,193, based on the median private payor rate.

myPath Melanoma is currently covered under a MoIDX LCD policy through Noridian that oversees laboratories in both Utah and Arizona. Noridian issued an LCD that became effective in June 2019. On September 6, 2019, myPath Melanoma was approved as a new ADLT. The rate for 2022 will be \$1,950.

TissueCypher is performed in our Pittsburgh, Pennsylvania laboratory and falls under the Medicare jurisdiction that is managed by Novitas. Novitas previously reviewed TissueCypher and we are receiving payments for claims according to the CLFS. For 2022, CMS published in its CLFS a payment amount of \$2,513 for the test.

Beginning in 2023, the rates for DecisionDx-Melanoma, DecisionDx-UM, and myPath Melanoma tests will be set annually based upon the median private payor rate for the first half of the second preceding calendar year. For example, the rate for 2023 will be set using median private payor rate data from January 1, 2021 to June 30, 2021.

In the second quarter of 2020, we submitted our technical assessment dossier for DecisionDx-SCC to Palmetto and Noridian. The dossier was accepted as complete in the third quarter of 2020. In early 2021, we submitted our technical assessment dossier for DecisionDx DiffDx-Melanoma. The dossier was accepted as complete in the first quarter of 2021. We expect that draft LCDs for DecisionDx-SCC and DecisionDx DiffDx-Melanoma could potentially be posted by the end of the second quarter of 2022 resulting in potentially final LCDs effective in 2023. However, there is no assurance that the timing of any draft or final LCD will match our expectations or our historical experience with LCDs for our other tests.

In the second quarter of 2021, Palmetto and the other MACs that participate in the MoIDX program posted a revised draft LCD for DecisionDx-Melanoma. The draft LCD includes commentary about two publications regarding the clinical utility of GEP tests and was posted to give providers an opportunity to comment. Each of the draft LCDs include an assessment stating that the MAC does not believe that the new data is sufficient to change the coverage criteria. We have submitted comments on the draft LCD. The comment period on the last of these draft LCDs closed on August 8, 2021. We are unable to predict when the final draft LCD will be posted.

Since becoming a public company, we have financed our operations with the revenue generated from the sale of our products, proceeds from our July 2019 IPO, follow-on public offerings of common stock in June 2020 and December 2020 and bank debt, which has since been repaid in full. We believe that our existing cash and cash equivalents and anticipated cash generated

from sales of our products will be sufficient to fund our operations for the next 12 months and into the foreseeable future. However, we have based these estimates on assumptions, including those related to the impact of COVID-19 on our financial condition, that may prove to be wrong, and could result in us depleting our capital resources sooner than expected.

Our net (loss) income may fluctuate significantly from period to period, depending on the timing of our planned development activities, the growth of our sales and marketing activities and the timing of revenue recognition under ASC 606. We expect our expenses will increase substantially over time as we:

- execute clinical studies to generate evidence supporting our current and future product candidates;
- execute our commercialization strategy for our current and future commercial products;
- continue our ongoing and planned development of new products in our pipeline;
- seek to discover and develop additional product candidates;
- hire additional scientific and research and development staff; and
- add additional operational, financial and management information systems and personnel.

Furthermore, we expect to continue to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses.

Impact of COVID-19 Pandemic

We are continuing to closely monitor the impact of the COVID-19 pandemic on our business and taking proactive efforts designed to protect the health and safety of our workforce, continue our business operations and advance our corporate objectives. We are providing the following update with respect to the impact of COVID-19 on our business:

- We have maintained, and expect to continue to maintain, uninterrupted business operations with adequate access to reagents and consumables needed for testing patient samples and normal turnaround times for our delivery of test reports. We have continued to maintain our previously implemented adjustments to our operations designed to keep employees safe and comply with federal, state and local guidelines, including those regarding social distancing.
- Following the onset of the COVID-19 pandemic, we experienced declines in orders and test report volume. For example, in the second quarter of 2020, test reports delivered for our lead product, DecisionDx-Melanoma, decreased 18.5% compared to the second quarter of 2019. For the year ended December 31, 2020, our growth in DecisionDx-Melanoma test report volume was 4.5%, compared to year-over-year growth of 29.1% for the year ended December 31, 2019. Our analysis of third-party data indicates that cutaneous melanoma diagnoses for the year ended December 31, 2020 were down approximately 20% compared to the year ended December 31, 2019. In the first quarter of 2021, test reports delivered for DecisionDx-Melanoma decreased by 11.2% compared to the first quarter of 2020. We believe these decreases in our test report volume were linked to delays and/or cancellations in patient visits, resulting in fewer diagnostic biopsies and thus a reduction in the number of diagnoses of cutaneous melanoma in response, as well as the cumulative impact on promotional responsiveness as a result of reduced sales calls per day and in-person sales call during the COVID-19 pandemic.
- We saw positive trends in orders and test report volumes in the second, third, and fourth quarters of 2021. In the second, third and fourth quarters of 2021, test reports delivered for DecisionDx-Melanoma increased by 70.5%, 25.0% and 32.7%, respectively, compared to the same quarters in 2020.
- Our commercial team uses a combination of in-person, virtual, and non-personal promotional and educational efforts. Since the beginning of 2021, we have seen improvements in the number of promotional calls per day, as well as a continued shift from virtual to in-person sales calls. During the three-months ended December 31, 2021, in-person sales calls accounting for over 90% of all calls during such period. However, we have not yet achieved pre-COVID-19 levels of calls per day per sales representative.
- Our future results will be dependent upon the extent and duration of the COVID-19 crisis, including the emergence and spread of variants of the virus, such as the Omicron variant, and government restrictions, which are beyond our control. Although state and local government restrictions put in place to slow the spread of the virus have been eased in certain locations, restrictions may be reinstated from time to time in various regions depending on the circumstances, potentially impacting the flow of future patient visits as well as access to our sales targets. Even with the easing of state and local restrictions and the availability of vaccinations, patient visits and diagnoses of cutaneous melanoma may be impacted by continued apprehension regarding possible exposure to the virus. For example, our

analysis of third-party data indicates that cutaneous melanoma diagnoses during the year ended December 31, 2021 remain approximately 11% below the pre-COVID, 2019 levels.

- We continue to believe our cash, cash equivalents and anticipated cash to be generated from sales of our products, will be sufficient to fund our operations for the next 12 months and into the foreseeable future.

As conditions are continuously evolving, we are unable to predict how our future test report volume will be impacted, or the extent to which our results of operations, financial condition or cash flows will be impacted, by the COVID-19 pandemic, or other future public health crises. Accordingly, the test report data presented above is not necessarily indicative of our results of operations that can be expected for future periods. For more information on the potential impact of the COVID-19 pandemic on our business, see the risk factors included under “Risks Related to Our Business” and the other risk factors included in Part I, Item 1A., “Risk Factors,” of this Annual Report on Form 10-K.

Factors affecting our performance

We believe there are several important factors that have impacted, and that we expect will continue to impact, our operating performance and results of operations, including:

- **Report volume.** We believe that the number of reports we deliver to physicians is an important indicator of the growth of adoption among the healthcare provider community. Our revenue and costs are affected by the volume of testing and mix of customers. Our performance depends on our ability to retain and broaden adoption with existing prescribing physicians, as well as attract new physicians. In the near term, our report volume may be negatively impacted by ongoing developments of the COVID-19 pandemic as discussed above.
- **Reimbursement.** We believe that expanding reimbursement is an important indicator of the value of our products. Payors require extensive evidence of clinical utility, clinical validity, patient outcomes and health economic benefits in order to provide reimbursement for diagnostic products. Our revenue depends on our ability to demonstrate the value of our products to these payors.
- **Gross margin.** We believe that our gross margin is an important indicator of the operating performance of our business. Higher gross margins reflect the average selling price of our tests, as well as the operating efficiency of our laboratory operations.
- **New product development.** A significant aspect of our business is our investment in research and development activities, including activities related to the development of new products. In addition to the development of new product candidates, we believe these studies are critical to gaining physician adoption of new products and driving favorable coverage decisions by payors for such products.

Information about certain metrics

The following provides additional information about certain metrics we have disclosed in this Management’s Discussion and Analysis of Financial Condition and Results of Operation.

Test reports delivered for DecisionDx-Melanoma, DecisionDx-SCC, myPath Melanoma/DecisionDx DiffDx-Melanoma, DecisionDx-UM and TissueCypher Barret’s Esophagus Assay represents the number of completed test reports delivered by us during the reporting period indicated. The period in which a test report is delivered does not necessarily correspond with the period the related revenue, if any, is recognized, due to the timing and amount of adjustments for variable consideration under ASC 606. We use this metric to evaluate the growth in adoption of our tests and to measure against our internal performance objectives. We believe this metric is useful to investors in evaluating the volume of our business activity from period-to-period that may not be discernible from our reported revenues under ASC 606. We also sometimes present, on a limited basis, data on the number of orders received. We believe order data can provide additional insight on current demand trends, particularly during the COVID-19 pandemic and with respect to new product launches, when considered in conjunction with test report volume. However, orders received in a particular period do not necessarily correspond with actual delivered test reports or reported revenues for the same period or subsequent periods.

New ordering clinicians for our dermatologic tests represents the number of clinicians who ordered a dermatologic test from us for the first time during the reporting period specified. Our dermatologic tests consist of DecisionDx-Melanoma, DecisionDx-SCC and our CDO. We believe this metric is useful in evaluating the effectiveness of our sales and marketing efforts in establishing new relationships with clinicians and increasing the adoption of our suite of dermatologic tests. We also believe this metric provides useful information to investors in assessing our ability to expand the use of our dermatologic tests. Since this metric is based upon the reporting period in which an order is placed, it does not necessarily correspond to the reporting period in which a test report was delivered or revenue was recognized.

Components of the Results of Operations

Net Revenues

We generate revenues from the sale of our products. Currently, our revenues are primarily derived from the sale of DecisionDx-Melanoma and DecisionDx-UM. We bill third-party payors and patients for the tests we perform.

Under ASC 606, we recognize revenue at the amount we expect to be entitled, subject to a constraint for variable consideration, in the period in which our tests are delivered to the treating physicians. We have determined that our contracts contain variable consideration under ASC 606 because the amounts paid by third-party payors may be paid at less than our standard rates or not paid at all, with such differences considered implicit price concessions. Variable consideration is recognized only to the extent it is probable that a significant reversal of revenue will not occur in future periods when the uncertainties are resolved. Variable consideration is evaluated each reporting period and adjustments are recorded as increases or decreases in revenues. Variable consideration for Medicare claims that are not covered by an LCD, including those claims subject to approval by an ALJ at an appeal hearing, is deemed to be fully constrained due to factors outside our influence (i.e., judgment or actions of third parties) and the uncertainty of the amount to be received is not expected to be resolved for a long period of time. For these fully constrained claims, we generally recognize revenue in the period the uncertainty is favorably resolved, if at all. Due to potential future changes in Medicare coverage policies and appeal cycles, insurance coverage policies, contractual rates and other trends in the reimbursement of our tests, our revenues may fluctuate significantly from period-to-period. Additionally, our ability to recognize revenue for our recently launched tests, DecisionDx-SCC and DecisionDx DiffDx-Melanoma, is dependent on the development of reimbursement experience and coverage decisions for these tests. Due to limited reimbursement experience, we are currently recognizing revenues for these two tests on the basis of actual cash collections.

Our ability to increase our revenues will depend on our ability to further penetrate our target markets, and, in particular, generate sales through our direct sales force, develop and commercialize additional tests, obtain reimbursement from additional third-party payors and increase our reimbursement rate for tests performed.

Cost of Sales (exclusive of amortization of acquired intangible assets)

The components of our cost of sales are material and service costs associated with testing samples, personnel costs (including salaries, bonuses, benefits and stock-based compensation expense), electronic medical record set up costs, order and delivery systems, shipping charges to transport samples, third-party test fees, and allocated overhead including rent, information technology costs, equipment and facilities depreciation and utilities. Costs associated with testing samples are recorded when the test is processed, regardless of whether and when revenues are recognized with respect to that test. As a result, our cost of sales as a percentage of revenues may vary significantly from period-to-period because we do not recognize all revenues in the period in which the associated costs are incurred. We expect cost of sales in absolute dollars to increase as the number of tests we perform increases. Additionally, we expect cost of sales to increase with the expansion of laboratory capacity and staffing in advance of the anticipated growth of our recently launched tests.

Gross margin and gross margin percentage are key indicators we use to assess our business. See the table in “Results of Operations—Comparison of the years ended December 31, 2021 and 2020” for details.

Research and Development

Research and development expenses include costs incurred to develop our genomic tests, collect clinical samples and conduct clinical studies to develop and support our products. These costs consist of personnel costs (including salaries, bonuses, benefits and stock-based compensation expense), prototype materials, laboratory supplies, consulting costs, regulatory costs, electronic medical records set up costs, costs associated with setting up and conducting clinical studies and allocated overhead, including rent, information technology, equipment depreciation and utilities. We expense all research and development costs in the periods in which they are incurred. We expect our research and development expenses to increase in absolute dollars as we continue to invest in research and development activities related to developing enhanced and new products.

We expect to use a portion of our cash and cash equivalents to further support and accelerate our research and development activities, including three important studies that are underway to support our DecisionDx-Melanoma test. The first is the PERSONALize study, in which we are evaluating DecisionDx-Melanoma for interactions with adjuvant therapies. The second is the CONNECTION study, which is collecting long-term outcomes for up to 10,000 patients who have been tested with DecisionDx-Melanoma. The third is the DECIDE study, which is designed to determine the association of GEP test results with SLNB surgical decisions in patients eligible for SLNB as well as to track outcomes for patients who did and did not undergo SLNB. Also, as noted above, we recently initiated a 4,800 patient, prospective, multi-center clinical study to develop, validate and bring to market a pipeline test aimed at predicting response to systemic therapy in patients with moderate to severe psoriasis, atopic dermatitis and related inflammatory skin conditions. We have also initiated two additional disease studies for pipeline tests for new indications.

Selling, General and Administrative

Selling, general and administrative (“SG&A”) expenses include executive, selling and marketing, legal, finance and accounting, human resources, billing and client services. These expenses consist of personnel costs (including salaries, bonuses, benefits and stock-based compensation expense), direct marketing expenses, audit and legal expenses, consulting costs, training and medical education activities, payor outreach programs and allocated overhead, including rent, information technology, equipment depreciation, and utilities. We expect continued increases in SG&A expenses related to compliance with the rules and regulations of the SEC and Nasdaq (in particular as we no longer qualify as an emerging growth company and a smaller reporting company, and have become a large accelerated filer), investor relations activities and additional insurance expenses. Other administrative and professional services expenses within SG&A are expected to increase with the scale of our business, but selling and marketing-related expenses are expected to increase significantly, consistent with our growth strategy.

Amortization of Acquired Intangible Assets

Amortization of acquired intangible assets are primarily associated with developed technology.

Other Operating Income

Other operating income consists of an automatic payment received from HHS for provider relief funds pursuant to the CARES Act.

Interest Income

Interest income consists primarily of earnings on cash and cash equivalents, primarily money market funds.

Interest Expense

Interest expense is primarily attributable to borrowings under our term debt, which was fully repaid in December 2020, and also includes the related amortization of debt discount and issuance costs.

Loss on Extinguishment of Debt

The loss on extinguishment of debt is associated with the early repayment of our term loan facility in December 2020.

Income Tax (Benefit) Expense

In connection with our acquisition of Cernostics in December 2021, and taking into consideration the additional deferred tax liabilities resulting from such acquisition, we determined that a portion of our valuation allowance should be reduced, which was reflected in our income tax benefit for the year ended December 31, 2021. Our consolidated financial statements do not reflect any federal or state income tax benefits attributable to the net losses we have incurred, due to the uncertainty of realizing a benefit from those items. As of December 31, 2021, we had federal NOL carryforwards of \$99.4 million, of which \$43.5 million will begin to expire in 2030 if not utilized to offset federal taxable income, and \$55.9 million may be carried forward indefinitely. Also, as of December 31, 2021, we had state NOL carryforwards of \$67.5 million, which begin to expire in 2028 if not utilized to offset state taxable income.

