Annual Report 2022

CASTLE BIOSCIENCES

Letter from Our CEO

DEAR FELLOW STOCKHOLDERS,

2022 was a year of significant growth and success for Castle, driven by strong execution and our steadfast commitment to improve patient care through our innovative, actionable tests.

▲46%	▲58%	198	81%
REVENUE	DELIVERED TEST REPORTS	NEW EMPLOYEES WELCOMED	EMPLOYEE ENGAGEMENT

2022 FINANCIAL AND OPERATIONAL HIGHLIGHTS

In 2022, we delivered strong year-over-year growth in revenue and test report volume, reflecting solid execution by our Castle team. Our full-year 2022 revenue increased by 46% over 2021 to $137 million, meeting the top end of our guided range. With commercial team expansions in both our Dermatology and Gastroenterology franchises and consistent execution of our sales objectives, we delivered 44,419 total test reports in 2022, an increase of 58% compared to 2021. Additionally, in 2022, we saw strong provider growth and continued adoption with 2,312 new ordering clinicians and 7,670 total ordering clinicians for our dermatologic tests.

KEY SUCCESSES WITHIN OUR FOUNDATIONAL GUIDEPOSTS

At our Investor Day in late September, we highlighted three foundational guideposts – Exceptional Employees, Continuous Evolution & Improvement and Customer & Solution Centric. These guideposts are grounded in our Mission, Vision and Values and guide how we operate our business. As I reflect on our accomplishments in 2022, I would like to celebrate a few highlights within each of these core areas from our many successes over the past year.

Exceptional Employees

Building our Castle team: Over the course of 2022, we welcomed 198 new individuals to the Castle family to help support our growing businesss – new team members with unique perspectives and strengths that we believe will help us continue to excel in the years to come.

Maintaining a strong culture: We are proud of the culture we have created at Castle, built on our values of excitement, collaboration, integrity, innovation, trust and excellence. In our annual employee engagement survey in June of 2022, we achieved an engagement score of 81%, compared to the benchmark average of only 53% for healthcare companies participating in the Top Workplaces program. Our engagement score indicates that 81% of Castle employees reported they are "engaged" or "highly engaged," suggesting they are motivated to deliver their best work, stay with Castle and recruit others to join the company. As a result of our strong engagement scores, Castle was named a Top Workplace in Arizona, Houston and the USA over the course of last year. We believe we have created something special at Castle and are committed to maintaining it.

Continuous Evolution & Improvement

NCI/SEER collaboration: Last year, we announced a collaboration with the National Cancer Institute (NCI) to link DecisionDx®-Melanoma testing data with data from the Surveillance, Epidemiology and End Results (SEER) Program's registries on cutaneous melanoma (CM) cases. Through the collaboration, patients who received DecisionDx-Melanoma test reports were linked to those who were entered into the SEER registries' database and had associated survival outcomes, using a third-party Honest Broker for the SEER registries. In the study, patients tested with DecisionDx-Melanoma had improved survival compared to untested patients, with a 27% (hazard ratio (HR)=0.73, p=0.028) and 21% (HR=0.79, p=0.006) Melanoma Specific Survival and Overall Survival benefit, respectively. These data provided direct evidence that the test's results have the potential to improve patient survival when used as part of a melanoma management plan.

Growing our body of clinical evidence: We are a leader in the field of molecular diagnostics by challenging the status quo with deep scientific expertise, unique value insight and strong data development. In 2022, we made great strides in demonstrating our tests' potential to transform how diseases are managed through the publication of 14 peer-reviewed studies across our innovative test portfolio and through our ongoing, robust clinical research efforts.

Customer & Solution Centric

Opportunities to impact patient care in new areas of unmet clinical need: Over the course of 2022, we made significant progress in developing our two newest franchises – Gastroenterology with our TissueCypher® Barrett's Esophagus test, and Mental Health with our IDgenetix® test. We believe the growth and early success we have seen in both of these franchises sets us up well for future progress in 2023 and beyond.

I am humbled by the drive and passion of our talented Castle team, who are dedicated to our mission of improving health through innovative tests that guide patient care. I believe it is their commitment to execution of our strategy and patient care that drove our successes in 2022. As we look ahead, we remain focused on value creation, which we expect to be powered by our ongoing momentum and steady steps toward achieving our vision of transforming disease management. On behalf of all of us at Castle, thank you for your ongoing support. We are excited about what is to come.

Sincerely,

DEREK J. MAETZOLD
Founder, President and CEO

"I am humbled by the drive and passion of our talented Castle team, who are dedicated to our mission of improving health through innovative tests that guide patient care."

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, 2022

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	**77-0701774**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
505 S. Friendswood Drive, Suite 401, Friendswood, Texas	**77546**
(Address of principal executive offices)	(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	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

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

Indicate by check mark whether the registrant 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. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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, 2022 (the last business day of the registrant’s most recently completed second fiscal quarter) was $472 million based on the closing price of the registrant’s common stock on June 30, 2022, as reported by the Nasdaq Global Market.

As of February 21, 2023, there were 26,575,616 shares of common stock, $0.001 par value per share, 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 2023 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, 2022.

Table of Contents

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 ("TAM"), future revenue and addressable patient populations, 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 geopolitical and macroeconomic developments, such as the ongoing conflict between Ukraine and Russia, related sanctions and 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, introducing our products to new customers, addressing areas of high clinical need or reducing healthcare costs;
- 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."

Risks Related to our Financial Condition

- A significant portion of our revenue comes from a small number of third-party payors.
- Due to how we recognize revenue, our quarterly and annual revenues 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 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.
- 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.
- We may need to raise additional capital to fund our existing operations, commercialize new products, or expand our operations.

Risks Related to our Business

- 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.
- Unfavorable U.S. and global economic conditions could adversely affect our business, financial condition, results of operations or cash flows.
- Public health crises, such as pandemics or similar outbreaks, could adversely impact our business.
- Billing for our products is complex and requires substantial time and resources to collect payment.
- We rely on third parties for sample collection, preparation and delivery.
- We rely on our database of samples for some of the development and improvement of our products. Depletion or loss of our samples 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 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 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.
- The sizes of the TAM 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 generally have limited reimbursement coverage for our products, 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 federal, state and foreign laboratory licensing requirements including those established by the Centers for Medicare and Medicaid ("CMS") and the applicable requirements of the U.S. Food and Drug Administration ("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.
- 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.
- 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 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.

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.
- Product or professional liability lawsuits against us could cause us to incur substantial liabilities and could limit our commercialization of our products.
- Our business could be adversely affected by natural disasters, public health epidemics and other events beyond our control.

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.
- We have and may continue to enter into related party transactions that create conflicts of interest, or the appearance of conflicts of interest, which 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.

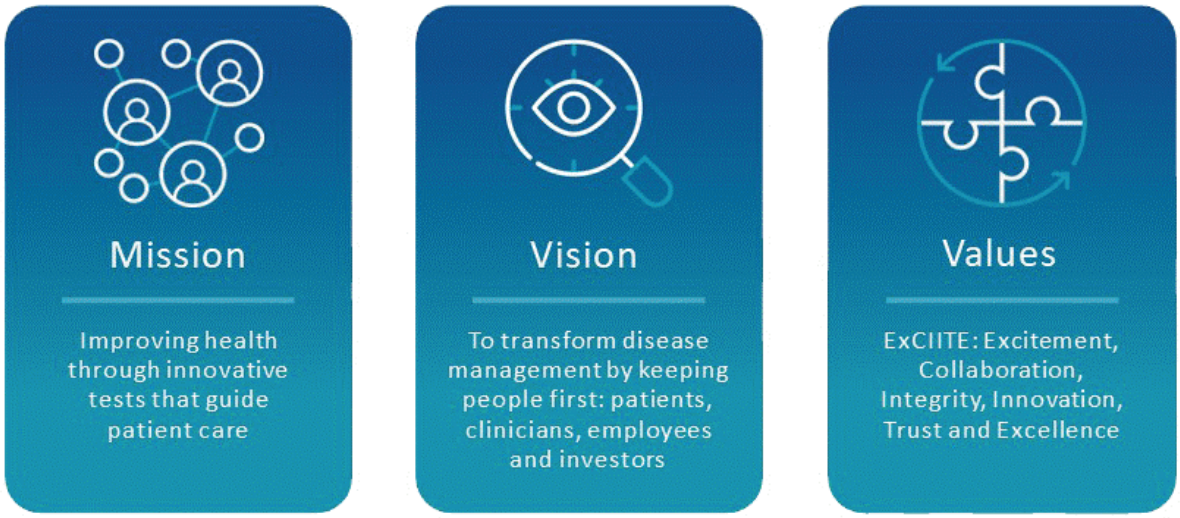
PART I

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.