Results of Operations

Certain prior year amounts in the tables below have been reclassified to conform to the current year presentation. Specifically, we no longer present gross margin on the face of our financial statements and therefore the cost of sales line is now presented within the operating expenses section. This reclassification had no impact on operating loss, loss before income taxes or net loss.

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the periods indicated (in thousands, except percentages):

	Years Ended December 31,		Change	
	2021	2020		
Net revenues	\$ 94,085	\$ 62,649	\$ 31,436	50.2 %
Operating expenses and other operating income:				
Cost of sales (exclusive of amortization of acquired intangible assets)	15,822	9,685	6,137	63.4 %
Research and development	29,646	13,256	16,390	123.6 %
Selling, general and administrative	86,738	48,132	38,606	80.2 %
Amortization of acquired intangible assets	1,958	—	1,958	NA ⁽¹⁾
Other operating income	—	(1,882)	1,882	100.0 %
Total operating expenses, net	134,164	69,191	64,973	93.9 %
Operating loss	(40,079)	(6,542)	(33,537)	(512.6)%
Interest income	68	373	(305)	(81.8)%
Interest expense	(1)	(2,634)	2,633	100.0 %
Loss on extinguishment of debt	—	(1,397)	1,397	100.0 %
Loss before income taxes	(40,012)	(10,200)	(29,812)	(292.3)%
Income tax (benefit) expense	(8,720)	84	(8,804)	NM ⁽²⁾
Net loss	\$ (31,292)	\$ (10,284)	\$ (21,008)	(204.3)%

(1) NA = Not applicable

(2) NM = Not meaningful

The following table indicates the amount of stock-based compensation expense reflected in the line items above (in thousands):

	Years Ended December 31,		Change
	2021	2020	
Cost of sales (exclusive of amortization of acquired intangible assets)	\$ 2,058	\$ 1,049	\$ 1,009
Research and development	4,522	1,492	3,030
Selling, general and administrative	15,160	5,768	9,392
Total stock-based compensation expense	\$ 21,740	\$ 8,309	\$ 13,431

The following table provides a disaggregation of net revenues by type (in thousands):

	Years Ended December 31,		Change
	2021	2020	
Dermatologic ⁽¹⁾	\$ 85,753	\$ 57,646	\$ 28,107
Other ⁽²⁾	8,332	5,003	3,329
Total net revenues	\$ 94,085	\$ 62,649	\$ 31,436

(1) Dermatologic includes DecisionDx-Melanoma, DecisionDx-SCC and CDO.

(2) Other consists primarily of DecisionDx-UM.

The following table presents the calculation of gross margin (in thousands, except percentages):

	Years Ended December 31,		
	2021	2020	Change
Net revenues	\$ 94,085	\$ 62,649	\$ 31,436
Less: Cost of sales (exclusive of amortization of acquired intangible assets)	15,822	9,685	6,137
Less: Amortization of acquired intangible assets	1,958	—	1,958
Gross margin	<u>\$ 76,305</u>	<u>\$ 52,964</u>	<u>\$ 23,341</u>
Gross margin percentage	81.1 %	84.5 %	(3.4)%

Net Revenues

Net revenues increased by \$31.4 million, or 50.2%, to \$94.1 million for the year ended December 31, 2021, primarily due to higher revenues from our dermatologic tests, which increased by \$28.1 million. The higher dermatologic test revenue was primarily attributable to higher volume from DecisionDx-Melanoma, which increased 25.2%, higher per-unit revenues for DecisionDx-Melanoma, which reflect the expanded LCD for the test that became effective in the fourth quarter of 2020, and increased revenues from DecisionDx-SCC and our CDO. We believe the higher test report volume for DecisionDx-Melanoma during the year ended December 31, 2021 reflects the relaxing of COVID-19 restrictions, and the related positive impacts on the flow of patient visits, as well as the effects of our sales force expansions discussed above. Revenues from other tests (non-dermatologic) contributed \$3.3 million to the overall increase in net revenues for the year ended December 31, 2021. This increase was principally due to the significantly higher Medicare rate for DecisionDx-UM that became effective January 1, 2021 and, to a lesser extent, the effect of a 16.0% increase in DecisionDx-UM test report volume. We believe the higher test report volume for DecisionDx-UM during the year ended December 31, 2021 is due in part to patients making up for missed eye exams from 2020 due to COVID-19 impacts. Net revenues include positive revenue adjustments related to tests delivered in previous periods, associated with changes in estimated variable consideration, of \$3.3 million for the year ended December 31, 2021 compared to \$0.2 million for the year ended December 31, 2020. The year-over-year increase is primarily attributable to favorable adjustments related to the settlement and collection during the year ended December 31, 2021 of certain groups of receivables from prior years.

Cost of Sales (exclusive of amortization of acquired intangible assets)

Cost of sales (exclusive of amortization of acquired intangible assets) for the year ended December 31, 2021 increased by \$6.1 million, or 63.4%, compared to the year ended December 31, 2020, primarily due to higher personnel costs due to additional headcount in our laboratory testing operations, and increased costs of supplies and services, attributable to the higher activity levels. The additional personnel costs included a year-over-year increase in stock-based compensation expense of \$1.0 million. Due to the nature of our business, a significant portion of our cost of sales expenses represent fixed costs associated with our testing operations. Accordingly, our cost of sales expense will not necessarily increase or decrease commensurately with the change in net revenues from period to period. We expect our cost of sales (exclusive of amortization of acquired intangible assets) to continue to increase in future periods as we hire additional laboratory personnel and related resources to support our expected growth in volume for our dermatologic, GI and pipeline tests

Gross Margin

Our gross margin percentage was 81.1% for the year ended December 31, 2021, compared to 84.5% for the same period in 2020. The decrease was largely due to amortization expense associated with our acquired intangible assets. In the near term, we expect that our gross margin percentage will decline as we invest in additional laboratory personnel and related resources to support the anticipated growth in our report volumes for tests in advance of obtaining reimbursement coverage. Additionally, our gross margin percentage will be negatively impacted by amortization of intangible assets associated with recent acquisitions.

Research and Development

Research and development expenses increased by \$16.4 million, or 123.6%, for the year ended December 31, 2021, compared to the year ended December 31, 2020, primarily due to increases in personnel costs and costs incurred in our clinical studies. Approximately 55% of the increase is attributable to higher personnel costs, due to expansions in headcount in support of our growth, including higher stock-based compensation expense of \$3.0 million compared to 2020. Approximately 27% of the increase was attributable to higher costs for clinical studies, including costs related to the PERSONALize, CONNECTION and DECIDE studies as well as our recently initiated a 4,800 patient, prospective, multi-center clinical study to develop, validate and bring to market a pipeline test for inflammatory skin diseases. Also, during the year ended December 31, 2021, we expanded evidence supporting our portfolio of tests with 15 peer-reviewed publications and initiated our collaboration with

NCI/SEER. We expect to continue to increase our research and development expenses as we fund ongoing evidence development for our existing products as well as additional pipeline programs.

Selling, General and Administrative

SG&A expense increased by \$38.6 million, or 80.2%, for the year ended December 31, 2021 compared to the year ended December 31, 2020. Approximately 67% of the increase is attributable to higher personnel costs, particularly due to increased headcount, which includes salaries, stock-based compensation and bonuses. We expanded our sales organization headcount in the third quarter of 2020 in preparation for the commercial launch of our DecisionDx DiffDx-Melanoma test and further expanded our sales team during the first and second quarters of 2021, bringing our dermatology-facing commercial team to the mid-60s. The higher personnel costs also reflect expanded headcount in our administrative support functions. Stock-based compensation expense included in SG&A expense was \$15.2 million for the year ended December 31, 2021 compared to \$5.8 million for the year ended December 31, 2020. The remainder of the increase in SG&A expense was primarily associated with training events, travel, professional fees and other general increases. The higher expenses for training events and travel reflect both a higher headcount as well a return to more in-person activities in 2021 as result of easing of COVID-19 restrictions.

Amortization of Acquired Intangible Assets

Amortization of acquired intangible assets was \$2.0 million for the year ended December 31, 2021 and was entirely associated with amortization of developed technology attributable to the acquisitions of Myriad myPath, LLC and Cernostics in May 2021 and December 2021, respectively. There was no such amortization during the year ended December 31, 2020. Amortization of acquired intangible assets is projected to be approximately \$6.7 million for the year ending December 31, 2022, but may increase in the future to the extent we complete additional acquisitions.

Other Operating Income

Other operating income of \$1.9 million for the year ended December 31, 2020 consisted entirely of the automatic payment received from HHS pursuant to the CARES Act for provider relief funds. We initially recognized income attributable to the payment in the second quarter of 2020 based on our expectation of meeting the requirements to retain the funds. However, due a change in requirements of the program in the third quarter of 2020, we reversed this income. However, in the fourth quarter of 2020, a legislative change was enacted affecting the program, under which we concluded it is reasonably assured we will qualify to retain the funds. Accordingly, we recognized the income again in the fourth quarter of 2020. There were no similar transactions during the year ended December 31, 2021. See Note 2 to the consolidated financial statements for additional information.

Interest Income

Interest income decreased by \$0.3 million for the year ended December 31, 2021, compared to the year ended December 31, 2020, as a result of lower interest rates, despite our higher average balances of cash and cash equivalents.

Interest Expense

Interest expense was essentially zero for the year ended December 31, 2021 compared to \$2.6 million for the year ended December 31, 2020. The decrease is a result of the early termination and repayment of all amounts due on our term loan facility in December 2020.

Loss on Extinguishment of Debt

We recorded an extinguishment loss of \$1.4 million during the year ended December 31, 2020 related to the early repayment and termination of our term loan facility. The extinguishment loss was attributable to the write-off of the unamortized discount and issuance costs as well as early termination and prepayment fees. There were no similar transactions during the year ended December 31, 2021.

Income Tax (Benefit) Expense

Income tax (benefit) expense was \$(8.7) million for the year ended December 31, 2021 compared to \$0.1 million for the year ended December 31, 2020. Substantially all of the income tax (benefit) in the year ended December 31, 2021 was attributable to a reduction in our valuation allowance on net deferred tax assets resulting from our acquisition of Cernostics in December 2021. Specifically, we took into consideration the additional deferred tax liabilities resulting from the acquisition and determined that a portion of our existing valuation allowance should be reduced to offset this liability. Other than this item, the recorded income tax (benefit) expense includes minimal amounts because in both the years ended December 31, 2021 and 2020, the income tax benefit of the net loss was largely offset by corresponding changes in the valuation allowance on net deferred tax assets, as we have determined that it is more likely than not that these benefits will not be realized.

Stock-Based Compensation Expense

Stock-based compensation expense, which is allocated among cost of sales, research and development expense and SG&A expense, totaled \$21.7 million for the year ended December 31, 2021 compared to \$8.3 million for the year ended December 31, 2020, which we attribute in part to the addition of 144 employees in 2021, a 71.6% increase from 2020. We expect material increases in stock-based compensation expense in future periods, reflecting additional awards outstanding due to expected growth in our headcount. As of December 31, 2021, the total unrecognized stock-based compensation cost related to outstanding awards was \$99.3 million, which is expected to be recognized on a straight-line basis over a weighted-average period of 3.3 years.

Liquidity and Capital Resources

Sources of Liquidity

Our principal sources of liquidity are our cash and cash equivalents and cash generated from the sale of our products. As of December 31, 2021 and 2020, we had cash and cash equivalents of \$329.6 million and \$409.9 million, respectively. In addition to the revenue generated from the sale of our commercial products, we have financed our operations through our IPO in July 2019, two follow-on public offerings of common stock in June 2020 and December 2020, and a \$25.0 million secured term loan credit facility, which we repaid in full in December 2020.

On December 14, 2020, we filed an automatically effective shelf registration statement on Form S-3 (File No. 333-251331) with the SEC as a “well-known seasoned issuer.” The registration statement allows us to issue an indeterminate number or amount of common stock, preferred stock, debt securities and warrants from time-to-time in one or more offerings. However, there can be no assurance that we will complete any such offerings of securities. Any future offerings under this registration statement will be dependent upon, among other factors, market conditions, available pricing, our financial condition, investor perception of our prospects, our capital needs and our ability to maintain status as a well-known seasoned issuer.

Public Offerings of Common Stock

On June 29, 2020 and July 2, 2020, we issued and sold 2,000,000 and 300,000 shares of our common stock, respectively, of our common stock in a follow-on public offering at a price of \$37.00 per share. We received \$79.5 million in aggregate net proceeds, after deducting underwriting discounts and commissions and offering costs. The shares issued and sold on July 2, 2020 reflect the underwriters’ exercise in full of their 30-day option to purchase additional shares at the public offering price, less underwriting discounts and commissions.

On December 18, 2020, we issued and sold 4,600,000 shares of our common stock (including the exercise in full by the underwriters of their option to purchase an additional 600,000 shares) in a follow-on public offering at a price of \$58.00 per share. We received \$250.5 million in aggregate net proceeds, after deducting underwriting discounts and commissions and offering costs (excluding \$0.4 million in offering costs that were incurred but not paid as of December 31, 2020). The shares issued and sold includes the underwriters’ exercise in full of their 30-day option to purchase additional shares at the public offering price, less underwriting discounts and commissions. On December 21, 2020, we used a portion of these proceeds to repay, in full, our outstanding term loan credit facility. See “Long-Term Debt” below for additional information.

As mentioned above, we expect to use a portion of these proceeds, as well as the approximately \$65.9 million of net proceeds from our IPO in July 2019, to further support and accelerate our research and development activities, including the clinical studies noted above.

Medicare Advance Payment

On April 16, 2020, we received an advance payment of \$8.3 million (“the Advance Payment”) from CMS under its Accelerated and Advance Payment Program, which was expanded to provide increased cash flow to service providers during the COVID-19 pandemic. CMS began recoupment of the Advance Payment in April 2021 by applying 25% of the Medicare payments otherwise owed to us against the balance of the Advance Payment. Recoupment of the full amount of the Advance Payment was complete by December 31, 2021.

Material Cash Requirements

Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, clinical research and development services, laboratory operations, equipment and related supplies, legal and other regulatory expenses, general administrative costs and, from time to time, expansion of our laboratory and office facilities in support of our growth. We anticipate that a substantial portion of our cash requirements in the foreseeable future will relate to the further commercialization of our currently marketed products, the development of our future product candidates in our pipeline and the potential commercialization of these pipeline products, should their development be successful.

In the past 12 months we completed two strategic opportunities, which we funded using our available cash on hand, and in the longer-term may evaluate and consummate other strategic acquisitions of businesses, assets, products or technologies, which we expect to be able to fund from our available cash and cash equivalents. In May 2021 and December 2021, we completed the acquisitions of the Myriad myPath Laboratory for \$32.5 million and Cernostics, Inc. for \$30.7 million, respectively. In both cases, the source of funding was from our existing cash and cash equivalents. Under the definitive agreement with Cernostics, we have also agreed to pay up to an additional \$50 million in cash or our common stock, at our sole discretion, based on the achievement of certain commercial milestones relating to the year ending December 31, 2022. Our liability with respect to the commercial milestone payments will depend on our ability to successfully integrate Cernostics into our suite of commercial product offerings, while future cash requirements arising from any additional strategic acquisitions will depend on, among other things, our identification of a target company with a product offering that we view as complementary to our product offerings. See Note 5 to the consolidated financial statements for additional information on recent acquisitions.

Since our inception, we have generally incurred significant losses and negative cash flows. For the year ended December 31, 2021 we had a net loss of \$31.3 million and an accumulated deficit of \$93.8 million as of December 31, 2021. Our ability to generate revenue sufficient to achieve profitability will depend heavily on the successful commercialization of our currently marketed products and the products we plan to launch in the future as well as our spending on research and development activities. We expect to incur additional expenses and losses in the future as we invest in the commercialization of our existing products, the development of our future product candidates and the commercialization of our product candidates. Further, we expect that any acquisitions of businesses, products, assets or technologies will also increase our expenses. We believe that our existing cash and cash equivalents and anticipated cash generated from the sale of our commercial products will be sufficient to fund our operations for the next twelve months. We believe we will meet longer-term expected cash requirements and obligations through a combination of existing cash and cash equivalents, anticipated cash generated from sales of our products and issuances of equity securities or debt offerings, including through our shelf registration statement on Form S-3 that became automatically effective in December 2020. However, we have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. There are numerous risks and uncertainties associated with developing genomic tests, including, among others, the uncertainty of:

- successful commencement and completion of clinical study protocols;
- successful identification and acquisition of tissue samples;
- the development and validation of genomic classifiers; and
- acceptance of new genomic tests by physicians, patients and third-party payors.

Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate our exact working capital requirements. Our future funding requirements will depend on, and could increase significantly as a result of, many factors, including those listed above as well as those listed in the section titled “Risk Factors.”

We do not currently have any committed external source of funds. In the event additional funding is required, we expect that we would use a combination of equity and debt financings, which may not be available to us when needed, on terms that we deem to be favorable or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends. Any disruptions to, or volatility in, the credit and financial markets or any deterioration in overall economic conditions may make any necessary debt or equity financing more difficult to obtain, more costly and/or more dilutive. If we are unable to raise additional funds through debt, or equity financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our product discovery and development activities or future commercialization efforts.

Leases

We have entered into various operating and finance leases, which are primarily associated with our laboratory facilities and office space. Total undiscounted future minimum payment obligations under our operating leases and finance leases as of December 31, 2021 totaled approximately \$10.6 million, of which \$1.4 million is payable in 2022 and \$9.2 million is payable through the end of 2033. The leases expire on various dates through 2033 and provide certain options to renew for additional periods. We expect our lease obligations will increase in the near term as we expand our facilities, operations and headcount in support of the anticipated growth in our portfolio of commercial products and pipeline tests. Refer to Note 9 to the consolidated financial statements for additional information on our leasing arrangements.

Cash Flows

The following table summarizes our sources and uses of cash and cash equivalents for each of the periods presented (in thousands):

	Years Ended December 31,	
	2021	2020
Net cash (used in) provided by operating activities	\$ (18,983)	\$ 9,865
Net cash used in investing activities	(66,657)	(4,748)
Net cash provided by financing activities	5,421	305,890
Net change in cash and cash equivalents	(80,219)	311,007
Cash and cash equivalents, beginning of year	409,852	98,845
Cash and cash equivalents, end of year	<u>\$ 329,633</u>	<u>\$ 409,852</u>

Operating Activities

Net cash used in operating activities of \$19.0 million for the year ended December 31, 2021 was primarily attributable to the net loss of \$31.3 million, deferred income taxes of \$8.7 million, recoupment of the Advance Payment of \$8.3 million and increases in accounts receivable of \$4.6 million, partially offset by stock compensation expense of \$21.7 million, increases in accrued compensation of \$6.2 million, depreciation and amortization of \$3.4 million and increases in other accrued liabilities of \$2.3 million.

Net cash provided by operating activities was \$9.9 million for the year ended December 31, 2020 and was primarily attributable to net non-cash charges of \$10.5 million (consisting of \$8.3 million in stock-based compensation expense, \$1.4 million of loss on extinguishment of debt, and \$0.8 million in amortization of debt discount and issuance costs), the receipt of the Advance Payment of \$8.3 million, increases in accrued compensation of \$3.3 million and decreases in accounts receivable of \$1.7 million, partially offset by the net loss of \$10.3 million and increases in prepaid expenses and other current assets of \$2.8 million, other assets of \$1.4 million and inventory of \$1.0 million.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2021 was primarily attributable to our asset acquisitions of Myriad myPath LLC and Cernostics (which collectively totaled \$63.2 million) and purchases of property and equipment of \$3.5 million.

Net cash used in investing activities for the year ended December 31, 2020 consisted entirely of purchases of property and equipment.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 consisted primarily of \$4.2 million of proceeds from exercise of common stock options and \$2.3 million of proceeds from contributions to the employee stock purchase plan, partially offset by payment of employees' taxes on vested restricted stock units of \$0.8 million and payment of common stock offering costs of \$0.3 million. We did not complete any public offerings of common stock during the year ended December 31, 2021.

Net cash provided by financing activities for the year ended December 31, 2020 consisted primarily of \$330.0 million of proceeds from two public offerings of our common stock (net of underwriting discounts, commissions and issuance costs), \$1.6 million of proceeds from contributions to the employee stock purchase plan and \$1.6 million of proceeds from exercise of common stock options, partially offset by repayments of term debt, including extinguishment costs, of \$27.4 million.

Inflation

We do not believe that inflation has had a material impact on our results of operations during the periods presented. However, recently, the rate of inflation in the U.S. has risen to levels not experienced in decades. We have begun to see some inflationary pressures, primarily in personnel and related costs. The extent of any future impacts from inflation on our business and our results of operations will be dependent upon how long the elevated inflation levels persist and if the rate of inflation were to further increase, neither of which we are able to predict.

Critical Accounting Estimates

Our consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our audited consolidated financial statements, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

We recognize revenue is recognized in accordance with ASC 606. In accordance with ASC 606, we follow a five-step process to recognize revenues: (1) identify the contract with the customer, (2) identify the performance obligations, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations and (5) recognize revenues when the performance obligations are satisfied. We have determined that we have a contract with the patient when the treating clinician orders the test. Our contracts generally contain a single performance obligation, which is the delivery of the test report, and we satisfy our performance obligation at a point-in-time upon the delivery of the test report to the treating physician, at which point we can bill for the report. The amount of revenue recognized reflects the amount of consideration to which we expect to be entitled, or the transaction price, and considers the effects of variable consideration.

All of our revenues from contracts with customers are associated with the provision of diagnostic and prognostic testing services. Most of our revenues are attributable to DecisionDx-Melanoma for cutaneous melanoma. We also provide a test for UM, DecisionDx-UM. We launched a test for patients with cutaneous SCC, DecisionDx-SCC in August 2020 and launched a test for use in patients with suspicious pigmented lesions, DecisionDx DiffDx-Melanoma in November 2020. We began offering a test for difficult-to-diagnose melanocytic lesions, myPath Melanoma, following an asset acquisition completed in May 2021 and began offering the TissueCypher® Barrett's Esophagus Assay for patients with BE following an asset acquisition completed in December 2021. Information on the disaggregation of revenues is included below.

Once we satisfy our performance obligations and bill for the service, the timing of the collection of payments may vary based on the payment practices of the third-party payor and the existence of contractually established reimbursement rates. Most of the payments for our services are made by third-party payors, including Medicare and commercial health insurance carriers. Certain contracts contain a contractual commitment of a reimbursement rate that differs from our list prices. However, absent a contractually committed reimbursement rate with a commercial carrier or governmental program, our diagnostic tests may or may not be covered by these entities' existing reimbursement policies. In addition, patients do not enter into direct agreements with us that commit them to pay any portion of the cost of the tests in the event that their insurance provider declines to reimburse us. We may pursue, on a case-by-case basis, reimbursement from such patients in the form of co-payments and co-insurance, in accordance with the contractual obligations that we have with the insurance carrier or health plan. These situations may result in a delay in the collection of payments.

The Medicare claims that are covered by policy under an LCD are generally paid at the established rate by our Medicare contractor within 30 days from receipt. Medicare claims that were either submitted to Medicare prior to the LCD's effective date or are not covered by the terms of the LCD, but meet the definition of being medically reasonable and necessary pursuant to the controlling Section 1862(a)(1)(A) of the Social Security Act are generally appealed and may ultimately be paid at the first (termed "redetermination"), second (termed "reconsideration") or third level of appeal (de novo hearing with an ALJ). A successful appeal at any of these levels results in payment.

In the absence of LCD coverage or contractually established reimbursement rates, we have concluded that our contracts include variable consideration because the amounts paid by Medicare or commercial health insurance carriers may be paid at less than our standard rates or not paid at all, with such differences considered implicit price concessions. Variable consideration attributable to these price concessions is measured at the expected value using the "most likely amount" method under ASC 606. The amounts are determined by historical average collection rates by test type and payor category taking into consideration the range of possible outcomes, the predictive value of our past experiences, the time period of when uncertainties expect to be resolved and the amount of consideration that is susceptible to factors outside of our influence, such as the judgment and actions of third parties. Such variable consideration is included in the transaction price only to the extent it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainties with respect to the amount are resolved. Variable consideration may be constrained and excluded from the transaction price in situations where

there is no contractually agreed upon reimbursement coverage or in the absence of a predictable pattern and history of collectability with a payor. Variable consideration for Medicare claims that are not covered by an LCD, including those claims subject to approval by an ALJ at an appeal hearing, is deemed to be fully constrained due to factors outside our influence (i.e., judgment or actions of third parties) and the uncertainty of the amount to be received is not expected to be resolved for a long period of time. Variable consideration is evaluated each reporting period and adjustments are recorded as increases or decreases in revenues. Included in revenues for the years ended December 31, 2021 and 2020 were \$3,324,000 and \$176,000, respectively, of revenue increases associated with changes in estimated variable consideration related to performance obligations satisfied in previous periods. These amounts include (i) adjustments for actual collections versus estimated amounts and (ii) cash collections and the related recognition of revenue in current period for tests delivered in prior periods due to the release of the constraint on variable consideration.

DecisionDx-Melanoma Claims Consolidation

In June 2017, we submitted to OMHA a formal request to participate in a program that OMHA developed with the intent of providing appellants a means to have large volumes of claim disputes adjudicated at an accelerated rate. The program consolidates outstanding claims at the ALJ level and uses a statistical-sampling approach where five ALJs will determine reimbursement results for a sample of claims which are then extrapolated to the universe of claims. Our consolidation includes 2,698 DecisionDx-Melanoma claims dating from 2013 through spring 2017. Hearings were held in April 2019 with a supplemental hearing in May 2019. On March 12, 2020, OMHA issued a decision denying payment on all claims in the consolidation. We have filed an appeal to the decision, although no ruling on such appeal has been issued to date. In accordance with ASC 606 and consistent with prior periods, we have not recognized (fully constrained the variable consideration) any revenues attributable to these claims in our consolidated financial statements pending the outcome of this matter.

Stock-Based Compensation

Stock-based compensation expense for equity instruments issued to employees and non-employees, including stock options, restricted stock units (“RSUs”) and purchase rights issued under our 2019 Employee Stock Purchase Plan (“ESPP”) is measured based on the grant date fair value of the awards. For stock options and purchase rights granted under the ESPP, we estimate the grant date fair value using the Black-Scholes option-pricing valuation model. For RSUs, we use the closing price of our common stock on the date of grant to determine the fair value. We recognize compensation costs on a straight-line basis for all stock-based compensation awards over the requisite service period of the awards, which is generally the awards’ vesting period, typically four years for options and RSUs and the two-year offering period for the ESPP. Forfeitures are accounted for as they occur.

Set forth below is a description of the significant assumptions used in the option pricing model:

- *Expected term.* The expected term is the period of time that granted options are expected to be outstanding. For stock options, we have set the expected term using the simplified method based on the weighted average of both the period to vesting and the period to maturity for each option, as we have concluded that our stock option exercise history does not provide a reasonable basis upon which to estimate the expected term. For the ESPP, the expected term is the period of time from the offering date to the purchase date.
- *Expected volatility.* Previously, because of the limited period of time our stock had been traded in an active market, we calculated expected volatility by using the historical stock prices of a group of similar companies looking back over the estimated life of the option or the purchase rights under our ESPP and averaging the volatilities of these companies. In the third quarter of 2021, we adjusted this calculation to include our own stock price on a relative basis to the peer group in the calculation of expected volatility, as our common stock has now been traded in an active market for more than two years.
- *Risk-free interest rate.* We base the risk-free interest rate used in the Black-Scholes valuation model on the market yield in effect at the time of option grant and at the offering date for ESPP provided from the Federal Reserve Board’s Statistical Releases and historical publications from the Treasury constant maturities rates for the equivalent remaining terms.
- *Dividend yield.* We have not paid, and do not have plans to pay, cash dividends. Therefore, we use an expected dividend yield of zero in the Black-Scholes option valuation model.

The fair value of our common stock is also an assumption used to determine the fair value of stock options. Prior to our IPO, the estimated fair value of our common stock had been determined by our board of directors as of the date of each award, with input from management, considering our most recently available third-party valuations of common stock and our board of directors’ assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant, which intended all options granted to be exercisable at price per share not less than the per share fair value of our common stock underlying those options on the grant date.

Subsequent to our IPO, the fair value of our common stock is the closing selling price per share of our common stock as reported on the Nasdaq Global Market on the date of grant or other relevant determination date.

The following table sets forth the assumptions used to determine the fair value of stock options:

	Years Ended December 31,	
	2021	2020
Average expected term (years)	6.1	6
Expected stock price volatility	66.50% - 68.83%	59.57%- 67.02%
Risk-free interest rate	0.51% - 1.48%	0.28% - 1.76%
Dividend yield	—%	—%

The following table sets forth assumptions used to determine the fair value of the purchase rights issued under the ESPP:

	Years Ended December 31,	
	2021	2020
Average expected term (years)	1.2	1.2
Expected stock price volatility	61.13% - 86.50%	56.80% - 100.49%
Risk-free interest rate	0.06% - 0.20%	0.12% - 0.95%
Dividend yield	—%	—%

Intangible Assets

Our intangible assets, which are comprised primarily of acquired developed technology, are considered to be finite-lived and are amortized on a straight-line basis over their estimated useful lives. Estimating the useful lives of our intangible assets requires considerable judgment. In determining the estimated useful lives, management considers factors such as historical experience, industry and regulatory factors, competition, patent expirations and commercial plans. If new information becomes available in future periods, we may be required to revise our estimated useful lives. If the revised useful lives are shorter than originally estimated, our future amortization expense will increase.

Contingent Consideration

Under the terms of business combinations or asset acquisitions, we may be required to pay additional consideration if specified future events occur or if certain conditions are met. With respect to the additional consideration that may be payable in connection with our acquisition of Cernostics, which was treated as an asset acquisition for accounting purposes, we account for the contingent consideration as liability in accordance with ASC 480, *Distinguishing Liabilities from Equity* (“ASC 480”), under the guidance for obligations that must or may be settled by issuance of a variable number of shares. In accordance with ASC 480, we record the contingent consideration initially and subsequently at fair value with changes in fair value recorded in the statements of operations and comprehensive loss each period. This liability is classified as a “Level 3” fair value measurement (as defined in Note 11 to our consolidated financial statements) due to the use of significant unobservable inputs and a Monte Carlo simulation to determine its fair value. The Monte Carlo simulation uses projections of the commercial milestones for the applicable period as well as the corresponding targets and approximate timing of payment based on the terms of the arrangement. The analysis also uses assumptions for expected volatility of the financial metrics and a risk-adjusted discount rate. The assumptions and estimates we use in the Monte Carlo simulation require considerable judgment and may change in future periods as a result of new information.

Recent Accounting Pronouncements

Refer to Note 2, “Summary of Significant Accounting Policies,” in the accompanying notes to our consolidated financial statements included in this Annual Report on Form 10-K for a discussion of recent accounting pronouncements.

JOBS Act Accounting Election

Previously, we were an emerging growth company within the meaning of the JOBS Act. Section 107(b) of the JOBS Act provides that an emerging growth company can leverage the extended transition period, provided in Section 102(b) of the JOBS Act, for complying with new or revised accounting standards. However, because the market value of our common stock held by non-affiliates exceeded \$700.0 million as of June 30, 2021, we are no longer an emerging growth company effective December 31, 2021. As a result, we now apply public company adoption dates for new or revised accounting standards. Further, we were required to comply with the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley regarding our internal control over financial reporting as of December 31, 2021.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

As a smaller reporting company, we are not required to provide the information required by this Item.