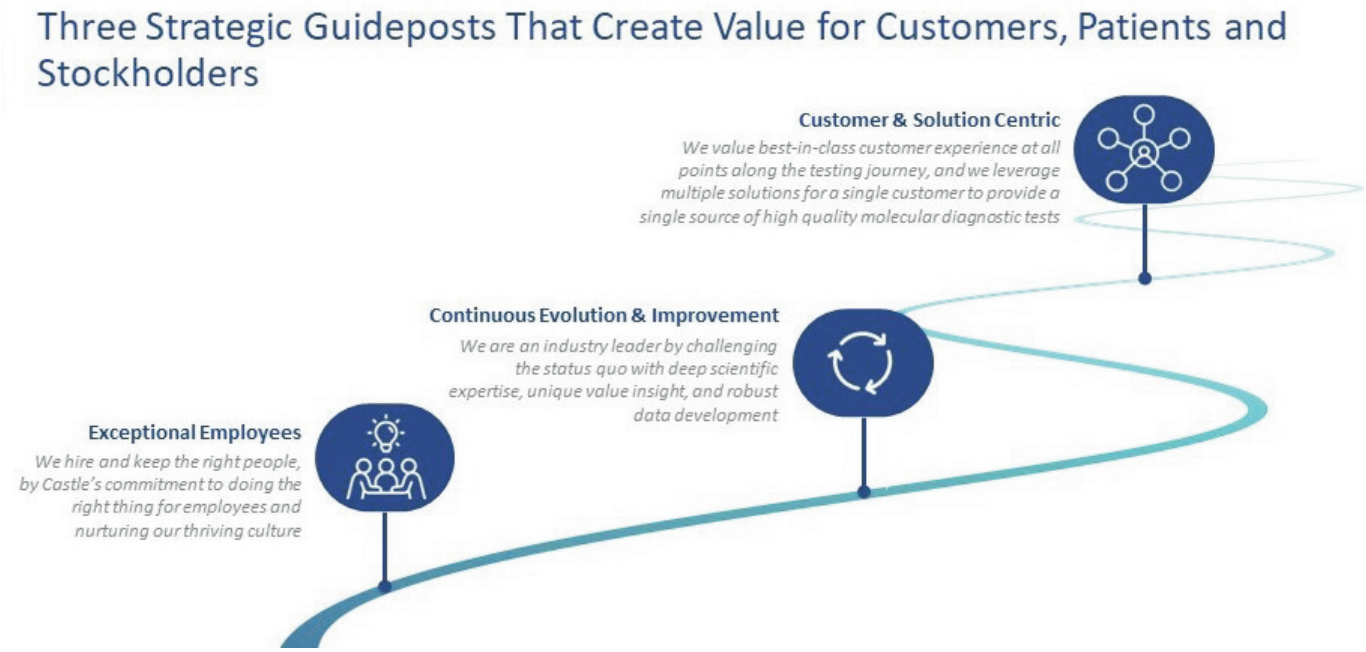
Overview

Castle Biosciences is applying innovative diagnostics to inform disease management and improve patient outcomes. 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 (or risk stratification) 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.

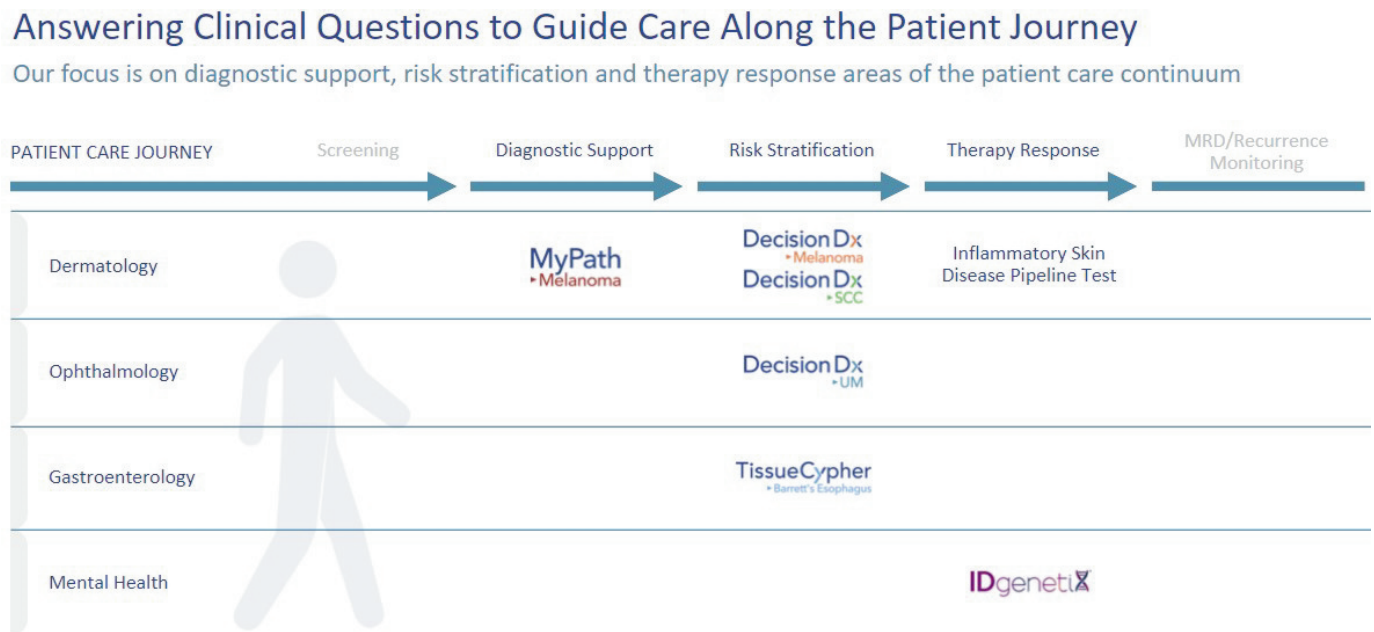


We have three strategic guideposts that create value for customers, patients and stockholders:

Exceptional Employees - We hire and keep the right people, by Castle's commitment to doing the right thing for employees and nurturing our thriving culture.

Continuous Evolution & Improvement - We are an industry leader by challenging the status quo with deep scientific expertise, unique value insight and robust data development.

Customer & Solution Centric - We value best-in-class customer experience at all points along the testing journey, and we leverage multiple solutions for a single customer to provide a single source of high quality molecular diagnostic tests.



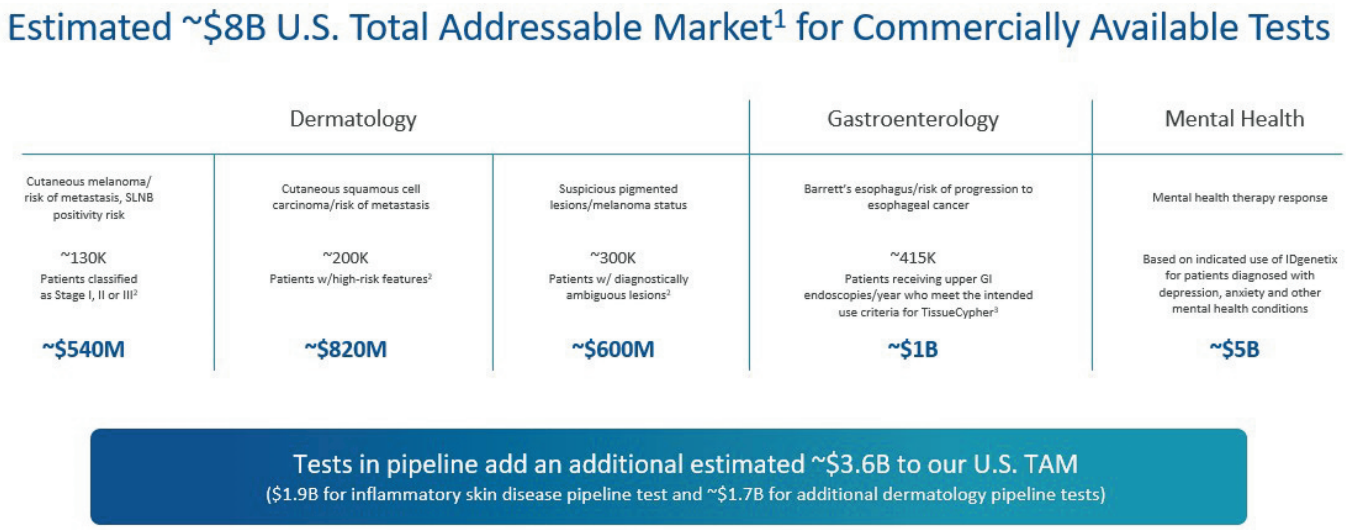
Our Test Portfolio

Currently, our revenue is primarily generated by our DecisionDx-Melanoma risk stratification test for cutaneous melanoma, although each of our other commercial tests do contribute to our overall revenue. We map out the patient journey 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 the following areas along the patient journey: providing diagnostic clarity in patients with signs or symptoms of disease, risk stratification and response to treatment. We have seven commercially available proprietary tests that assist clinicians and patients along this continuum.

Our commercially available proprietary tests focus on answering clinical questions arising during the treatment of:

- Dermatologic cancers—DecisionDx-Melanoma, DecisionDx®-SCC, MyPath® Melanoma and DiffDx®-Melanoma
- Uveal melanoma ("UM")—DecisionDx®-UM
- Barrett's esophagus ("BE")—TissueCypher® Barrett's Esophagus Test
- Mental health conditions—IDgenetix®

Together, we believe these commercial products support an estimated TAM of $8.0 billion in the United States.



1) U.S. TAM based on estimated patient population assuming average reimbursement rate among all payors.

2) 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.

3) 415,000 upper GI endoscopies/year with confirmed dx of BE (ND, IND, LGD, EXCLUDING HGD) x $2,513 = U.S. only TAM of ~$1 billion.

In 2022, we developed expanded evidence supporting portfolio of innovative tests through the acceptance/ publication of 14 peer-reviewed studies across all franchises. As of December 2022, over 100 peer-reviewed articles have been published demonstrating the analytical validity, clinical validity and clinical utility of our tests.

The primary source of revenue for our products is reimbursement from third-party payors, which includes government payors, such as Medicare, and commercial payors, such as insurance companies. We currently have Medicare coverage for DecisionDx-Melanoma, DecisionDx-SCC, MyPath Melanoma, DecisionDx-UM, TissueCypher and IDgenetix. 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. For further detail, see "—Reimbursement" below.

Commercial Launches

We launched DecisionDx-UM in January 2010, a proprietary, risk stratification gene expression profile ("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. Based on the substantial clinical evidence that we have developed, we have received Medicare coverage for DecisionDx-UM, and we believe patients 65 years of age and older represents approximately 45% of the addressable patient population for this test. We estimate approximately 2,000 patients in the United States are diagnosed annually with UM.

We launched DecisionDx-Melanoma in May 2013, a proprietary risk stratification GEP test that predicts the risk of metastasis or recurrence for patients diagnosed with invasive cutaneous melanoma. 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 clinicians 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. Based on the substantial clinical evidence that we have developed, we have received Medicare coverage for DecisionDx-Melanoma which we believe represents approximately 50% of the addressable patient population for this test.

We commercially launched DecisionDx-SCC in August 2020, our cutaneous squamous cell carcinoma ("SCC") proprietary risk stratification GEP test, for use in patients with one or more risk factors (also referred to as "high-risk" SCC). We commercially launched DiffDx-Melanoma in November 2020, our proprietary GEP test for use in patients with difficult-to-diagnose melanocytic lesions, meaning there is uncertainty related to the malignancy of the biopsied lesion. We believe that these two 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.

Acquisitions

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.

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 DiffDx-Melanoma test. Initially, we offered both our MyPath Melanoma test and our DiffDx-Melanoma test under an offering that we referred to as our Diagnostic GEP offering to leverage the strength of both tests. Our internal data indicates that we have improved the technical performance of MyPath Melanoma such that it is now comparable to the technical performance of DiffDx-Melanoma. As such, following an internal assessment of the clinical value of offering both tests, we made the decision to suspend the clinical offering of DiffDx-Melanoma in February 2023.

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, for total consideration of $49.0 million, consisting of cash consideration of $30.7 million and contingent consideration with an acquisition date fair value of $18.3 million. 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 ("HGD") and/or esophageal cancer in patients with non-dysplastic ("ND"), indefinite dysplasia ("IND") or low-grade dysplasia ("LGD") 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.

In April 2022, we completed our acquisition of AltheaDx, Inc. ("AltheaDx"), a commercial-stage molecular diagnostics company specializing in the field of pharmacogenomic ("PGx") testing services that are focused on certain mental health diagnoses, and the provider of IDgenetix, a PGx test for mental health conditions, for a total consideration of $47.6 million, consisting of cash consideration of $30.5 million and equity consideration of $17.1 million. Traditional PGx tests focus on drug-gene interactions where our IDgenetix test also incorporates drug-drug interactions and lifestyle factors into the final patient report, which we believe offers additional value to clinicians and patients. This acquisition enabled us to offer a testing solution that we believe has the potential to accelerate our impact on patient care in an area of high unmet clinical need, significantly expanded our in-market estimated U.S. TAM by approximately $5 billion and offer incremental value to patients and clinicians over the standard of care trial-and-error approach. A randomized controlled trial showed that patients diagnosed with depression, who were

assessed with the IDgenetix test, showed a 2.5 times improvement in remission rates compared to those who did not have their genes tested.

Pipeline Initiatives

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 ended 2022 with more than 50 active clinical study sites, exceeding our initial target. 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 pipeline 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.

Test Report Volume and Revenue

The number of test reports we generate is a key indicator that we use to assess our business. The numbers of test reports delivered by us and our net revenues during the past five years are presented in the table below:

	Years Ended December 31,				
	2022	2021	2020	2019	2018
DecisionDx-Melanoma	27,803	20,328	16,232	15,529	12,032
DecisionDx-SCC[1]	5,967	3,510	485	—	—
Diagnostic GEP offering[2]	3,561	2,662	73	—	—
Dermatologic Total	37,331	26,500	16,790	15,529	12,032
DecisionDx-UM	1,711	1,618	1,395	1,526	1,413
TissueCypher Barrett's Esophagus Test[3]	2,128	27	—	—	—
IDgenetix[4]	3,249	—	—	—	—
Grand Total	44,419	28,145	18,185	17,055	13,445
Net Revenues (in thousands)	$ 137,039	$ 94,085	$ 62,649	$ 51,865	$ 22,786

(1) On August 31, 2020, we commercially launched our cutaneous SCC proprietary GEP test for use in patients with one or more risk factors.

(2) Includes MyPath Melanoma and DiffDx-Melanoma. On November 2, 2020, we commercially launched our DiffDx-Melanoma test. We began offering MyPath Melanoma following our acquisition of the Myriad MyPath Laboratory on May 28, 2021. We offered both MyPath Melanoma and DiffDx-Melanoma under our Diagnostic GEP offering until February 2023 when we suspended the clinical offering of DiffDx-Melanoma, as discussed above.

(3) We began offering the TissueCypher Barrett's Esophagus Test on December 3, 2021, following the completion of our acquisition of Cernostics.

(4) We began offering the IDgenetix test on April 26, 2022, following our acquisition of AltheaDx. Includes both single-gene and multi-gene tests.

Our Markets Overview

Our current test portfolio serves the markets for dermatologic cancers, UM, BE and mental health conditions. The sections that follow provide an overview of each of these markets.

Dermatologic Market Overview

The foundation of our business is our dermatologic cancer franchise, and our lead product is DecisionDx-Melanoma. DecisionDx-Melanoma is a proprietary 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 SLN negative biopsy result so that clinicians 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. 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.

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, which may give rise to SCC.

Cutaneous Melanoma

Melanoma is a malignancy of the pigment-producing melanocytes in the basal layer of the epidermis and is growing in incidence in the United States. Published statistics suggest that there were nearly 300,000 new cases of melanoma diagnosed worldwide, and an estimated annual incidence of 130,000 in the United States, representing an estimated U.S. TAM of $540 million. This estimated annual incidence number is based upon a calculation using data from the U.S. Surveillance, Epidemiology, and End Results ("SEER") registries and subsequently adjusted for the documented underreporting of melanoma diagnoses which range from 30%-72%. Based on currently available data, we estimate the targetable clinician base treating melanoma is between 11,000 and 15,000.

After a diagnosis of invasive cutaneous melanoma, healthcare providers have traditionally relied solely on clinical and pathological 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 based on thickness of tumor (Breslow thickness), presence of ulceration, and presence of regional or distant disease spread.

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.

Guideline committees base recommendations for the invasive SLNB surgery on an estimated risk of the likelihood of positivity determined by Breslow thickness and ulceration and the presence of certain adverse pathologic features, such as high mitotic rate or transected base. If the likelihood of a positive SLN result is less than 5%, SLNB surgery is not recommended. If the likelihood of a positive SLN result falls between 5% and 10%, then consideration of an SLNB surgery is recommended, and if the likelihood exceed 10%, then discussing and offering SLNB surgery is recommended. 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). Clinicopathologic staging factors provide an imprecise population-based estimation of risk of SLN positivity and do not evaluate nor incorporate the biology of the patient's primary tissue biology. A positive SLN biopsy result, meaning that at least one melanoma cell was seen in the SLN tissue, leads to re-staging the patient from stage I or II to stage III, indicating regional spread of disease.

Importantly, the National Cancer Institute (the "NCI") recently completed 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 compared to those who merely underwent observation, indicating that SLNB surgery is prognostic, and not therapeutic.

On average, 12% of patients undergoing the SLNB surgery will have an SLN-positive biopsy result, indicating that 88% of patients will not derive clinical benefit from the procedure. The 88% SLN-negative rate in these surgeries carries significant patient and healthcare system implications. 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 clinicians should either consider (5%) or offer (10%) the procedure to their patients. The SLNB surgery requires the use of general anesthesia leading to an average reimbursed cost of $20,000 to $24,000. Thus, patients undergoing SLNB surgery are exposed to the complications from surgery, including general anesthesia risks, high medical costs and a median false negative rate of 18%.