Item 8. Financial Statements and Supplementary Data.

The financial statements and supplementary data required by this item are included after the Signature page of this Annual Report on Form 10-K beginning on page F-1.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.**Evaluation of Disclosure Controls and Procedures**

We maintain “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021. Based upon the evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2021, our disclosure controls and procedures were effective at the reasonable assurance level.

Management’s Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term as defined in Exchange Act Rule 13a-15(f). Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America.

As of December 31, 2021, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control-Integrated Framework (2013 Framework)*. Based on this assessment, our management concluded that, as of December 31, 2021, our internal control over financial reporting was effective based on those criteria.

Under guidelines established by the SEC, companies are allowed to exclude acquisitions from their assessment of internal control over financial reporting during the first year of an acquisition while integrating the acquired company. Accordingly, our assessment of internal controls excluded our acquisition of Cernostics, completed on December 3, 2021. See Note 5 to the consolidated financial statements included in this Annual Report on Form 10-K for additional information on our acquisition of Cernostics. Operations from this acquisition represented approximately 13% of our total assets and 0% of our total revenue as of and for the year ended December 31, 2021.

Our independent registered public accounting firm, KPMG LLP, has audited the effectiveness of our internal control over financial reporting as of December 31, 2021, as stated in its report contained in Item 15 of this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) or 15d-15(f) of the Exchange Act) that occurred during the fourth quarter of 2021 that have materially affected, or are reasonably likely to materially affect, the Company’s internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K since we intend to file our definitive proxy statement for our 2022 Annual Meeting of Stockholders (“the Proxy Statement”) pursuant to Regulation 14A of the Exchange Act, not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and certain information to be included in the Proxy Statement is incorporated herein by reference.

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is to be included in the Proxy Statement as follows:

- The information relating to our executive officers is to be included in the section entitled “Executive Officers,”
- The information relating to our directors and nominees for director is to be included in the section entitled “Proposal 1: Election of Directors,”
- The information relating to our audit committee and audit committee financial expert is to be included in the section entitled “Information Regarding the Board of Directors and Corporate Governance,” and
- If required, the information regarding compliance with Section 16(a) of the Exchange Act is to be included in the section entitled “Delinquent Section 16(a) Reports.”

Such information will be included in the Proxy Statement and is incorporated herein by reference.

We have adopted a written Code of Business Conduct and Ethics (“Ethics Code”) that applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The Ethics Code is available on our website at www.CastleBiosciences.com. If we make any substantive amendments to the Ethics Code or grant any waiver from a provision of the Ethics Code to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website or in a Current Report on Form 8-K.

Item 11. Executive Compensation.

The information required by this item is to be included in our Proxy Statement under the section entitled “Executive Compensation” and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item with respect to equity compensation plans is to be included in our Proxy Statement under the section entitled “Equity Compensation Plan Information” and the information required by this item with respect to security ownership of certain beneficial owners and management is to be included in our Proxy Statement under the section entitled “Security Ownership of Certain Beneficial Owners and Management” and in each case is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item is to be included in our Proxy Statement under the sections entitled “Transactions with Related Persons and Indemnifications—Related Person Transactions Policy and Procedures” and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

Our independent registered public accounting firm is KPMG LLP, San Diego, CA, Audit Firm ID: 185.

The information required by this item is to be included in our Proxy Statement under the section entitled “Proposal 2: Ratification of Selection of Independent Registered Public Accounting Firm” and is incorporated herein by reference.

PART IV

Item 15. Exhibit and Financial Statement Schedules.

(a)(1) Financial Statements.

The consolidated financial statements and supplementary data required by this item are included after the Signature page of this Annual Report on Form 10-K beginning on page F-1.

(a)(2) Financial Statement Schedules.

All schedules have been omitted because they are not required or because the required information is given in the Consolidated Financial Statements or Notes thereto.

(a)(3) Exhibits.

The exhibits listed in the Exhibit Index below are filed or incorporated by reference as part of this Annual Report on Form 10-K.

Exhibit Index

Exhibit Number	Description of document
2.1†^	Agreement and Plan of Merger, dated October 18, 2021, by and among the Company, Space Merger Sub, Inc., Cernostics, Inc., and Shareholder Representative Services LLC, incorporated by reference to Exhibit 2.1 of the Registrant's Current Report on Form 8-K, as amended, originally filed with the SEC on December 6, 2021.
3.1	Amended and Restated Certificate of Incorporation of the Registrant, incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K filed with the SEC on July 29, 2019.
3.2	Amended and Restated Bylaws of the Registrant, incorporated by reference to Exhibit 3.2 of the Registrant's Current Report on Form 8-K filed with the SEC on July 29, 2019.
4.1	Description of securities registered under Section 12 of the Exchange Act, incorporated by reference to Exhibit 4.1 of the Registrant's Annual Report on Form 10-K filed with the SEC on March 10, 2020.
4.2	Form of Common Stock Certificate of the Registrant, incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
4.3	Sixth Amended and Restated Investors' Rights Agreement, dated July 12, 2019, by and among the Registrant and certain of its stockholders, incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.1+	Form of Indemnity Agreement by and between the Registrant and its directors and officers, incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.2+	Castle Biosciences, Inc. 2008 Stock Plan, incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.3+	Forms of Stock Option Agreement, Exercise Notice and Investment Representation Statement under the 2008 Stock Plan, incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.4+	Castle Biosciences, Inc. 2018 Equity Incentive Plan, as amended, incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.5+	Forms of Stock Option Grant Notice, Option Agreement and Notice of Exercise under the 2018 Equity Incentive Plan, incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.6+	Castle Biosciences, Inc. 2019 Equity Incentive Plan, incorporated by reference to Exhibit 99.3 of the Registrant's Registration Statement on Form S-8 (File No. 333-232884), originally filed with the SEC on July 29, 2019.
10.7+	Forms of Stock Option Grant Notice, Option Agreement and Notice of Exercise under the 2019 Equity Incentive Plan, incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.8+	Forms of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Equity Incentive Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed with the SEC on November 9, 2020.

Exhibit Number	Description of document
10.9+	Castle Biosciences, Inc. 2019 Employee Stock Purchase Plan, incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.10+	Form of Director Agreement by and between the Registrant and certain of its directors, incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.11+*	Non-Employee Director Compensation Policy, as amended effective January 28, 2022.
10.12+	Amended and Restated Executive Employment Agreement, dated September 20, 2012, as amended, by and between the Registrant and Derek J. Maetzold, incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.13+	Offer Letter Agreement, dated March 2, 2016, by and between the Registrant and Bernhard Spiess, incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.14+	Offer Letter Agreement, dated November 9, 2017, by and between the Registrant and Frank Stokes, incorporated by reference to Exhibit 10.13 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.15+	Employment Separation Agreement dated December 29, 2021, by and between Castle Biosciences, Inc. and Bernhard E. Spiess, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed with the SEC on January 5, 2022.
10.16+#	Master Services Agreement dated December 29, 2021, by and between Castle Biosciences, Inc. and Bernhard E. Spiess, incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed with the SEC on January 5, 2022.
10.17+	Executive Employment Agreement, dated September 15, 2008, as amended, by and between the Registrant and Kristen Oelschlager, incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2021.
10.18+	Executive Employment Agreement, dated October 1, 2008, as amended, by and between the Registrant and Tobin Juvenal, incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2021.
10.19+	Consulting Agreement, dated May 7, 2021, by and among the Registrant and Joseph C. Cook III, incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2021.
10.20+	Separation Agreement dated May 29, 2020, by and between the Registrant and Federico A. Monzon, M.D., incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed with the SEC on June 2, 2020.
10.21+	Master Services Agreement dated May 29, 2020, by and between the Registrant and Genomic Path LLC, incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed with the SEC on June 2, 2020.
10.22	Standard Office Lease, dated as of October 5, 2015, by and between the Registrant and Merced Restart Phoenix Investors II, LLC, incorporated by reference to Exhibit 10.14 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.23	First Amendment to Lease, dated December 4, 2018, by and between the Registrant and Alturas Siete I, LLC, incorporated by reference to Exhibit 10.15 of the Registrant's Annual Report on Form 10-K, filed with the SEC on March 10, 2020.
10.24	Office Building Lease, dated as of March 11, 2015, by and between the Registrant and RMG Leasing (a/k/a Cedarwood Professional Building), as amended, incorporated by reference to Exhibit 10.15 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
10.25	Standard Office Lease, dated December 16, 2019, by and between the Registrant and Alturas Siete, II, LLC, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed with the SEC on December 19, 2019.
10.26	Second Amendment to Standard Office Lease, dated December 16, 2019, by and between the Registrant and Alturas Siete I, LLC, incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed with the SEC on December 19, 2019.
10.27	First Amendment to Standard Office Lease, dated February 16, 2021, by and between the Registrant and Alturas Siete III, LLC, incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2021.

Exhibit Number	Description of document
10.28	Second Amendment to Standard Office Lease, dated November 29, 2021, by and between the Company and Alturas Siete, II, LLC, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed with the SEC on December 3, 2021.
10.29	Third Amendment to Standard Office Lease, dated November 29, 2021, by and between the Company and Alturas Siete, I, LLC, incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed with the SEC on December 3, 2021.
10.30	Commercial Lease, dated December 17, 2019, by and between the Registrant and Tannos Land Holding III, LLC, incorporated by reference to Exhibit 10.3 of the Registrant's Current Report on Form 8-K filed with the SEC on December 19, 2019.
10.31	First Amendment to Commercial Lease, dated November 13, 2020, by and between the Registrant and Tannos Land Holdings III, LLC, incorporated by reference to Exhibit 10.23 of the Registrant's Annual Report on Form 10-K filed with the SEC on March 11, 2021.
10.32#	Exclusive License Agreement, dated as of November 14, 2009, by and between the Registrant and The Washington University, incorporated by reference to Exhibit 10.17 of the Registrant's Registration Statement on Form S-1 (File No. 333-232369), as amended, originally filed with the SEC on June 26, 2019.
21.1*	Subsidiaries of the Registrant.
23.1*	Consent of KPMG LLP, Independent Registered Public Accounting Firm.
31.1*	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) of the Exchange Act.
31.2*	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) of the Exchange Act.
32.1**	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rules 13a-14(b) or 15d-14(b) of the Exchange Act, and 18 U.S.C. Section 1350.
101.INS*	Inline XBRL Instance Document—the instance document does not appear in the Interactive Data File as its XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema.
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase.
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase.
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase.
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase.
104*	Cover Page Interactive Data File (embedded within the Inline XBRL and contained in Exhibit 101).

* Filed herewith

** Furnished herewith.

+ Indicates management contract or compensatory plan.

Certain portions of this exhibit (indicated by “[***]”) have been omitted as we have determined (i) the omitted information is not material and (ii) the omitted information would likely cause harm to us if publicly disclosed.

† Schedules and exhibits to the Agreement have been omitted pursuant to Item 601(a)(5) of Regulation S-K. A copy of any omitted schedule and/or exhibit will be furnished to the Securities and Exchange Commission upon request.

^ Pursuant to Item 601(b)(10) of Regulation S-K, certain portions of this exhibit have been omitted (indicated by “[***]”) because the Company has determined that the information is not material and is the type that the Company treats as private or confidential.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

CASTLE BIOSCIENCES, INC.

Date: February 28, 2022

By: /s/ Derek J. Maetzold

Derek J. Maetzold
President and Chief Executive Officer
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacity and on the dates indicated.

SIGNATURE	TITLE	DATE
<u> /s/ Derek J. Maetzold</u> (Derek J. Maetzold)	President, Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	February 28, 2022
<u> /s/ Frank Stokes</u> (Frank Stokes)	Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	February 28, 2022
<u> /s/ Daniel M. Bradbury</u> (Daniel M. Bradbury)	Chairman of the Board of Directors	February 28, 2022
<u> /s/ Mara G. Aspinall</u> (Mara G. Aspinall)	Member of the Board of Directors	February 28, 2022
<u> /s/ Kimberlee S. Caple</u> (Kimberlee S. Caple)	Member of the Board of Directors	February 28, 2022
<u> /s/ G. Bradley Cole</u> (G. Bradley Cole)	Member of the Board of Directors	February 28, 2022
<u> /s/ Ellen Goldberg</u> (Ellen Goldberg)	Member of the Board of Directors	February 28, 2022
<u> /s/ Miles D. Harrison</u> (Miles D. Harrison)	Member of the Board of Directors	February 28, 2022
<u> /s/ Tiffany P. Olson</u> (Tiffany P. Olson)	Member of the Board of Directors	February 28, 2022

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INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Castle Biosciences, Inc.:

Opinion on Internal Control Over Financial Reporting

We have audited Castle Biosciences, Inc. and subsidiaries' (the Company) 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. 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 Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2021 and December 31, 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2021, and the related notes (collectively, the consolidated financial statements), and our report dated February 28, 2022 expressed an unqualified opinion on those consolidated financial statements.

The Company acquired Cernostics, Inc. during 2021, and management excluded from its assessment of the effectiveness of the Company's internal control over financial reporting as of December 31, 2021, Cernostics, Inc.'s internal control over financial reporting associated with 13% of total assets and 0% of total revenues included in the consolidated financial statements of the Company as of and for the year ended December 31, 2021. Our audit of internal control over financial reporting of the Company also excluded an evaluation of the internal control over financial reporting of Cernostics, Inc.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit 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 audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ KPMG LLP

San Diego, California
February 28, 2022

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Castle Biosciences, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Castle Biosciences, Inc. and subsidiaries (the Company) as of December 31, 2021 and December 31, 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2021, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and December 31, 2020, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission, and our report dated February 28, 2022 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company has changed its method of accounting for leases as of January 1, 2021 due to the adoption of ASC 842, *Leases*.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the 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. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter 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 matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Measurement of Test Revenue

As discussed in Notes 2 and 3 of the consolidated financial statements, test revenue is recognized when the performance obligation is satisfied, upon delivery of the test report. The amount of revenue recognized reflects the amount of consideration to which the Company expects to be entitled and considers the effects of variable consideration. The measurement of test revenue is determined by contractually established rates as well as historical average collection rates by test type and payor category taking into consideration the range of possible outcomes, the predictive value of the Company's past experiences, the time period of when uncertainties expect to be resolved and the amount of consideration that is susceptible to factors outside of the Company's influence, such as the judgment and actions of third parties. The Company reported net revenues of \$94,085 thousand for the year ended December 31, 2021, a portion of which related to test revenue.

We identified the evaluation of the measurement of test revenue as a critical audit matter. Evaluating the measurement of test revenue, specifically the estimation of the amount of test revenue expected to be collectible related to commercial payors and certain others, required especially complex and subjective auditor judgment.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain internal controls related to the estimation of the expected collectible test revenue related to commercial payors and certain others. This included controls related to management's review of the assumptions and inputs used in the determination of test revenue expected to be collectible from commercial payors and certain others. For a selection of tests, we evaluated certain historical data inputs that are used in management's model to estimate test revenue expected to be collectible by comparing the data from the model to physician test requisition forms, proof of delivery, and cash collection activity. These data inputs included collection activity, amounts of historical claims, insurance payor categories, test dates, test types, claim aging categories, and revenue recognition dates. In addition, we inquired of the individuals who are responsible for monitoring and tracking the status of anticipated collections to understand the progress of these activities and any impact to management's estimates.

/s/ KPMG LLP

We have served as the Company's auditor since 2018.

San Diego, California
February 28, 2022

CASTLE BIOSCIENCES, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31,	
	2021	2020
ASSETS		
Current Assets		
Cash and cash equivalents	\$ 329,633	\$ 409,852
Accounts receivable, net	17,282	12,759
Inventory	2,021	2,217
Prepaid expenses and other current assets	4,807	4,766
Total current assets	353,743	429,594
Long-term accounts receivable, net	1,308	1,096
Property and equipment, net	9,501	7,102
Operating lease assets	7,383	—
Intangible assets, net	88,922	—
Other assets – long-term	1,715	1,536
Total assets	\$ 462,572	\$ 439,328
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities		
Accounts payable	\$ 2,546	\$ 2,098
Accrued compensation	15,483	9,108
Medicare advance payment	—	6,615
Operating lease liabilities	1,179	—
Other accrued and current liabilities	5,678	3,055
Total current liabilities	24,886	20,876
Contingent consideration	18,287	—
Noncurrent operating lease liabilities	6,900	—
Noncurrent portion of Medicare advance payment	—	1,735
Deferred tax liability	635	—
Other liabilities	124	1,026
Total liabilities	50,832	23,637
Commitments and Contingencies (Note 12)		
Stockholders' Equity		
Preferred stock, \$0.001 par value; 10,000,000 shares authorized as of December 31, 2021 and 2020; no shares issued and outstanding as of December 31, 2021 and 2020.	—	—
Common stock, \$0.001 par value; 200,000,000 authorized as of December 31, 2021 and 2020, respectively; 25,378,520 and 24,812,487 shares issued and outstanding as of December 31, 2021 and 2020, respectively.	25	25
Additional paid-in capital	505,482	478,162
Accumulated deficit	(93,767)	(62,496)
Total stockholders' equity	411,740	415,691
Total liabilities and stockholders' equity	\$ 462,572	\$ 439,328

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

CASTLE BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except per share data)

	Years Ended December 31,	
	2021	2020
NET REVENUES	\$ 94,085	\$ 62,649
OPERATING EXPENSES AND OTHER OPERATING INCOME		
Cost of sales (exclusive of amortization of acquired intangible assets)	15,822	9,685
Research and development	29,646	13,256
Selling, general and administrative	86,738	48,132
Amortization of acquired intangible assets	1,958	—
Other operating income	—	(1,882)
Total operating expenses, net	134,164	69,191
Operating loss	(40,079)	(6,542)
Interest income	68	373
Interest expense	(1)	(2,634)
Loss on extinguishment of debt	—	(1,397)
Loss before income taxes	(40,012)	(10,200)
Income tax (benefit) expense	(8,720)	84
Net loss and comprehensive loss	\$ (31,292)	\$ (10,284)
 Loss per share attributable to common stockholders:		
Basic	\$ (1.24)	\$ (0.54)
Diluted	\$ (1.24)	\$ (0.54)
 Weighted-average shares outstanding:		
Basic	25,137	18,929
Diluted	25,137	18,929

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

CASTLE BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share data)

	Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount			
BALANCE, JANUARY 1, 2020	—	\$ —	17,130,907	\$ 17	\$ 137,308	\$ (52,212)	\$ 85,113
Stock-based compensation expense	—	—	—	—	8,309	—	8,309
Exercise of common stock options	—	—	459,074	1	1,592	—	1,593
Exercise of common stock warrants	—	—	241,052	—	—	—	—
Public offerings of common stock, net of underwriting discounts, commissions and offering costs	—	—	6,900,000	7	329,657	—	329,664
Issuance of common stock under the employee stock purchase plan	—	—	81,454	—	1,296	—	1,296
Net loss	—	—	—	—	—	(10,284)	(10,284)
BALANCE, DECEMBER 31, 2020	—	\$ —	24,812,487	\$ 25	\$ 478,162	\$ (62,496)	\$ 415,691
Adoption of ASU No. 2016-02	—	—	—	—	—	21	21
Stock-based compensation expense	—	—	—	—	21,740	—	21,740
Exercise of common stock options	—	—	416,037	—	4,234	—	4,234
Issuance of common stock from vested restricted stock units and payment of employees' taxes	—	—	39,548	—	(781)	—	(781)
Public offerings of common stock, adjustment to offering costs	—	—	—	—	39	—	39
Issuance of common stock under the employee stock purchase plan	—	—	110,448	—	2,088	—	2,088
Net loss	—	—	—	—	—	(31,292)	(31,292)
BALANCE, DECEMBER 31, 2021	—	\$ —	25,378,520	\$ 25	\$ 505,482	\$ (93,767)	\$ 411,740

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

CASTLE BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,	
	2021	2020
OPERATING ACTIVITIES		
Net loss	\$ (31,292)	\$ (10,284)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Depreciation and amortization	3,407	472
Stock-based compensation expense	21,740	8,309
Amortization of debt discounts and issuance costs	—	839
Deferred income taxes	(8,736)	—
Loss on extinguishment of debt	—	1,397
Other	—	(16)
Change in operating assets and liabilities:		
Accounts receivable	(4,631)	1,663
Prepaid expenses and other current assets	617	(2,815)
Inventory	327	(980)
Operating lease assets	931	—
Other assets	(180)	(1,401)
Accounts payable	(182)	169
Operating lease liabilities	(852)	—
Accrued compensation	6,208	3,329
Medicare advance payment	(8,350)	8,350
Other accrued liabilities	2,286	561
Other liabilities	(276)	272
Net cash (used in) provided by operating activities	<u>(18,983)</u>	<u>9,865</u>
INVESTING ACTIVITIES		
Purchases of property and equipment	(3,483)	(4,751)
Asset acquisitions, net of cash and cash equivalents acquired	(63,184)	—
Proceeds from sale of property and equipment	10	3
Net cash used in investing activities	<u>(66,657)</u>	<u>(4,748)</u>
FINANCING ACTIVITIES		
Proceeds from public offerings of common stock, net of underwriting discounts, commissions and offering costs	—	330,041
Payment of common stock offering costs	(336)	—
Repayment of term debt	—	(27,359)
Proceeds from exercise of common stock options	4,234	1,593
Payment of employees' taxes on vested restricted stock units	(781)	—
Proceeds from contributions to the employee stock purchase plan	2,312	1,615
Repayment of principal portion of finance lease liabilities	(8)	—
Net cash provided by financing activities	<u>5,421</u>	<u>305,890</u>

CASTLE BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS (Continued)
(in thousands)

	Years Ended December 31,	
	2021	2020
NET CHANGE IN CASH AND CASH EQUIVALENTS	(80,219)	311,007
Beginning of year	409,852	98,845
End of year	\$ 329,633	\$ 409,852
 SUPPLEMENTAL DISCLOSURE OF CASH PAID FOR:		
Interest	\$ 1	\$ 1,978
Income taxes	\$ 16	\$ 102
 DISCLOSURE OF NON-CASH INVESTING AND FINANCING ACTIVITIES:		
Accrued purchases of property and equipment	\$ 33	\$ 58
Property and equipment acquired with tenant improvement allowance	\$ 54	\$ 714
Asset acquisition, receivable for purchase price adjustment	\$ 519	\$ —
Asset acquisition, liability for contingent consideration	\$ 18,287	\$ —
Common stock offering costs incurred but not paid	\$ —	\$ 377
Cashless exercise of common stock warrants	\$ —	\$ 250

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

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Description of Business

Castle Biosciences, Inc. (the “Company”, “we”, “us”, or “our”) was incorporated in the state of Delaware on September 12, 2007. We are a commercial-stage diagnostics company focused on providing physicians and their patients with personalized, clinically actionable information to clinicians and their patients to inform treatment decisions and improve health outcomes. We are based in Friendswood, Texas (a suburb of Houston, Texas) and laboratory operations are conducted at our facilities located in Phoenix, Arizona and in Pittsburgh, Pennsylvania.

Impact of COVID-19 Pandemic

Since the COVID-19 pandemic began in March 2020, we have maintained uninterrupted business operations with normal turnaround times for delivery of test reports, but have experienced declines in test report volume in certain periods, which we believe is linked to delays and/or cancellations in patient visits in response to COVID-19, resulting in reduced diagnostic biopsies and thus reduced diagnoses of cutaneous melanoma. The extent to which COVID-19 may further impact our business, consolidated results of operations, consolidated financial condition and consolidated cash flows will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

2. Summary of Significant Accounting Policies

Basis of Presentation

Our consolidated financial statements include the accounts of Castle Biosciences, Inc. and our wholly owned subsidiaries and have been prepared in conformity with accounting principles generally accepted in the United States of America (“U.S. GAAP”). All intercompany accounts and transactions have been eliminated in consolidation.

Reclassification

Certain prior year amounts in our consolidated statements of operations and comprehensive loss have been reclassified to conform to the current year presentation. Specifically, we no longer present gross margin on our statements of operations and comprehensive loss and therefore the cost of sales line is now presented within the operating expenses section. This reclassification had no impact on operating loss, loss before income taxes, net loss, comprehensive loss or loss per share.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Significant items subject to such estimates include revenue recognition, the valuation of stock-based compensation, assessing future tax exposure and the realization of deferred tax assets, the useful lives and recoverability of long-lived assets, the valuation of acquired intangible assets, the valuation of contingent consideration and other contingent liabilities. We base these estimates on historical and anticipated results, trends, and various other assumptions that we believe are reasonable under the circumstances, including assumptions as to future events. These estimates form the basis for making judgments about the carrying values of assets and liabilities and recorded revenues and expenses that are not readily apparent from other sources. Actual results could differ from those estimates and assumptions. We have considered the potential impact of the COVID-19 pandemic on our estimates and assumptions. The extent to which the COVID-19 pandemic may impact our estimates in future periods is uncertain and subject to change.

Operating Segments

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. The Company views its operations and manages its business as one operating segment. All revenues are attributable to U.S.-based operations and all assets are held in the United States.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Cash and Cash Equivalents including Concentrations of Credit Risk

Cash equivalents consist of short-term, highly liquid investments with original maturities of three months or less. Our cash equivalents consist of money market funds, which are not insured by the Federal Deposit Insurance Corporation (“FDIC”), that are primarily invested in short-term U.S. government obligations. Cash deposits at financial institutions may exceed the amount of insurance provided by the FDIC. Management believes that we are not exposed to significant credit risk on our cash deposits due to the financial position of the institutions in which deposits are held. We have not experienced any losses on our cash or cash equivalents.

Revenue Recognition

Revenue is recognized in accordance with Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (“ASC”) Topic 606, *Revenue from Contracts with Customers* (“ASC 606”). In accordance with ASC 606, we follow a five-step process to recognize revenues: (1) identify the contract with the customer, (2) identify the performance obligations, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations and (5) recognize revenues when the performance obligations are satisfied. We have determined that we have a contract with the patient when the treating clinician orders the test. Our contracts generally contain a single performance obligation, which is the delivery of the test report, and we satisfy our performance obligation at a point in time upon the delivery of the test report to the treating physician, at which point we can bill for the report. The amount of revenue recognized reflects the amount of consideration to which we expect to be entitled, or the transaction price, and considers the effects of variable consideration. See Note 3 for further details.

Accounts Receivable and Allowance for Credit Losses

We classify accounts receivable balances that are expected to be paid more than one year from the consolidated balance sheet date as non-current assets. The estimated timing of payment utilized as a basis for classification as non-current is determined by analyses of historical payor-specific payment experience, adjusted for known factors that are expected to change the timing of future payments.

We accrue an allowance for credit losses against our accounts receivable based on management’s current estimate of amounts that will not be collected. Management’s estimates are typically based on historical loss information adjusted for current conditions. We generally do not perform evaluations of customers’ financial condition and generally do not require collateral. Historically, our credit losses have not been significant. The allowance for credit losses was zero as of December 31, 2021 and 2020. Adjustments for implicit price concessions attributable to variable consideration, as discussed above, are incorporated into the measurement of the accounts receivable balances and are not part of the allowance for credit losses.

Inventory

We carry inventories of test supplies in our laboratory facilities. The inventories are carried at the lower of weighted average cost and net realizable value and expensed through cost of sales as the supplies are used.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, generally between five and ten years. Leasehold improvements are amortized using the straight-line method over the shorter of the estimated useful life of the asset or the term of the lease. Our leasehold improvements primarily relate to our office and laboratory facilities in Friendswood, Texas and Phoenix, Arizona, and are generally being amortized through the end of the lease terms in 2025 and 2033, respectively. Maintenance and repairs are charged to expense as incurred, and material improvements are capitalized. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the consolidated balance sheet and any resulting gain or loss is reflected in the consolidated statements of operations and comprehensive loss in the period realized.

Intangible Assets

Our intangible assets, which are comprised primarily of acquired developed technology, are considered to be finite-lived and are amortized on a straight-line basis over their estimated useful lives.

Long-Lived Assets

We review long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of the assets may not be recoverable. An impairment loss is recognized when the total of estimated future undiscounted cash flows, expected to result from the use of the asset and its eventual disposition, are less than the carrying amount. Impairment, if

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

any, would be calculated based on the excess of the carrying amount of the long-lived asset over the long-lived asset's fair value. There were no impairment charges recognized for the years ended December 31, 2021 and 2020.

Acquisitions

We assess acquisitions under ASC 805, *Business Combinations*, to determine whether a transaction represents the acquisition of assets or a business combination. Under this guidance, we apply a two-step model. The first step involves a screening test where we evaluate whether substantially all of the fair value of the gross assets acquired is concentrated in a single asset or a group of similar assets. If the screening test is met, we account for the set as an asset acquisition. If the screening test is not met, we apply the second step of the model to determine if the set meets the definition of a business based on the guidance in ASC 805. If so, the transaction is treated as a business combination. Otherwise, it is treated as an asset acquisition. Asset acquisitions are accounted for by allocating the cost of the acquisition, including transaction costs, to the individual assets acquired and liabilities assumed on a relative fair value basis without recognition of goodwill. Business combinations are accounted for using the acquisition method. Under the acquisition method, goodwill is measured as a residual amount equal to the fair value of the consideration transferred less the net recognized fair value of the identifiable assets acquired and the liabilities assumed, as of the acquisition date, and transaction costs are expensed as incurred.

Contingent Consideration

Under the terms of business combinations or asset acquisitions, we may be required to pay additional consideration if specified future events occur or if certain conditions are met. With respect to the additional consideration that may be payable in connection with the Cernostics, Inc. ("Cernostics") asset acquisition, we account for the contingent consideration as liability in accordance with ASC 480, *Distinguishing Liabilities from Equity* ("ASC 480"), under the guidance for obligations that must or may be settled by issuance of a variable number of shares. In accordance with ASC 480, we record the contingent consideration initially and subsequently at fair value with changes in fair value recorded in the statements of operations and comprehensive loss each period. For additional information on the contingent consideration, see Notes 5 and 11.

Other Operating Income

On April 10, 2020, we received an automatic payment of \$1.9 million from the U.S. Department of Health and Human Services ("HHS") pursuant to the Coronavirus Aid, Relief and Economic Security Act enacted on March 27, 2020, also known as the CARES Act, out of relief funds allocated by HHS to healthcare providers to reimburse healthcare related expenses or lost revenues attributable to COVID-19. This automatic payment was calculated by HHS in proportion to the providers' share of Medicare fee-for-service reimbursements in 2019 and was applicable to all facilities and providers that received Medicare fee-for-service reimbursements in 2019. In the second quarter of 2020, based on guidance issued by HHS at the time that stated any reasonable method could be used to calculate lost revenues attributable to COVID-19, we concluded it would qualify to retain the relief funds and recognized the funds received as other operating income during the three months ended June 30, 2020. On September 19, 2020, HHS issued a notice of reporting requirements that changed the methodology for determining lost revenues to be based on a patient care operating income metric, as defined by HHS. Due to this change in methodology and uncertainty in its application, we determined that it was no longer reasonably assured of keeping the funds. Therefore, in the three months ended September 30, 2020, we reversed the previously recognized income. However, in the fourth quarter of 2020, a legislative change was enacted affecting the program, under which we concluded it is reasonably assured we will qualify to retain the funds. Accordingly, we recognized the income again in the fourth quarter of 2020.