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). While Stage I and II patients have a lower population-based estimated risk of melanoma specific death, due to the higher incidence of these 'lower risk' stage groups, these lower risk stages 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 III patients is 77% without any intervention. 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 immune-oncology 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.

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 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 clinicians. 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 Eighth Edition staging system 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 Seventh Edition staging system 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 clinicians 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 for DecisionDx-SCC

included 321 patients, of which 93% had one or more high-risk features. Within this study cohort, 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 clinician 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.

Difficult-to-Diagnose Melanocytic Lesions

Difficult-to-diagnose melanocytic lesions are pigmented 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 clinician 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 were benign, the recommendation in the majority of cases would be no additional intervention. Thus, the tendency of clinicians to treat an indeterminate diagnosis as melanoma leads to significant over-treatment decisions, complications and increased healthcare costs.

MyPath Melanoma and DiffDx-Melanoma are independent GEP tests that together comprised Castle's Diagnostic GEP offering of molecular testing solutions for difficult-to-diagnose melanocytic lesions, representing an estimated U.S. TAM of $600 million. Our internal data indicates that we have improved the technical performance of MyPath Melanoma such that it is now comparable to the technical performance of DiffDx-Melanoma. As such, following an internal assessment of the clinical value of offering both tests, we made the decision to suspend the clinical offering of DiffDx-Melanoma in February 2023.

Uveal Melanoma Market Overview

The incidence of UM has remained relatively constant over time with approximately 2,000 patients diagnosed annually in the United States, representing an estimated U.S. TAM of $9.3 million. UM 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. UM may also be referred to as ocular melanoma.

Approximately 97% of patients with UM 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 UM 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 UM. 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 UM tumors.

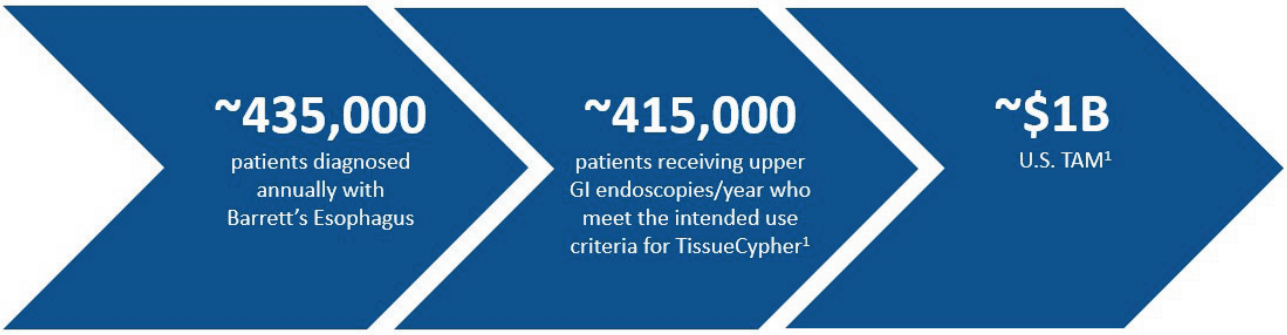
Barrett's Esophagus Market Overview

Barrett's esophagus is a protective response to chronic acid reflex resulting in the replacement of normal esophageal squamous mucosa with specialized intestinal metaplasia that is more resistant to acidic environments and is the only known precursor to esophageal adenocarcinoma ("EAC"), which is one of the fastest increasing

cancers in incidence in the United States with a five-year survival rate of approximately 20%. There are approximately 4 million patients in the U.S. currently diagnosed with BE and approximately 435,000 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 Test, which we acquired through our acquisition of Cernostics on December 3, 2021.

Patients with BE symptoms undergo an endoscopic biopsy procedure to both visualize lesions that may be present in a patient's esophagus as well as collect one or more biopsy specimens. These biopsy specimens serve as the diagnostic specimens to determine if the patient has BE, perhaps esophageal cancer, another disease or no diagnosed disease. The extent of BE dysplasia, which represents the extent of abnormality detected in the tissue that may precede development of cancer, is graded by the pathologist as either non-dysplastic ("NDBE"), IND, LGD or HGD. Treatment plans for BE are risk stratified according to these grades. Patients with HGD and many LGD patients receive esophageal eradication therapy with the intent of eliminating the BE lesion. They may also receive varying levels of repeat endoscopic biopsy procedures, which can occur at frequent or less frequent intervals, with the goal of detecting progression to HGD or EAC.

Similar to the staging limitations that are seen in cutaneous melanoma, at least half of the patients who progress to HGD or esophageal cancer are originally diagnosed as ND or IND patients at lower risk for disease progression based on pathological assessment alone due to the high relative incidence of ND/IND diagnoses relative to LGD/HGD diagnoses. This highlights the poor sensitivity of diagnosis by histology in predicting progression and inadequacy of surveillance to detect progression in patients originally diagnosed with low-risk NDBE. Thus, improvement is needed in the assessment of the risk of progression in patients with Barrett's esophagus to better inform risk-aligned treatment plans.



1. 415,000 upper GI endoscopies/year with confirmed dx of BE (ND, IND, LGD, excluding HGD) x $2,513 = U.S. only TAM of ~$1 billion.

Mental Health Market Overview

Finding an optimal medication for patients diagnosed with a mental illness has traditionally relied on trial and error, often times resulting in inadequate therapy response, low remission rates, and a high rate of adverse drug events. Using current standard-of-care treatment approaches, less than half of patients with major depressive disorder achieve an adequate response to first line treatment and nearly 3 of 4 do not achieve remission. There is a high prevalence of adverse drug events and increasing rates of discontinuation with repeated medication trials. This frustration has led to a need in the mental health community for more personalized care with selection of an optimal therapy the first time, achieving a fast response/remission with few to no side effects and at a low out of pocket cost. For the approximately 50 million patients experiencing mental health illness in the United States, meeting these expectations could require a new approach to medication selection. PGx can help improve medication selection and avoid the need for multiple medication trials. A traditional PGx test is designed to assess a patient's DNA to identify variances that result in drug-gene interactions. These interactions can lead to variation in medication responses by altering drug metabolism or impacting how the body responds to a drug. In addition to drug-gene interactions, our IDgenetix test also incorporates drug-drug interactions and lifestyle factors into the final patient report, which we believe offers additional value to clinicians and patients.

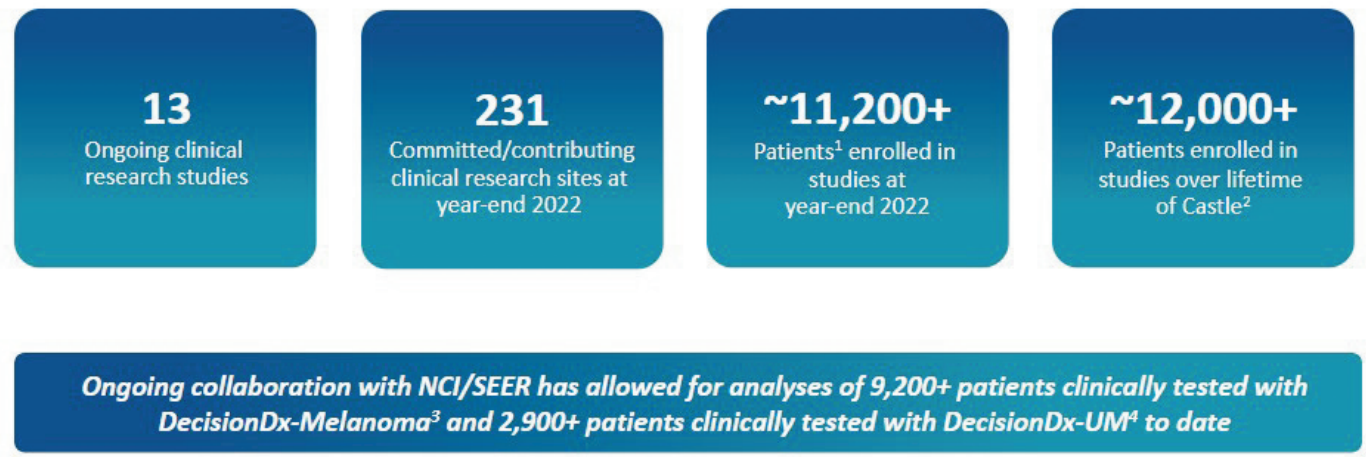
Our Testing Solutions

We use multi-analyte assays with algorithmic analysis ("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 clinician 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 clinician adoption, reimbursement success and guideline inclusion.

We currently offer five proprietary MAAA tests for use in the dermatologic, ocular and gastroenterology fields: DecisionDx-Melanoma, DecisionDx-SCC, MyPath Melanoma, DecisionDx-UM and TissueCypher. We also offer our proprietary PGx test, IDgenetix, to guide optimal drug treatment for patients diagnosed with depression, anxiety and other mental health conditions. The accuracy of each product in our portfolio is typically supported by multiple studies published in peer-reviewed journals following completion of the initial clinical validation studies. Also, multiple clinical impact studies have demonstrated a significant impact on clinician 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-SCC, DecisionDx-UM, TissueCypher, MyPath Melanoma and IDgenetix 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 140,000 clinical patient samples across our product portfolio.

Significant Scientific Evidence Through Robust Clinical Research Program Across Our Testing Portfolio



Data as of Dec. 31, 2022

1. One TissueCypher study involves patients and ~250 physicians. 2. Number reflects studies that span Castle's dermatology, ophthalmology and gastroenterology portfolios. 3. SEER cancer registries linked CM cases diagnosed from 2013-2018 to data for patients with stage I-III CM tested with the 31-GEP as of Dec. 31, 2022; includes patients in studies not yet published. 4. SEER cancer registries linked UM cases diagnosed in 2018 for patients with primary uveal melanoma tested with the 15-GEP; includes patients in studies not yet published.

Our products are designed to provide the following benefits:

- ***Clinically Actionable Information for Clinicians.*** Our commercial tests provide clinicians 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 GEP 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. Clinicians 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 clinicians 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

DecisionDx-MELANOMA

Overview

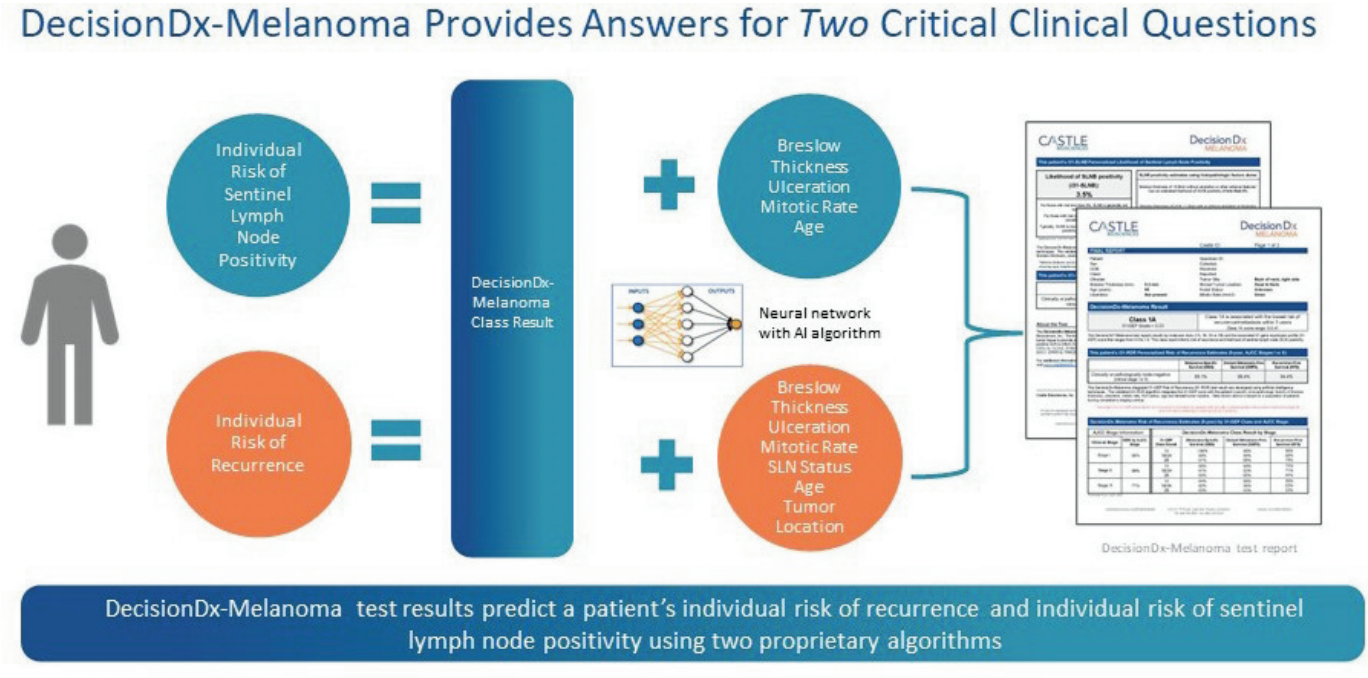
DecisionDx-Melanoma is our proprietary risk stratification GEP test developed to identify the risk of metastasis, or recurrence, for patients diagnosed with invasive cutaneous melanoma, a deadly skin cancer. Under the traditional staging methods, patients with melanoma are classified into low or and high-risk categories based on population-wide clinical and pathology features, and risk of recurrence guides a clinician's treatment plan recommendations about whether or not to offer invasive SLNB surgery, frequency and use of clinical imaging and follow-up, and/or consider referral for adjuvant therapy.

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. 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 identify tumors at high risk for metastasis from patients receiving a Stage I, II or III diagnosis. DecisionDx-Melanoma is administered from the formalin-fixed, paraffin embedded biopsy or wide local excision tissue used to diagnose and stage melanoma and assesses the expression of 31 genes to result in classification of metastatic risk as Class 1A (lowest risk), Class 1B/2A (increased risk) and Class 2B (highest risk). DecisionDx-Melanoma has been validated to provide additional information on a patient's risk of metastasis not obtainable from staging alone and can improve the accuracy of risk stratification beyond traditional staging approaches. The results of the test have been incorporated into clinical practice to inform important decisions about recommendation for invasive SLNB surgery, use of advanced imaging for active surveillance, and frequency and specialty for clinical follow-up. As of February 28, 2023, we have received orders from more than 11,200 clinicians for an aggregate of more than 120,000 tests.

In March 2021, we announced that DecisionDx-Melanoma utilizes an Integrated Test Result ("ITR"), designed to provide more precise risk stratification for patients with Stage I, II or III melanoma. The ITR uses an independently validated algorithm ("i31-SLNB") that integrates the DecisionDx-Melanoma continuous score with clinical and pathological features, including Breslow thickness, ulceration, mitotic rate and age 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 with Breslow thickness, ulceration, mitotic rate, SLN status, age and tumor location to provide a prediction of an individual patient's risk of metastasis and recurrence ("i31-ROR"). This new i31-ROR algorithm includes the additional endpoints of recurrence-free survival ("RFS") and distant metastasis-free survival, which are not currently provided by the AJCC 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-ROR algorithm guide discussions and recommendations, within current risk-based guidelines, for the SLNB surgical procedure or for surveillance methodologies.



Two intended uses for DecisionDx-Melanoma

Source: Whitman et al. JCO PO 2021; Jarell et al. JAAD 2022.

In 2021, we initiated a collaboration with the NCI to link SEER Program registries' data on cutaneous melanoma cases with DecisionDx-Melanoma testing data. Data from this large, real-world and unselected patient population found that when controlling for clinicopathologic as well as socioeconomic factors, patients who received DecisionDx-Melanoma as part of their clinical care had improved melanoma-specific survival compared to patients who did not have the DecisionDx-Melanoma test as part of their clinical care. 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 2023. 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 in the first half of 2023 and beyond.

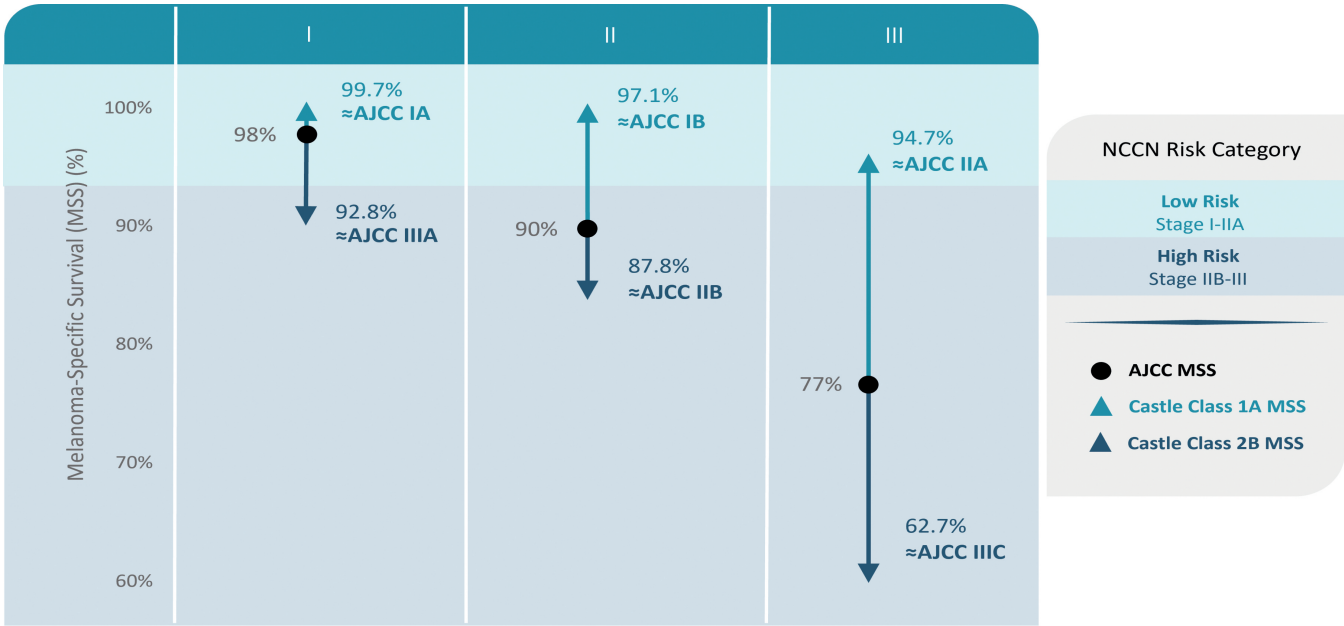
Clinical Validation

More than 40 peer-reviewed articles have been published demonstrating the analytical validity, clinical validity and clinical utility of DecisionDx-Melanoma. We believe the clinical validation studies represent the largest clinical validation program of the metastatic risk of cutaneous melanoma ever conducted. In 2022, we developed expanded evidence supporting DecisionDx-Melanoma through the acceptance/publication of seven peer-reviewed studies. Based on our published data, we have shown that DecisionDx-Melanoma is an accurate, independent predictor of the risk of metastasis or recurrence.