Leases

Effective January 1, 2021, we account for leases in accordance with ASC 842, *Leases*. We categorize leases at their commencement as either operating or finance leases based on the criteria in ASC 842. Under ASC 842, we record right-of-use ("ROU") assets and lease liabilities for each lease arrangement identified, except that we have elected the short-term lease exemption for all leases with a term of 12 months or less. Lease liabilities are recorded at the present value of future lease payments discounted using our incremental borrowing rate for the lease established at the commencement date and ROU assets are measured at the amount of the lease liability plus any initial direct costs, less any lease incentives received before commencement. For our operating leases, we recognize a single lease cost over the lease term on a straight-line basis. We have elected the practical expedient of not separating nonlease components from lease components in all leases. Periods prior to January 1, 2021 have not been restated for the adoption of ASC 842 and continue to reflect the accounting treatment of leases in accordance with the prior lease accounting guidance, ASC 840, *Leases*. Under ASC 840, landlord/tenant incentives, rent holidays and escalations in the base price of rent payments under operating leases were recognized on a straight-line basis over the lease term. Deferred rent balances were classified as current or non-current in the consolidated balance sheets based upon the period when reversal of the liability was expected to occur. See Note 9 for details on our leases.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Cost of Sales (exclusive of amortization of acquired intangible assets)

Cost of sales is expensed as incurred and includes material and service costs associated with testing samples, personnel costs (including salaries, bonuses, benefits and stock-based compensation expense), electronic medical records, order and delivery systems, shipping charges to transport samples, third-party test fees, and allocated overhead including rent, information technology costs, equipment and facilities depreciation and utilities.

Research and Development

Research and development costs are charged to operations as incurred. 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. Upfront and milestone payments due to third parties that perform research and development services on behalf of us will be expensed as services are rendered or when the milestone is achieved.

Research and development costs include, but are not limited to, payroll and personnel-related expenses, stock-based compensation expense, materials, laboratory supplies, and consulting costs.

Selling, General and Administrative Expenses

Selling, general and administrative (“SG&A”) expenses are attributable to sales, marketing, executive, finance and accounting, legal and human resources functions. These expenses consist of personnel costs (including salaries, employee benefit costs, bonuses and stock-based compensation expenses), customer services expenses, direct marketing expenses, educational and promotional expenses, market research, audit and legal expenses, and consulting. We expense all SG&A costs as incurred.

Accrued Compensation

We accrue for liabilities under discretionary employee and executive bonus plans. These estimated compensation liabilities are based on progress against corporate objectives approved by our board of directors, compensation levels of eligible individuals, and target bonus percentage levels. The board of directors reviews and evaluates the performance against these objectives and ultimately determines what discretionary payments are made. We also accrue for liabilities under employee sales incentive bonus plans with accruals based on performance achieved to date compared to established targets. As of December 31, 2021 and 2020, we accrued approximately \$12,071,000 and \$7,175,000, respectively, for liabilities associated with these bonus plans. These amounts are classified as current or noncurrent accrued liabilities in the balance sheets based on the expected timing of payment.

Retirement Plan

We have an Internal Revenue Code (“IRC”) Section 401(k) profit sharing plan (the “Plan”) for eligible employees. The Plan is funded by employee contributions and provides for discretionary contributions in the form of matching and/or profit-sharing contributions. For the years ended December 31, 2021 and 2020, we provided a discretionary matching contribution of \$2,036,000 and \$789,000, respectively. The higher amount for the year ended December 31, 2021 reflects both an increase in the number of employees and a higher matching contribution rate compared to the year ended December 31, 2020.

Income Taxes

We recognize deferred tax assets and liabilities for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using statutory tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the period that includes the statutory enactment date. Valuation allowances are established to reduce deferred tax assets when it is more likely than not that some portion or all of the deferred tax assets will not be realized.

Tax benefits are recognized only for tax positions that are more likely than not to be sustained upon examination by tax authorities. The amount recognized is measured as the largest amount of benefit that is greater than 50% likely to be realized upon settlement. A liability for unrecognized tax benefits is recorded for any tax benefits claimed in our tax returns that do not meet these recognition and measurement standards.

Our policy for recording interest and penalties associated with uncertain tax positions is to record such items as a component of tax expense. No material amounts of tax-related interest or penalties were recorded during the years ended December 31, 2021 and 2020.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Stock-Based Compensation

Stock-based compensation expense for equity instruments issued to employees is measured based on the grant-date fair value of the awards. The fair value of employee stock options and offerings under the 2019 Employee Stock Purchase Plan (the “ESPP”) are estimated on the date of grant using the Black-Scholes option-pricing valuation model. For restricted stock units (“RSUs”), the fair value is equal to the closing price of our common stock on the date of grant. We recognize compensation costs on a straight-line basis for all employee stock-based compensation awards over the requisite service period of the awards. For options and RSUs, the requisite service period is generally the awards’ vesting period (typically four years). For the ESPP, the requisite service period is generally the period of time from the offering date to the purchase date. Forfeitures are accounted for as they occur.

Comprehensive Loss

Comprehensive loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. Our comprehensive loss was the same as our reported net loss for all periods presented.

CARES Act Payroll Tax Deferral

The CARES Act permits employers to defer the payment of the employer share of social security taxes due for the period beginning March 27, 2020 and ending December 31, 2020. Of the amounts deferred, 50% were required to be paid by December 31, 2021 and the remaining 50% are required to be paid by December 31, 2022. We began deferring payment of the employer share of social security taxes in May 2020. Of the \$551,000 originally deferred, 50% was repaid during the year ended December 31, 2021. As of December 31, 2021, the remaining \$276,000 of such taxes was classified as a current liability on the consolidated balance sheet.

Recently Adopted Accounting Pronouncements

We were previously an emerging growth company (“EGC”) within the meaning of the Jumpstart Our Business Startups Act, as amended, (the “JOBS Act”) and elected to delay the adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements were made applicable to private companies, as permitted under the JOBS Act. Because the market value of our common stock held by non-affiliates exceeded \$700.0 million as of June 30, 2021, we ceased to be an EGC effective December 31, 2021. Accordingly, we are no longer permitted to delay the adoption of new or revised accounting pronouncements and as such we adopted the pronouncements discussed below in the fourth quarter of 2021 effective as of the dates noted.

In February 2016, the FASB issued Accounting Standards Update (“ASU”) No. 2016-02, *Leases* (Topic 842) (“ASU 2016-02”), which supersedes ASC 840, *Leases*. ASU 2016-02 establishes ASC 842, *Leases*, and provides principles for the recognition, measurement, presentation and disclosure of leases for both lessees and lessors. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification determines whether lease expense is recognized based on an effective interest method for finance leases or on a straight-line basis over the term of the lease for operating leases. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of classification. Leases with a term of 12 months or less may be accounted for similar to existing guidance for operating leases. We adopted ASU 2016-02 and ASC 842 using the modified retrospective approach with an effective date of January 1, 2021. Periods prior to January 1, 2021 have not been restated for the adoption of ASC 842 and continue to reflect the accounting treatment of leases in accordance with ASC 840. In connection with the adoption, we elected the package of practical expedients to not reassess prior conclusions about lease identification, lease classification and capitalized indirect costs. We did not elect the use of hindsight practical expedient. Upon adoption, effective January 1, 2021 we recognized operating lease right-of-use assets of \$5,405,000, operating lease liabilities of \$6,076,000, reductions to noncurrent liabilities of \$751,000, reductions to current assets of \$59,000 and a credit to accumulated deficit of \$21,000. See Note 9 for disclosures about our leases.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments - Credit Losses* (Topic 326): *Measurement of Credit Losses on Financial Instruments*, which requires the measurement of expected credit losses for financial instruments carried at amortized cost, such as accounts receivable, held at the reporting date based on historical experience, current conditions and reasonable forecasts. The main objective of this ASU is to provide financial statement users with more decision-useful information about the expected credit losses on financial instruments and other commitments to extend credit held by a reporting entity at each reporting date. We adopted the standard effective January 1, 2021 using the modified retrospective approach. The adoption of this standard had no impact on our consolidated financial statements.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* (“ASU 2019-12”), which eliminates certain exceptions to the general principles in Topic 740 and simplifies other areas of the existing guidance. The adoption of ASU 2019-12 effective January 1, 2021 had no impact on our consolidated financial statements.

3. Revenue

All of our revenues from contracts with customers are associated with the provision of diagnostic and prognostic testing services. Most of our revenues are attributable to DecisionDx®-Melanoma for cutaneous melanoma. We also provide a test for uveal melanoma, DecisionDx®-UM. We launched a test for patients with cutaneous squamous cell carcinoma, DecisionDx®-SCC in August 2020 and launched a test for use in patients with suspicious pigmented lesions, DecisionDx® DiffDx™-Melanoma in November 2020. We began offering a test for difficult-to-diagnose melanocytic lesions, myPath Melanoma, following an asset acquisition completed in May 2021 and began offering the TissueCypher® Barrett’s Esophagus Assay for patients with BE following an asset acquisition completed in December 2021. Information on the disaggregation of revenues is included below.

Once we satisfy our performance obligations and bill for the service, the timing of the collection of payments may vary based on the payment practices of the third-party payor and the existence of contractually established reimbursement rates. Most of the payments for our services are made by third-party payors, including Medicare and commercial health insurance carriers. Certain contracts contain a contractual commitment of a reimbursement rate that differs from our list prices. However, absent a positive coverage policy, with or without a contractually committed reimbursement rate, with a commercial carrier or governmental program, our diagnostic tests may or may not be paid by these entities. In addition, patients do not enter into direct agreements with us that commit them to pay any portion of the cost of the tests in the event that their insurance provider declines to reimburse us. We may pursue, on a case-by-case basis, reimbursement from such patients in the form of co-payments and co-insurance, in accordance with the contractual obligations that we have with the insurance carrier or health plan. These situations may result in a delay in the collection of payments.

The Medicare claims that are covered by policy under a Local Coverage Determination (“LCD”) are generally paid at the established rate by our Medicare contractor within 30 days from receipt. Medicare claims that were either submitted to Medicare prior to the LCD coverage commencement date or are not covered by the terms of the LCD but meet the definition of being medically reasonable and necessary pursuant to the controlling Section 1862(a)(1)(A) of the Social Security Act are generally appealed and may ultimately be paid at the first (termed “redetermination”), second (termed “reconsideration”) or third level of appeal (de novo hearing with an Administrative Law Judge (“ALJ”). A successful appeal at any of these levels results in payment.

In the absence of LCD coverage or contractually established reimbursements rates, we have concluded that our contracts include variable consideration because the amounts paid by Medicare or commercial health insurance carriers may be paid at less than our standard rates or not paid at all, with such differences considered implicit price concessions. Variable consideration attributable to these price concessions is measured at the expected value using the “most likely amount” method under ASC 606. The amounts are determined by historical average collection rates by test type and payor category taking into consideration the range of possible outcomes, the predictive value of our past experiences, the time period of when uncertainties expect to be resolved and the amount of consideration that is susceptible to factors outside of our influence, such as the judgment and actions of third parties. Such variable consideration is included in the transaction price only to the extent it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainties with respect to the amount are resolved. Variable consideration may be constrained and excluded from the transaction price in situations where there is no contractually agreed upon reimbursement coverage or in the absence of a predictable pattern and history of collectability with a payor. Accordingly, in such situations revenues are recognized on the basis of actual cash collections. Variable consideration for Medicare claims that are not covered by an LCD, including those claims subject to approval by an ALJ at an appeal hearing, is deemed to be fully constrained due to factors outside our influence (i.e., judgment or actions of third parties) and the uncertainty of the amount to be received is not expected to be resolved for a long period of time. Variable consideration is evaluated each reporting period and adjustments are recorded as increases or decreases in revenues. Included in revenues for the years ended December 31, 2021 and 2020 were \$3,324,000 and \$176,000, respectively, of revenue increases associated with changes in estimated variable consideration related to performance obligations satisfied in previous periods. These amounts include (i) adjustments for actual collections versus estimated amounts and (ii) cash collections and the related recognition of revenue in current period for tests delivered in prior periods due to the release of the constraint on variable consideration.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Because our contracts with customers have an expected duration of one year or less, we have elected the practical expedient in ASC 606 to not disclose information about our remaining performance obligations. Any incremental costs to obtain contracts are recorded as selling, general and administrative expense as incurred due to the short duration of our contracts. Contract balances consisted of accounts receivable (both current and noncurrent) as of December 31, 2021 and 2020 and the Medicare advance payment (discussed further below) as of December 31, 2020.

Medicare Advance Payment

On April 16, 2020, we received an advance payment of \$8.3 million (the “Advance Payment”) from the Centers for Medicare & Medicaid Services (“CMS”) under its Accelerated and Advance Payment Program, which was expanded to provide increased cash flow to service providers during the COVID-19 pandemic. CMS began recoupment of the Advance Payment in April 2021 by applying 25% of the Medicare payments otherwise owed to us against the balance of the Advance Payment. Recoupment of the full amount of the Advance Payment was complete by December 31, 2021.

DecisionDx-Melanoma Claims Consolidation

In June 2017, we submitted to the Office of Medicare Hearings and Appeals (“OMHA”) a formal request to participate in a program that OMHA developed with the intent of providing appellants a means to have large volumes of claim disputes adjudicated at an accelerated rate. The program consolidates outstanding claims at the ALJ level and uses a statistical-sampling approach where five ALJs will determine reimbursement results for a sample of claims which are then extrapolated to the universe of claims. The consolidation includes 2,698 DecisionDx-Melanoma claims dating from 2013 through spring 2017. Hearings were held in April 2019 with a supplemental hearing in May 2019. On March 12, 2020, OMHA issued a decision denying payment on all claims in the consolidation. We have filed an appeal to the decision, although no ruling on such appeal has been issued to date. In accordance with ASC 606 and consistent with prior periods, we have not recognized (fully constrained the variable consideration) any revenues attributable to these claims in our consolidated financial statements pending the outcome of this matter.

Disaggregation of revenues

The table below provides the disaggregation of revenue by type (in thousands):

	Years Ended December 31,	
	2021	2020
Dermatologic	\$ 85,753	\$ 57,646
Other	8,332	5,003
Total net revenues	\$ 94,085	\$ 62,649

Payor Concentration

We rely upon reimbursements from third-party government payors (primarily Medicare) and private-payor insurance companies to collect accounts receivable related to sales of our diagnostic tests.

Our significant third-party payors and their related revenues as a percentage of total revenues and accounts receivable balances are as follows:

	Percentage of Revenues		Percentage of Accounts Receivable (current)		Percentage of Accounts Receivable (non-current)	
	Year Ended December 31,		As of December 31,		As of December 31,	
	2021	2020	2021	2020	2021	2020
Medicare	57 %	58 %	24 %	15 %	— %	— %
Medicare Advantage plans	28 %	29 %	40 %	40 %	— %	25 %
BlueCross BlueShield plans	7 %	6 %	22 %	26 %	58 %	44 %

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

4. Loss Per Share

Basic loss per share is computed by dividing net loss for the period by the weighted-average number of common shares outstanding during the period. Diluted loss per share reflects the additional dilution from potential issuances of common stock, such as stock issuable pursuant to the exercise of stock options or purchases under the 2019 Employee Stock Purchase Plan (“ESPP”). The treasury stock method is used to calculate the potential dilutive effect of these common stock equivalents. However, potentially dilutive shares are excluded from the computation of diluted loss per share when their effect is antidilutive.

Due to us reporting a net loss for all periods presented, all potentially dilutive securities are antidilutive and are excluded from the computation of diluted loss per share for such periods.