Across multiple validation studies including more than 10,000 patients, DecisionDx-Melanoma has demonstrated improved prognostication of recurrence, distant metastasis, and melanoma-related death independent of traditional clinical and pathological factors defined by the AJCC and NCCN and clinical utility in improving risk-aligned management, indicating the test adds information and can be used as an adjunct to AJCC staging to further risk stratify within stages. DecisionDx-Melanoma has over 70% sensitivity for predicting distant metastasis and death, even in node-negative (Stage I-II) patients. Moreover, a low-risk Class 1A result is associated with excellent survival outcomes (~99% melanoma-free survival). Our long-term outcomes 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. Within patients diagnosed with Stage I melanoma, a DecisionDx-Melanoma high-risk Class 2B result 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 low-risk Class 1A results

indicate a 99.7% likelihood of survival from melanoma at five years. Within patients diagnosed with Stage II melanoma, a high-risk Class 2B result is associated with a higher risk of death from melanoma that is similar to a patient with Stage IIB melanoma, whereas a low-risk Class 1A result can identify patients who have a very low risk of death from melanoma (>97.1% likelihood of survival at 5-years). Within patients diagnosed with Stage III melanoma, high-risk Class 2B results can identify patients who have a risk of death from melanoma similar to a patient with Stage IIIC melanoma, whereas a low-risk Class 1A likelihood of death from melanoma is similar to a patient with Stage IIA 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.



Wisco et al. *Melanoma Research* 2021; n=911

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 1A test result. An update to this study published in 2021 that included long-term outcomes of these patients demonstrated consistent findings, with patients with a Class 1A result maintaining significantly improved survival outcomes over patients with Class 2B results. Moreover, this study demonstrated that patients diagnosed with early stage I-IIA disease that received a Class 2B result had risk of recurrence and death from melanoma similar to that of patients with stage IIB-III disease for whom NCCN guidelines recommend increased intensity of management, indicating the level of risk associated with a high-risk result is meaningful and actionable. A total of 8 publications from 6 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.

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-GEP 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 clinicians 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 six clinical utility studies 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	Results
Yamamoto et al. CMRO 2023	Prospective, multi-center study evaluating impact of GEP and clinical and pathological features in impacting decision to perform SLNB	193	85% of decisions relating to SLNB performance were influenced by test results
Dillon et al. CMRO 2022	Long term follow-up of prospective, multi-center study evaluating pre-test and post-test management.	509	51% of patients had a change in management
Berger et al. CMRO 2016	Prospectively tested cohort, multi-center. Retrospective pre-test / post-test management.	156	53% of patients had a change in management
Dillon et al. SKIN J Cutan Med 2018	Prospective, multi-center: evaluating pre-test / post-test management.	247	49% of patients had a change in management
Farberg et al. J Drugs Derm 2017	169 physician impact study: patient vignettes with pre-test / post-test management.	n/a	47-50% of patients had a change in management
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% of patients had a change in management

In 2022, additional follow-up from a prospective, multi-center study evaluated 5-year management plan changes for lab work, frequency of clinical visits and imaging in 509 patients pre- and post-31-GEP results. After receiving results, 51% of patients had a change in management plans in clinical visits, lab work or surveillance imaging. The changes were risk-aligned with GEP result in 76.1% of Class 1 results and 79% of Class 2 results. In early 2023, a publication of a prospective, multi-center study evaluating the impact of DecisionDx-Melanoma to guide SLNB decisions showed the test influenced 52% of clinical decisions to forego SLNB and 33% of decisions to perform SLNB. Compared to the baseline rate of SLNB performance in a contemporary cohort, there were 29% less SLNB procedures performed in patients with a Class 1A result.

Building on our clinical utility evidence, in October 2020, the publication in Future Oncology of a retrospective study, titled “Integrating the melanoma 31-GEP 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 clinicians 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. From 2020 – 2022, three independent expert physician panels published consensus guidelines on incorporation of the DecisionDx-Melanoma test into clinical practice based on this evidence.

Health Economics

We believe our products have the potential to reduce overall healthcare costs by enabling clinicians 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

DecisionDx-SCC has been validated to improve prediction for the risk of metastasis in patients with cutaneous SCC and one or more risk factors, as identified by clinical and pathological staging criteria. The current staging systems that rely on a combination of clinical or pathological factors to stage or classify risk of metastasis suffer from a low PPV for risk of metastasis. 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-GEP 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. 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 clinicians and patients.

We commercially launched DecisionDx-SCC on August 31, 2020. Fourteen peer-reviewed publications support the analytic validity, clinical validity and clinical utility of DecisionDx-SCC. In 2022, we developed expanded evidence supporting DecisionDx-SCC through the acceptance/publication of five peer-reviewed studies. Clinical validation studies demonstrate that DecisionDx-SCC is an independent predictor of metastatic risk and that integrating with prognostic methods can add PPV to clinician decisions regarding staging and management.

Clinical Validation

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 from an expanded 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.

Clinical Utility

Prospective studies including nearly 600 physicians have consistently demonstrated that DecisionDx-SCC delivers clinically actionable results that can change clinician assessment of risk of metastasis and potentially change patient management plans in a risk-aligned manner within NCCN guideline recommendations.

In 2022, Hooper *et al.* published "Real-world evidence shows clinicians appropriately use the prognostic 40-GEP test for high-risk cutaneous squamous cell carcinoma patients". This study was a real-world clinical study involving

clinicians (n=34) who have adopted the DecisionDx-SCC test for patients with one or more high risk factors and shows that integrating the DecisionDx-SCC test result significantly impacted recommended patient treatment plans in a risk-aligned manner within the context of the NCCN guidelines, including changes to surveillance imaging, nodal assessment, and adjuvant radiation.

In addition, an initial analysis of a prospective, multi-center clinical utility study was published by Saleeby et. al., titled “A prospective, multi-center clinical utility study demonstrates that the 40-gene expression profile (40-GEP) test impacts clinical management for Medicare-eligible patients with high-risk SCC”. In this study, the DecisionDx-SCC was the single most influential factor in determining management plans for 42% of Medicare patients and resulted in a pre-test to post-test management change in 24% of patients. These data demonstrate clinical actionability on par with other contemporaneously developed molecular diagnostic tests used to guide similar clinical decisions, particularly in disease states, such as breast and prostate cancer.

Diagnostic GEP 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 clinician generally leans towards making a conservative decision and assumes that the lesion is melanoma.

DecisionDx DiffDx-Melanoma is 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 (GEP suggestive of benign neoplasm); intermediate-risk (gene express profile cannot exclude malignancy); or malignant (GEP 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. Similar to DiffDx-Melanoma, MyPath Melanoma is a proprietary GEP test that we acquired from Myriad Genetics. 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 13 publications supporting the accurate diagnosis of benign or malignant lesions by the test.

DiffDx-Melanoma, in tandem with MyPath Melanoma, were provided under our Diagnostic GEP offering of molecular testing solutions for difficult-to-diagnose melanocytic lesions. Our Diagnostic GEP offering had robust diagnostic resolution for melanocytic lesions with unknown malignant potential, with validation studies demonstrating accurate diagnosis of benign and malignant lesions for greater than 98% of cases tested. Our internal data indicates we have improved the technical performance of MyPath Melanoma such that it is now comparable to the technical performance of DiffDx-Melanoma. As such, following an internal assessment of the clinical value of offering both tests, we made the decision to suspend the clinical offering of DiffDx-Melanoma in February 2023.

Clinical Validation

The development and validation study of DiffDx-Melanoma titled “Development and Validation of a Diagnostic 35-Gene Expression Profile Test for Ambiguous or Difficult-To-Diagnose Suspicious Pigmented Skin Lesions,” showed that our 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 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. MyPath Melanoma was developed in a training cohort of 464 melanocytic lesions and subsequently validated in three separate cohorts comprised of more than 1,300 melanocytic neoplasms, independent from the training cohort. These clinical validation studies utilized both histopathologic interpretation by experts and actual patient outcomes as reference standards, and MyPath Melanoma demonstrated strong diagnostic accuracy against both reference standards. Across multiple

validation studies, MyPath Melanoma differentiated malignant melanoma from benign nevi with a sensitivity of 90-94%, and accurately classified benign nevi with a specificity of 89-96%.