The table below provides the weighted-average number of potential common shares associated with outstanding securities not included in our calculation of diluted loss per share for the years ended December 31, 2021 and 2020 because to do so would be antidilutive (in thousands):

	Years Ended December 31,	
	2021	2020
Stock options and restricted stock units	3,459	2,789
Common stock warrants	—	35
Employee stock purchase plan	62	100
Total	3,521	2,924

In addition, in connection with the acquisition of Cernostics, we may issue shares of our common stock to satisfy the contingent consideration obligation, pending the outcome of certain commercial milestones, as discussed in Note 5.

5. Asset Acquisitions

Myriad myPath, LLC

On May 28, 2021, we completed the acquisition of all of the equity of Myriad myPath, LLC, a laboratory in Salt Lake City where the myPath Melanoma test for difficult-to-diagnose melanocytic lesions was developed and offered, for a cash purchase price of \$32,500,000. Following the completion of the acquisition, we became the sole provider of the myPath Melanoma test. Based on the guidance in ASC 805, we concluded that substantially all of the fair value of the gross assets acquired was concentrated in a single identifiable asset and therefore the transaction represents an asset acquisition. We incurred \$684,000 of direct transaction costs that were included in the cost of the acquisition. The allocation of the acquisition to individual assets resulted in an intangible asset representing developed technology of \$33,054,000 and inventory of \$130,000. The intangible asset has an estimated useful life of 12 years and is being amortized on a straight-line basis.

Cernostics, Inc.

On December 3, 2021, we completed the acquisition of Cernostics, Inc., which offers the TissueCypher® Barrett’s Esophagus Assay for patients with BE. We acquired Cernostics for an upfront cash purchase price of \$30,732,000, including \$653,000 of direct transaction costs. A portion of the upfront cash consideration is being held in escrow for a specified period following closing to secure post-closing adjustments and indemnification claims, if any. Our consolidated balance sheet at December 31, 2021 reflects a receivable of \$519,000 for the post-closing purchase price adjustment, representing the difference between actual and estimated cash and working capital at closing, among other things. We have also agreed to pay up to an additional \$50.0 million in cash or shares of our common stock, at our sole discretion, based on the achievement of certain commercial milestones relating to the year ending December 31, 2022 (“Earnout Payments”). The portion of any Earnout Payments that may be settled in shares of our common stock is subject to certain limitations and the aggregate number of shares that may be issued for the Earnout Payments may not exceed 5,034,653 shares. Any Earnout Payments in shares of our common stock will be based on the volume weighted-average price of our common stock for the 15 trading days ending December 30, 2022. The Earnout Payments represent contingent consideration. ASC 480, *Distinguishing Liabilities from Equity*, provides guidance on accounting for certain obligations that must or may be settled by issuance of a variable number of shares. In accordance with that guidance, we recognized a liability of \$18,287,000, which represents the fair value of the obligation as of the acquisition date. See Note 11 for additional information on the measurement of the contingent consideration. Based on the guidance in ASC 805, we concluded that substantially all of the fair value of the gross assets acquired was concentrated in a single identifiable asset and therefore the transaction represents an asset acquisition.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The cost of the acquisition, which is comprised of the cash consideration, transaction costs and contingent consideration, was allocated to the assets acquired and the liabilities assumed as follows (in thousands):

	December 3, 2021
Cash and cash equivalents	\$ 1,251
Accounts receivable	104
Prepaid expenses and other current assets	198
Property and equipment	455
Intangible assets	57,827
Accounts payable	(655)
Accrued compensation	(167)
Other accrued and current liabilities	(386)
Finance lease liabilities	(237)
Deferred tax liabilities	(9,371)
Total cost allocated	\$ 49,019

The intangible assets were comprised of developed technology of \$57,264,000 with an estimated useful life of 15 years and a developed workforce of \$563,000, with an estimated useful life of five years, and each is being amortized on a straight-line basis.

6. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	As of December 31,	
	2021	2020
Leasehold improvements	\$ 5,044	\$ 1,388
Lab equipment ⁽¹⁾	3,727	2,037
Computer equipment	2,457	1,305
Furniture and fixtures	1,288	436
Construction-in-progress	27	3,590
Total	12,543	8,756
Less accumulated depreciation ⁽¹⁾	(3,042)	(1,654)
Property and equipment, net	\$ 9,501	\$ 7,102

(1) Includes lab equipment under a finance lease of \$237 thousand and accumulated depreciation of \$8 thousand.

Depreciation expense was recorded in the consolidated statements of operations and comprehensive loss as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Cost of sales (exclusive of amortization of acquired intangible assets)	\$ 478	\$ 341
Research and development	248	31
Selling, general and administrative	722	100
Total	\$ 1,448	\$ 472

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

7. Intangible Assets, Net

Our intangible assets, net consist of the following (in thousands):

	December 31, 2021			Weighted-Average Remaining Life (in years)
	Gross carrying value	Accumulated amortization	Net	
Developed technology	\$ 90,317	\$ (1,949)	\$ 88,368	13.2
Assembled workforce	563	(9)	554	4.9
Total intangible assets, net	\$ 90,880	\$ (1,958)	\$ 88,922	

There were no intangible assets as of December 31, 2020.

The estimated future aggregate amortization expense as of December 31, 2021 is as follows (in thousands):

Years Ending December 31,	
2022	\$ 6,681
2023	6,681
2024	6,700
2025	6,681
2026	6,672
Thereafter	55,507
Total	\$ 88,922

Amortization expense of intangible assets was \$2.0 million for the year ended December 31, 2021. No amortization expense was recorded for the year ended December 31, 2020.

8. Other Accrued and Current Liabilities

Other accrued liabilities consisted of the following (in thousands):

	As of December 31,	
	2021	2020
Accrued service fees	\$ 1,905	\$ 1,543
Clinical studies	1,655	348
Employee stock purchase plan contributions	760	536
Payroll tax liabilities	695	276
Accrued payor refunds	386	—
Other	277	352
Total	\$ 5,678	\$ 3,055

9. Leases

Operating Leases

We lease office space in Friendswood, Texas (the “Friendswood Lease”) for use as our corporate headquarters. The Friendswood Lease commenced in late 2020 under a 60-month term and a renewal option for one additional five-year term.

We lease two facilities in Phoenix, Arizona for laboratory and office space. For both leases, the current term extends until April 2033 with options to renew for two additional five-year terms.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

We have not included the optional renewal periods in the measurement of the lease obligations because it is not reasonably certain that we will exercise these renewal options.

Our other operating leases primarily consist of office equipment.

Finance Lease

In connection with the December 2021 acquisition of Cernostics, we assumed a finance lease for laboratory equipment.

Discount Rates

We discount our lease obligations using our incremental borrowing rate at the commencement date. The incremental borrowing rate is the rate of interest we would have to pay to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. We primarily consider industry data, our credit rating and the lease term to determine our incremental borrowing rate.

Lease Balances and Costs

Lease balances reflected in the consolidated balance sheet were as follows (in thousands):

Lease Balance	Classification	December 31, 2021
Lease Assets		
Operating	Operating lease assets	\$ 7,383
Finance	Property and equipment, net	\$ 229
Lease Liabilities		
Current		
Operating	Operating lease liabilities	\$ 1,179
Finance	Other accrued and current liabilities	\$ 105
Noncurrent		
Operating	Noncurrent operating lease liabilities	\$ 6,900
Finance	Other liabilities	\$ 124

Costs associated with our leases were included in the consolidated statement of operations and comprehensive loss as follows (in thousands):

Lease Cost	Year Ended December 31, 2021
Operating lease cost⁽¹⁾	\$ 1,450
Finance lease cost	
Amortization of lease assets	8
Interest on finance lease liabilities	1
Short-term lease cost	29
Total lease cost	\$ 1,488

(1) Includes variable lease cost of \$187 thousand for the year ended December 31, 2021.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Other Information

Supplemental cash flow information on leases is as follows (in thousands):

	Year Ended December 31, 2021
Cash paid for amounts included in the measurement of lease liabilities	
Operating cash flows from operating leases	\$ 1,145
Operating cash flows from interest paid on finance leases	\$ 1
Financing cash flows from finance leases	\$ 8

During the year ended December 31, 2021, we recorded \$2.9 million in lease liabilities arising from obtaining ROU assets.

Information regarding the weighted-average lease term and weighted-average discount rate is presented below:

	December 31, 2021
Weighted-average remaining lease term (years)	
Operating leases	9.1
Finance leases	2.3
 Weighted-average discount rate	
Operating leases	4.9 %
Finance leases	5.0 %

The following is a maturity analysis of our operating lease and finance lease liabilities as of December 31, 2021 (in thousands):

	Operating leases	Finance leases
Years Ending December 31,		
2022	\$ 1,258	\$ 108
2023	1,287	108
2024	1,302	26
2025	1,218	—
2026	689	—
Thereafter	4,609	—
Total lease payments	10,363	242
Less: Interest component	(2,284)	(13)
Present value of lease payments	\$ 8,079	\$ 229

As of December 31, 2021, we have no material leases that have not yet commenced.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Disclosures Under ASC 840

Future non-cancellable commitments under all operating leases were as follows as of December 31, 2020 (in thousands):

Years Ending December 31,	
2021	\$ 1,164
2022	1,148
2023	1,142
2024	1,154
2025	1,119
Thereafter	1,037
	<u>\$ 6,764</u>

Rent expense was \$548,000 for the year ended December 31, 2020.

10. Long-Term Debt

We had a Loan and Security Agreement with Oxford Finance LLC (“Oxford”) as collateral agent, and Oxford and Silicon Valley Bank as equal syndicated lenders (the “2018 LSA”). The 2018 LSA consisted of a \$25.0 million secured term loan credit facility (the “Term Loan”). The Term Loan bore interest at a floating rate equal to the greater of (1) 8.55% and (2) the 30-day U.S. LIBOR rate as reported in The Wall Street Journal on the last business day of the month that preceded the month in which the interest was to accrue, plus 6.48%. We were permitted to make interest-only payments on the Term Loan through May 31, 2020. As required, we began to repay the principal in 30 equal monthly installments of \$833,333 each beginning on June 1, 2020. All unpaid principal and accrued and unpaid interest were to be due at maturity on November 1, 2022. However, on December 21, 2020, we terminated the 2018 LSA and repaid in full all amounts due, which totaled \$21.6 million as of such date, including the outstanding principal balance, the final payment amount, early termination and prepayment fees and accrued interest. The termination of the 2018 LSA resulted in the recognition of an extinguishment loss of \$1.4 million, which was reflected in our statement of operations and comprehensive loss for the year ended December 31, 2020.

11. Fair Value Measurements

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market in an orderly transaction between market participants at the measurement date. The fair value hierarchy prioritizes the inputs to valuation techniques used in measuring fair value. There are three levels to the fair value hierarchy based on the reliability of inputs, as follows:

Level 1 – Observable inputs that reflect quoted prices (unadjusted) for identical assets or liabilities in active markets.

Level 2 – Inputs other than quoted prices included in Level 1 that are observable for the asset or liability, either directly or indirectly.

Level 3 – Unobservable inputs in which little or no market data exists, therefore requiring us to develop our own assumptions.

Financial instruments measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. Our assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. The use of different assumptions and/or estimation methodologies may have a material effect on estimated fair values. Accordingly, the fair value estimates disclosed, or amounts recorded may not be indicative of the amount that us or holders of the instruments could realize in a current market exchange.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The table below provides information (in thousands), by level within the fair value hierarchy, of our financial assets and liabilities that are accounted for at fair value on a recurring basis as of December 31, 2021 and 2020 (in thousands):

	As of December 31, 2021			
	Quoted Prices in Active Markets for Identical Items (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Money market funds ⁽¹⁾	\$ 327,721	\$ —	\$ —	\$ 327,721
Liabilities:				
Contingent consideration	\$ —	\$ —	\$ 18,287	\$ 18,287
	As of December 31, 2020			
	Quoted Prices in Active Markets for Identical Items (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Money market funds ⁽¹⁾	\$ 409,480	\$ —	\$ —	\$ 409,480

(1) Classified as “Cash and cash equivalents” in the consolidated balance sheets.

Contingent Consideration

In connection with our acquisition of Cernostics, we have recorded a contingent consideration liability for the Earnout Payments. This liability is classified as a Level 3 fair value measurement due to the use of significant unobservable inputs and a Monte Carlo simulation to determine its fair value. The Monte Carlo simulation uses projections of the commercial milestones for the applicable period as well as the corresponding targets and approximate timing of payment based on the terms of the arrangement. The analysis also uses assumptions for expected volatility of the financial metrics and a risk-adjusted discount rate, which were 20.0% and 16.1%, respectively, at initial measurement on December 3, 2021. The contingent consideration liability is remeasured at fair value at each reporting period taking into account any updated assumptions or changes in circumstances. Any change in the fair value is recorded as a gain or loss in our consolidated statement of operations and comprehensive loss. There was no change in fair value from the initial recognition on December 3, 2021 through December 31, 2021.

The following table discloses the summary of changes in the contingent consideration liability measured at fair value using Level 3 inputs during the year ended December 31, 2021 (in thousands):

	Year Ended December 31, 2021
Balance at beginning of period	\$ —
Acquisition of Cernostics	18,287
Change in fair value	—
Balance at end of period	\$ 18,287

12. Commitments and Contingencies

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. We believe there is no threatened litigation or litigation pending that could have, individually or in the aggregate, a material adverse effect on our financial position, results of operations or cash flows.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

13. Stockholders' Equity

Capital Stock

The Company's Amended and Restated Certificate of Incorporation, dated July 29, 2019, authorizes the Company to issue up to 200,000,000 shares of common stock with a par value of \$0.001 per share. The Company is also authorized to issue up to 10,000,000 shares of preferred stock with a par value of \$0.001 per share. No dividends were declared or paid during the years ended December 31, 2021 or 2020.

On June 29, 2020, we issued and sold 2,000,000 shares of our common stock in a follow-on public offering at a price of \$37.00 per share. We received \$69,079,000 in net proceeds, after deducting underwriting discounts, commissions and offering costs. In connection with the offering, we granted the underwriters a 30-day option to purchase up to 300,000 additional shares of common stock at the public offering price, less underwriting discounts and commissions. On July 2, 2020, we issued and sold an additional 300,000 shares of common stock pursuant to the underwriters' exercise in full of their option to purchase additional shares, which resulted in an additional net proceeds to us of \$10,425,000. On December 18, 2020, we issued and sold 4,600,000 shares of our common stock in a follow-on public offering, including 600,000 shares associated with the full exercise of the underwriters' option to purchase additional shares, at a price to the public of \$58.00 per share. We received \$250,201,000 in aggregate net proceeds, after deducting underwriting discounts and commissions and offering costs.

Common Stock Warrants

The Company issued an aggregate of 209,238 shares and 31,814 shares of common stock December 11, 2020 and December 29, 2020, respectively, pursuant to net exercises by the holders of common stock warrants outstanding. In accordance with the net exercise provisions of the warrants, shares of common stock were withheld to satisfy the cost of these exercises.

There were no common stock warrants outstanding as of December 31, 2021 or 2020.

The common stock warrants were classified as stockholders' equity and no adjustments were recorded for changes in fair value.

14. Stock Incentive Plans and Stock-Based Compensation

Stock Incentive Plans

Our stock incentive plans provide for the granting of options to purchase common stock and other equity-based awards to our employees, directors and consultants. On September 6, 2008, we adopted the 2008 Stock Plan (the "2008 Plan"), on August 15, 2018, we adopted the 2018 Stock Plan (the "2018 Plan") and on July 24, 2019, we adopted the 2019 Equity Incentive Plan (the "2019 Plan"). Following the adoption of the 2018 Plan, no additional stock awards were granted under the 2008 Plan and following the adoption of the 2019 Plan, no additional stock awards were granted under the 2018 Plan.