Clinical Utility

Clinical utility has been demonstrated by DiffDx-Melanoma and MyPath Melanoma. Four studies have been published demonstrating that dermatopathologists use diagnostic GEP testing to improve diagnostic accuracy and impact treatment recommendations, and that dermatologists incorporate test results to adjust treatment plans, including reduction of re-excisions in 63-76% of cases with benign results. These tests provide opportunities for clinicians to deliver more informed patient management plans.

The offering of both MyPath Melanoma and DiffDx-Melanoma in an integrated workflow to enhance both accuracy and technical reliability of diagnostic testing is supported by 15 peer-reviewed publications. Our internal data indicates we have improved the technical performance of MyPath Melanoma such that it is now comparable to the technical performance of DiffDx-Melanoma. As such, following an internal assessment of the clinical value of offering both tests, we made the decision to suspend the clinical offering of DiffDx-Melanoma in February 2023.

DecisionDx-UM

DecisionDx-UM

Overview

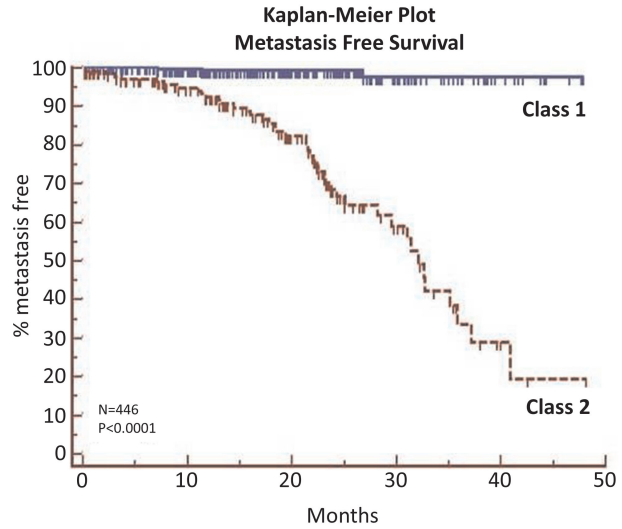
At the time of diagnosis nearly all patients with UM have no evidence of metastasis yet, approximately 30% of UM patients will metastasize within five years and nearly 50% of UM patients will metastasize at some point. Traditional clinical staging and molecular diagnostic tests for UM have been commercialized, 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 UM. 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 UM without evidence of metastatic disease. DecisionDx-UM identifies patients at low risk for progression of their UM so that their clinicians can appropriately de-escalate the level of care provided. 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 45% of the addressable patient population as well as widespread commercial payor coverage. 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, and it is estimated that nearly 8 in 10 patients diagnosed with UM in the United States receive the DecisionDx-UM test as part of their diagnostic workup.

As of December 31, 2022, 24 peer-reviewed publications involving more than 3,600 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 NPV 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 UM), using Cox multivariate

analysis, and found that the only statistically significant factor in predicting a likelihood of metastasis was DecisionDx-UM.



Variable	Cox Multivariate Analysis	
	HR	P-value
↑ patient age	1.9	0.2
Ciliary body involved	1.1	0.9
↑ tumor diameter	2.0	0.2
↑ tumor thickness	0.8	0.6
Mixed/epith. cell type	1.3	0.6
Loss of chromosome 3	2.8	0.2
DecisionDx-UM Class 2	20.5	0.006

The seminal prospective, multi-center COOG study validated the clinical accuracy of the DecisionDx-UM test (Kaplan-Meier plot on the left) as well as independence and superiority over existing clinical, pathologic and molecular factors (Cox multivariate analysis on right).

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 UM (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. We expect that the second ongoing COOG study, commonly referred to as COOG2, will report findings in 2023 that continue to support DecisionDx-UM as the strongest prognostic factor for identifying patients at high risk of metastasis and mortality from UM. We anticipate that these results may inform clinical improvements in the value of our UM test.

TissueCypher

TissueCypher
Barrett's Esophagus

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 gastroesophageal reflux disease ("GERD") and a risk factor for the development of esophageal cancer.

There are approximately 4 million patients in the United States diagnosed with BE, and annually, approximately 435,000 endoscopies are performed on BE patients. The TissueCypher Barrett's Esophagus Test addresses an unmet need in BE, as it is designed to objectively and accurately predict progression from ND, IND and LGD BE to HGD 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, 2023, nine peer-reviewed publications have demonstrated the clinical validity and utility of the TissueCypher Barrett's Esophagus Test. Recent presentations at major gastroenterology conferences have further supported the validity and utility of the TissueCypher Barrett's Esophagus Test. At Digestive Diseases Week 2022, results from a new study were presented showing that TissueCypher outperforms pathologist diagnoses when predicting progression in patients diagnosed with BE with LGD. A presentation at the American College of Gastroenterology 2022 annual meeting reported that use of the TissueCypher test results to guide patient management decisions significantly increased the likelihood of BE patients with LGD receiving appropriate management per their known outcome, and use of the test results also improved the consistency of management decisions for BE patients with LGD by reducing the impact of variable pathology review. An independent, peer-reviewed article published by investigators at the Mayo Clinic in the journal *Clinical Gastroenterology and Hepatology* reinforced the ability of TissueCypher to significantly improve

predictions of progression to esophageal cancer in patients with BE, compared to predictions based on clinical and pathology variables alone, allowing for more informed disease management decisions. In the study, a TissueCypher high-risk score independently predicted increased risk of progression to HGD/esophageal cancer, with improved accuracy over expert pathologist diagnoses of LGD and IND. Further, a TissueCypher high-risk score was associated with a strong independent risk of progression in NDBE patients.

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 HGD, LGD, IND and 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 the majority 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 Test 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.

IDgenetix

Finding an optimal medication for patients diagnosed with a mental illness has traditionally relied on trial and error, resulting in inadequate therapy response, low remission rates, and a high rate of adverse drug events. Using current standard-of-care treatment approaches, less than half of patients with major depressive disorder achieve an adequate response to first line treatment and nearly 3 of 4 do not achieve remission. There is a high prevalence of adverse drug events and increasing rates of discontinuation with repeated medication trials. This frustration has led to a need in the mental health community for more personalized care with selection of an optimal therapy the first time, achieving a fast response/remission with few to no side effects and at a low out of pocket cost. For the 50 million patients experiencing mental health illness in the United States, meeting these expectations will require a new approach to medication selection. PGx can improve medication selection and avoid the need for multiple medication trials. Traditional PGx tests are designed to assess a patient's DNA to identify variances that result in drug-gene interactions. These interactions can lead to variation in medication responses by altering drug metabolism or impacting how the body responds to a drug. In addition to drug-gene interactions, our IDgenetix test

incorporates drug-drug interactions and lifestyle factors into the final patient report, which we believe offers additional value to clinicians and patients.

Following our acquisition of AltheaDx in April 2022, we began offering a proprietary PGx test service focused on mental health, IDgenetix, a PGx test for depression, anxiety and other mental health conditions designed to analyze a patient's genetic make-up to guide timely and evidence-based decisions on the optimal drug for each patient. IDgenetix is designed to provide important genetic information to clinicians to help guide personalized treatment plans for their patients, with the potential to help patients achieve a faster therapeutic response and improve their chances of remission by identifying appropriate medications more efficiently than the standard of care trial-and-error approach. IDgenetix is supported by a published, peer-reviewed randomized controlled trial that demonstrated clinical utility over the standard of care when physicians used IDgenetix prior to prescribing a medication. The trial was conducted across 20 independent clinical sites within the United States specializing in Psychiatry, Internal Medicine, Obstetrics & Gynecology, and Family Medicine. A total of 685 patients were randomized by disease and severity and allocated in a 1:1 ratio to the experimental group (guided by the IDgenetix test) or control group (using standard of care) and followed for a period of twelve weeks. Medication changes in the experimental group were aligned with the report recommendations 70% of the time, as compared to only 29% alignment in random selection in the control group. More importantly, clinical decision-making based on IDgenetix resulted in a two-fold increase over the control group for response (p=0.001) and a 2.5x increase over the control group for remission (p=0.02). Collectively, these data speak to the ability of the IDgenetix test to guide provider decision making and to significantly improve clinical outcomes. IDgenetix is currently reimbursed by Medicare for the following eight mental health conditions: major depressive disorder, schizophrenia, bipolar disorder, anxiety disorders, social phobia, obsessive-compulsive personality disorder, post-traumatic stress disorder, and attention deficit hyperactivity disorder.

Our Commercial Channel

Sales and Marketing

Our sales and marketing efforts are primarily focused on the United States skin cancer, gastroenterology and mental health markets. We employ a direct sales and marketing strategy to educate clinicians, nurses, laboratory and pathology personnel, and finance administrators 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.