Options under the plans may be granted as incentive stock options ("ISOs") or non-statutory stock options ("NSOs"). ISOs may only be granted our employees (including directors who are also considered employees). NSOs may be granted our employees, directors and consultants. Options may be granted for terms up to ten years from the date of grant, as determined by the Board of Directors; provided, however, that with respect to an ISO granted to a person who owns stock representing more than 10% of the voting power of all classes of stock of ours, the terms shall be for no more than five years from the date of grant. The exercise price of options granted must be no less than 100% of the fair market value of the shares on the date of grant, provided, however, that with respect to an ISO granted to an employee who at the time of grant of such options owns stock representing more than 10% of the voting power of all classes of stock of ours, the exercise price shall not be less than 110% of the fair market value of the shares on the date of grant. Options generally vest over four years (generally 25% after one year and monthly thereafter), subject to the option holder's continued service with us. We issue new shares to satisfy option exercises.

As of December 31, 2021, 46,741 shares remained available for grant under the 2019 Plan. On January 1, 2022, an additional 1,268,926 shares became available under the 2019 Plan pursuant to an automatic annual increase.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Stock Options

Stock option activity under our stock plans for the years ended December 31, 2021 and 2020 is set forth below:

	Stock Options Outstanding	Weighted-Average		Aggregate Intrinsic Value (in thousands)
		Exercise Price	Remaining Contractual Term (Years)	
Balance as of January 1, 2020	2,637,966	\$ 13.30		
Granted	1,286,065	\$ 49.63		
Exercised	(460,207)	\$ 3.53		
Forfeited/Cancelled	(94,322)	\$ 27.51		
Balance as of December 31, 2020	3,369,502	\$ 28.11		
Granted	841,336	\$ 48.97		
Exercised	(414,890)	\$ 10.13		
Forfeited/Cancelled	(209,260)	\$ 33.97		
Balance as of December 31, 2021	<u>3,586,688</u>	\$ 34.75	8.3	\$ 45,970
Exercisable at December 31, 2021 ⁽¹⁾	<u>1,332,487</u>	\$ 23.31	7.5	\$ 28,845

(1) Vested and exercisable options. Additionally, outstanding unvested options to purchase an aggregate of 10,255 shares of common stock with a weighted-average exercise price of \$2.39 per share may be exercised prior to vesting as of December 31, 2021 under early-exercise provisions. In the event of such exercise, the shares obtained upon exercise would be restricted and subject to forfeiture prior to vesting. No such early exercises have occurred as of December 31, 2021.

Restricted Stock Units

RSUs represent the right to receive shares of our common stock at a specified future date, subject to vesting. Our RSUs generally vest annually from the grant date in four equal installments subject to the holder's continued service with us. We issue new shares to satisfy RSUs upon vesting.

The following table summarizes our RSU activity for the years ended December 31, 2021 and December 31, 2020:

	Restricted Stock Units Outstanding	Weighted- Average Grant Date Fair Value
Balance as of January 1, 2020	—	\$ —
Granted	161,477	\$ 59.16
Vested	—	\$ —
Forfeited/Cancelled	—	\$ —
Balance as of December 31, 2020	161,477	\$ 59.16
Granted	958,361	\$ 43.05
Vested ⁽¹⁾	(56,002)	\$ 61.07
Forfeited/Cancelled	(13,662)	\$ 62.80
Balance as of December 31, 2021	<u>1,050,174</u>	<u>\$ 44.31</u>

(1) The aggregate number of shares withheld upon vesting for employee tax obligations was 16,440 for the year ended December 31, 2021.

RSU Awards to Related Parties

On October 1, 2021, the Audit Committee of our Board of Directors approved, at the recommendation of our Compensation Committee, a one-time award of RSUs to three employees who are the children of our Chief Executive Officer ("CEO") which we have determined to be outside the ordinary course of business. Under the Internal Revenue Code ("IRC"), those owning more than a specified percentage of a company's stock are not eligible to receive certain preferential tax benefits that are afforded to qualifying stock compensation arrangements. In determining eligibility under the Code, when calculating the number of shares of common stock owned, an individual must attribute all shares owned by specified family members. Because

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

of the stock ownership of our CEO and this attribution requirement, the three children have not been eligible to participate in the ESPP and, at times, have not qualified to receive stock option grants on terms as favorable as those received by other similar employees. Our Compensation Committee recommended, and our Audit Committee approved, a one-time grant of restricted stock units designed to compensate the three children for these differences. The aggregate number of shares underlying the restricted stock units granted to the three children was 17,275 which are included in the table above. The awards had an aggregate grant date fair value of \$1,129,000, vested immediately upon grant and was recognized as stock-based compensation expense, included in selling, general and administrative expenses, during the year ended December 31, 2021.

Employee Stock Purchase Plan

The ESPP became effective July 24, 2019. Offerings under the ESPP are generally 24 months in length with four six-month purchase periods unless terminated earlier, as described below. Eligible employees who enroll in an offering are able to purchase shares of our common stock at a discount through payroll deductions, subject to certain limitations. The purchase price of the shares of common stock is the lesser of (i) 85% of the fair market value of such shares on the offering date and (ii) 85% of the fair market value of such shares on the purchase date. A new offering begins approximately every six months. Offerings are concurrent, but in the event the fair market value of a share of common stock on the first day of any purchase period during an offering (the “New Offering”) is less than or equal to the fair market value of a share of common stock on the offering date for an ongoing offering (the “Ongoing Offering”), then the Ongoing Offering terminates immediately following the purchase of shares on the purchase date immediately preceding the New Offering and the participants in the terminated Ongoing Offering are automatically enrolled in the New Offering. In such case, we account for this event as a modification of the Ongoing Offering. Notwithstanding the above, our Board of Directors (or an authorized committee thereof) may modify the terms of or suspend any future offerings prior to their commencement.

As of December 31, 2021, 639,466 shares remained available for issuance under the ESPP. The ESPP provides for certain automatic increases in the number of shares of common stock reserved for issuance, which resulted in an additional 253,785 shares becoming available under the ESPP effective January 1, 2022. We issue new shares to satisfy ESPP purchases.

Determining Fair Value - Summary of Assumptions

We use the Black-Scholes option pricing model to estimate the fair value of stock options and purchase rights granted under the ESPP at the date of grant, start of the offering or other relevant measurement date. Set forth below is a description of the significant assumptions used in the option pricing model:

- *Expected term.* The expected term is the period of time that granted options are expected to be outstanding. For stock options, we have set the expected term using the simplified method based on the weighted average of both the period to vesting and the period to maturity for each option, as we have concluded that its stock option exercise history does not provide a reasonable basis upon which to estimate the expected term. For the ESPP, the expected term is the period of time from the offering date to the purchase date.
- *Expected volatility.* Previously, because of the limited period of time our stock had been traded in an active market, we calculated expected volatility by using the historical stock prices of a group of similar companies looking back over the estimated life of the option or the ESPP purchase right and averaging the volatilities of these companies. In the third quarter of 2021, we adjusted this calculation to include our own stock price on a relative basis to the peer group in the calculation of expected volatility, as our common stock has now been traded in an active market for more than two years.
- *Risk-free interest rate.* We base the risk-free interest rate used in the Black-Scholes valuation model on the market yield in effect at the time of option grant and at the offering date for the ESPP, provided from the Federal Reserve Board’s Statistical Releases and historical publications from the Treasury constant maturities rates for the equivalent remaining terms.
- *Dividend yield.* We have not paid, and does not have plans to pay, cash dividends. Therefore, we use an expected dividend yield of zero in the Black-Scholes option valuation model.

The fair value of our common stock is also an assumption used to determine the fair value of stock options. Prior to our initial public offering of common stock on July 29, 2019 (the “IPO”), our common stock was not publicly traded, therefore we estimated the fair value of our common stock. Following the IPO, the fair value of our common stock is the closing selling price per share of its common stock as reported on the Nasdaq Global Market on the date of grant or other relevant determination date.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

We use the Black-Scholes option pricing model to estimate the fair value of each option grant on the date of grant or any other measurement date. The following table sets forth the assumptions used to determine the fair value of stock options:

	Years Ended December 31,	
	2021	2020
Average expected term (years)	6.1	6
Expected stock price volatility	66.50% - 68.83%	59.57% - 67.02%
Risk-free interest rate	0.51% - 1.48%	0.28% - 1.76%
Dividend yield	—%	—%

The following table sets forth assumptions used to determine the fair value of the purchase rights issued under the ESPP:

	Years Ended December 31,	
	2021	2020
Average expected term (years)	1.2	1.2
Expected stock price volatility	61.13% - 86.50%	56.80% - 100.49%
Risk-free interest rate	0.06% - 0.20%	0.12% - 0.95%
Dividend yield	—%	—%

We use the closing price of our common stock on the date of grant to determine the fair value of RSUs.

Stock-Based Compensation Expense

Stock-based compensation expense is included in the consolidated statements of operations and comprehensive loss as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Cost of sales (exclusive of amortization of acquired intangible assets)	\$ 2,058	\$ 1,049
Research and development	4,522	1,492
Selling, general and administrative	15,160	5,768
Total stock-based compensation expense	<u>\$ 21,740</u>	<u>\$ 8,309</u>

For the years ended December 31, 2021 and 2020, the weighted-average grant date fair value of stock options was \$29.89 and \$28.95 per option, respectively, and the weighted-average grant date fair value of the purchase rights granted under the ESPP was \$27.60 and \$17.43 per share, respectively. As of December 31, 2021, the total unrecognized stock-based compensation cost related to outstanding awards was \$99,251,000, which is expected to be recognized on a straight-line basis over a weighted-average period of 3.3 years. The total unrecognized compensation cost will be adjusted for forfeitures in future periods as they occur. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2021 and 2020 was \$27,191,000 and \$18,377,000, respectively. The aggregate intrinsic value of shares issued under the ESPP was \$6,341,000 and \$1,797,000 during the years ended December 31, 2021 and 2020, respectively. The aggregate fair value of restricted stock units that vested during the year ended December 31, 2021 was \$2,698,000. No tax benefits related to stock-based compensation were recorded in the consolidated statements of operations and comprehensive loss during the years ended December 31, 2021 and 2020 due to the valuation allowance on net deferred tax assets.

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

15. Income Taxes

The components of income tax expense (benefit) are as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Current tax expense		
U.S. Federal	\$ —	\$ —
State and local	16	84
Total current	<u>16</u>	<u>84</u>
Deferred tax (benefit) expense		
U.S. Federal	(8,726)	—
State and local	(10)	—
Total deferred	<u>(8,736)</u>	<u>—</u>
Total income tax (benefit) expense	<u>\$ (8,720)</u>	<u>\$ 84</u>

The differences between income taxes expected at the U.S. federal statutory rate (21%) and the reported income tax expense (benefit) are summarized as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Pre-tax loss	\$ (40,012)	\$ (10,200)
U.S. federal taxes at statutory rate	(8,402)	(2,142)
State income taxes	(1,764)	(311)
Non-deductible meals	—	235
Research and development (“R&D”) tax credit	(1,658)	(703)
Change in valuation allowance	2,570	2,784
Stock-based compensation	(880)	(781)
Non-deductible officers’ compensation	1,571	963
Other	(157)	39
Total income tax (benefit) expense	<u>\$ (8,720)</u>	<u>\$ 84</u>

CASTLE BIOSCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Significant components of deferred tax assets and liabilities are as follows (in thousands):

	As of December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss (“NOL”) carryforwards	\$ 24,316	\$ 13,720
Accrued liabilities	4,168	2,730
Lease liabilities	2,114	—
Intangible assets	—	46
Stock-based compensation	2,202	761
R&D tax credit	3,670	1,777
Other	240	—
Total deferred tax assets	<u>36,710</u>	<u>19,034</u>
Less valuation allowance	<u>(17,774)</u>	<u>(15,204)</u>
Deferred tax assets, net	<u>\$ 18,936</u>	<u>\$ 3,830</u>
Deferred tax liabilities:		
Prepaid expenses	\$ (330)	\$ (289)
Property and equipment	(2,285)	(776)
Intangible assets	(12,913)	—
ROU assets	(2,166)	—
Section 481(a) adjustment (cash to accrual)	<u>(1,877)</u>	<u>(2,765)</u>
Total deferred tax liabilities	<u>(19,571)</u>	<u>(3,830)</u>
Net deferred tax asset (liability)	<u>\$ (635)</u>	<u>\$ —</u>

At December 31, 2021, we had NOL carryforwards for federal income tax purposes of approximately \$99,365,000 of which \$43,513,000 will begin to expire in 2030 if not utilized to offset taxable income, and \$55,852,000 may be carried forward indefinitely. Future changes in ownership, as defined by Section 382 of the IRC, could limit the amount of NOL carryforwards used in any one year. Also, as of December 31, 2021, we had state net operating loss carryforwards of approximately \$67,453,000, which begin to expire in 2028 if not utilized to offset state taxable income. Our R&D tax credit carryforwards of \$3,670,000 at December 31, 2021 will begin to expire in 2034 if not utilized to offset federal income tax.

In general, under Section 382 and 383 of the IRC, a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its pre-change NOLs and certain tax credits, to offset future taxable income and tax. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders changes by more than 50 percentage points over such stockholders’ lowest percentage of ownership during the testing period (generally three years). We performed a Section 382 analysis from inception through the year ended December 31, 2021 and concluded we had experienced an ownership change in 2011, 2014 and 2020. These changes in ownership did not result in the expiration of any NOLs or R&D credits. However, future changes in ownership may further limit the ability of us to utilize our NOL carryforwards and R&D tax credit carryforwards.

During the year ended December 31, 2021, in connection with the acquisition of Cernostics, we recorded additional net deferred tax liabilities of \$9,371,000, primarily due to book-tax differences related to the acquired intangible assets. As a result of these additional deferred tax liabilities, we determined that \$8,726,000 of our existing valuation allowance should be reduced, which was reflected in our income tax benefit for the year ended December 31, 2021. At December 31, 2021 and 2020, we placed a valuation allowance of \$17,774,000 and \$15,204,000, respectively, against our net deferred tax asset balances, as we have determined that it is more likely than not that they will not be realized.

We assessed whether we had any significant uncertain tax positions related to open tax years and concluded there were none. Accordingly, no reserve for uncertain tax positions has been recorded as of December 31, 2021 and 2020. We are generally no longer subject to tax examinations for U.S. federal income tax purposes for fiscal years prior to 2018 and fiscal years prior to 2017 for multiple state jurisdictions. However, since we have been in an NOL position since 2008, our 2008 to 2017 federal tax returns and our 2008 to 2016 state tax returns are potentially subject to examination adjustments to the extent of those NOL carryforwards.

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STOCKHOLDER INFORMATION

Corporate Offices

Castle Biosciences, Inc.
505 S. Friendswood Drive, Suite 401
Friendswood, Texas 77546
866.788.9007

Annual Meeting of Stockholders

June 2, 2022, at 11:00 a.m. (local time)
The San Luis Resort, Spa and Conference Center
5222 Seawall Boulevard
Galveston, Texas 77551

Independent Registered Public Accounting Firm

KPMG LLP
San Diego, California

Transfer Agent

Broadridge Corporate Issuer Solutions, Inc.
P.O. Box 1342
Brentwood, New York 11717
877.830.4936
shareholder@broadridge.com

Investor Contact

Camilla Zuckero
Vice President, Investor Relations & Corporate Affairs
czuckero@castlebiosciences.com

Exchange

Our common stock is traded on The Nasdaq Global Market under the ticker symbol "CSTL".

Note on Forward-Looking Statements

This annual report contains forward-looking statements within the meaning of the federal securities laws. Actual results could differ materially from those implied by any forward-looking statements. See the section titled "Special Note Regarding Forward-Looking Statements" in our 2021 Annual Report on Form 10-K for additional information. We disclaim any intent or obligation to update these forward-looking statements, and you should not unduly rely on them.

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Derek J. Maetzold

*Founder, President, CEO, and Director
Castle Biosciences, Inc.*

EXECUTIVE OFFICERS

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Founder, President, CEO, and Director

Tobin W. Juvenal

Chief Commercial Officer

Kristen M. Oelschlager, R.N.

Chief Operating Officer

Frank Stokes

Chief Financial Officer



For more information, please visit:
CastleBiosciences.com

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