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 DiffDx-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 September 2022, we established a new commercial sales team dedicated to our Diagnostic GEP offering, with the current dermatologic commercial team shifting to focus primarily on DecisionDx-Melanoma and DecisionDx-SCC. We expect the new sales team to be fully integrated into our commercial operations by the second quarter of 2023.

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 Test. This dedicated team focuses on gastroenterology specialists that diagnose and manage patients with BE. In September 2022, we added additional outside territories for our TissueCypher Barrett's Esophagus Test.

In April 2022, we added a mental health commercial team covering approximately 20 outside sales territories through our acquisition of AltheaDx.

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 clinicians by providing highly technical interactions that focus on optimizing the appropriate use of our proprietary and ancillary products.

We will continue to assess market response in determining further commercial expansions.

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 with our integrated accounts.

Medical Affairs

We also deploy an experienced medical affairs group to assist education of treating clinicians 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 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.

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 Medicare coverage for our DecisionDx-Melanoma, DecisionDx-SCC, MyPath Melanoma, DecisionDx-UM, TissueCypher and IDgenetix tests which meet certain criteria for Medicare and Medicare Advantage beneficiaries, representing approximately 60 million covered lives. The Medicare rates discussed below are prior to giving effect to applicable sequestration in effect from time to time as described in further detail under "Government Regulation and Product Approval—Healthcare Reform" included in Part 1, Item 1, “Business”, in this Annual Report on Form 10-K. A ‘‘covered life’’ means a subscriber, or a dependent of a subscriber, who is insured under an insurance carrier’s policy.

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 (“LCD”) are made through an evidence-based process by Medicare Administrative Contractors (“MACs”) with opportunities for public participation. Coverage and payment may also be obtained from MACs through medical review and pricing in absence of an LCD. The Medicare rates discussed below are prior to giving effect to applicable sequestration in effect from time to time as described in further detail under "Government Regulation and Product Approval—Healthcare Reform" below.

Palmetto GBA MolDX (“Palmetto”) is the MAC responsible for administering MolDX, the program that assesses molecular diagnostic technologies. Noridian Healthcare Solutions, LLC (“Noridian”) is the MAC responsible for administering claims for laboratory services performed in Arizona and California laboratories. Novitas Solutions (“Novitas”) is the MAC responsible for administering claims for laboratory services performed in Pennsylvania laboratories.

Advanced Diagnostic Laboratory Tests

Advanced Diagnostic Laboratory Test (“ADLT”) status is a designation granted by CMS for clinical diagnostic laboratory tests covered under Medicare Part B that is offered and furnished only by a single laboratory. Additionally, an ADLT cannot be sold for use by a laboratory other than a single laboratory that designed the test or a successor owner, and must meet one of the following criteria:

Criterion A: The test:

- Is an analysis of multiple biomarkers of DNA, RNA or proteins: When combined with an empirically derived algorithm, yields a result that predicts the probability a specific individual patient will develop a certain condition or conditions, or respond to a particular therapy or therapies;
- Provides new clinical diagnostic information that cannot be obtained from any other test or combination of tests; and
- May include other tests.

Criterion B: The test is cleared or approved by the FDA. Laboratories requesting ADLT status under this criterion are required to submit documentation of premarket approval or premarket notification from the FDA.

DecisionDx-Melanoma

LCD

Palmetto 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 adopted the same coverage policy as Palmetto and also issued an expanded final LCD for DecisionDx-Melanoma, effective December 6, 2020.

In the second quarter of 2021, Palmetto and the other MACs that participate in the MolDX program posted a revised draft LCD for DecisionDx-Melanoma. The draft LCD included commentary about two publications regarding the clinical utility of GEP tests and included an assessment stating that the new data is not sufficient to change the coverage criteria. There was an open public comment period, and we submitted comments in support of Medicare coverage. The comment period ended on August 8, 2021. Palmetto issued a final LCD on May 19, 2022 with Noridian issuing the same on June 16, 2022. The final LCDs did not result in any change in coverage.

ADLT

On May 17, 2019, CMS determined that DecisionDx-Melanoma meets the criteria for "new ADLT" status. From July 1, 2019 through March 31, 2020, the Medicare reimbursement rate was equal to the initial list price of $7,193 per test. From April 1, 2020 through December 31, 2021, the rate was also $7,193 per test, which was calculated based upon the median private payor rate for DecisionDx-Melanoma from July 1, 2019 to November 30, 2019.

Beginning in 2022, the rate for DecisionDx-Melanoma has been 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 was set using median private payor rate data from January 1, 2021 to June 30, 2021. Our rate for 2022 was $7,193 per test and will continue to be $7,193 per test for 2023.

DecisionDx-UM

LCD

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 UM and to guide surveillance and referral to medical oncology for those patients. Similar to cutaneous melanoma, the median age at diagnosis for UM is estimated at 58-62 years old. The Medicare eligible population represents close to 45% of the addressable market.

ADLT

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. For example, the rate for 2023 was set using median private payor rate data from January 1, 2021 to June 30, 2021. Our rate for 2021 was $7,776 per test. Our rate remained at $7,776 per test for 2022 and will remain at $7,776 per test for 2023.

Diagnostic GEP Offering

Our Diagnostic GEP offering included MyPath Melanoma and DiffDx-Melanoma. We began offering MyPath Melanoma following our acquisition of the Myriad MyPath Laboratory on May 28, 2021. Our internal data indicates that we have improved the technical performance of MyPath Melanoma such that it is now comparable to the technical performance of DiffDx-Melanoma. As such, following an internal assessment of the clinical value of offering both tests, we made the decision to suspend the clinical offering of DiffDx-Melanoma in February 2023.

MyPath Melanoma

MyPath Melanoma is currently covered under a MolDX LCD policy. 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 was $1,950. Beginning in 2023, the rates for our MyPath Melanoma test 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 was set using median private payor rate data from January 1, 2021 to June 30, 2021. The rate for 2023 is set at $1,755 per test based on data submitted by the predecessor owner of the Myriad MyPath Laboratory relating to the first half of 2021. Rates for our MyPath Melanoma test will continue to be set annually based upon the median private payor rate for the first half of the second preceding calendar year.

DiffDx-Melanoma

In early 2021, we submitted our technical assessment dossier for DiffDx-Melanoma. The dossier was accepted as complete in the first quarter of 2021. In June 2022, Palmetto and Noridian each posted a draft LCD that would provide coverage criteria for DiffDx-Melanoma, and each of the comment periods closed during the third quarter of 2022. We believe the LCD for DiffDx-Melanoma will be finalized by the end of the second quarter of 2023. However, there is no assurance that any draft or final LCD will match our expectations, be posted in a timeframe consistent with our historical experience or will be posted at all.

In the second quarter of 2022, we obtained a Proprietary Laboratory Analyses ("PLA") code for DiffDx-Melanoma. DiffDx-Melanoma will go through CMS's Gapfill pricing process in 2023, which we expect to conclude in late 2023.

DecisionDx-SCC

We issue our DecisionDx-SCC tests from our Arizona and Pittsburgh labs, with a majority of tests being issued from our Pittsburgh lab. As previously discussed, the Palmetto MolDX program oversees MAAA tests that are reported from our Arizona laboratory and Noridian is the MAC responsible for administering claims for test reports issued by our Arizona laboratory. Novitas is the MAC responsible for administering claims for test reports issued by our Pittsburgh laboratory.

Novitas

On June 9, 2022, Novitas posted a draft oncology biomarker LCD that proposes to rely upon evidentiary reviews sourced from three databases for all oncology biomarker tests: ClinGen, OncoKB and NCCN. We believe the purpose of the proposals in this draft LCD are to streamline future reviews. Two of the databases do not review GEP tests and NCCN has not yet, to our knowledge, reviewed DecisionDx-SCC. If finalized as proposed, then DecisionDx-SCC would not be included as a covered test in the associated billing and coding article. The comment period for the draft LCD ended on September 6, 2022. We cannot predict whether this draft LCD will be finalized as proposed or what the timing of any final LCD might be.

In the second quarter of 2022, following the completion of a requested medical review and pricing of our DecisionDx-SCC test by Novitas, we obtained a PLA code and began receiving reimbursement from Novitas for DecisionDx-SCC at a rate of approximately $3,800 per test. In November 2022, CMS set our rate of reimbursement for DecisionDx-SCC at $3,873 per test. DecisionDx-SCC will go through CMS's Gapfill pricing process in 2023, which we expect to conclude in late 2023. We expect our current rate of $3,873 per test to be maintained through the Gapfill process and for the Gapfill rate to go into effect in 2024.

Palmetto MolDX

In the second quarter of 2020, we submitted our technical assessment dossier for DecisionDx-SCC to Palmetto. The dossier was accepted as complete in the third quarter of 2020. To date, Palmetto has not issued a draft LCD for DecisionDx-SCC. 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.

TissueCypher

TissueCypher is processed in our Pittsburgh, Pennsylvania laboratory and falls under the Medicare jurisdiction managed by Novitas which previously reviewed TissueCypher. We receive payments for claims according to the published CLFS rate. For 2022, the published CLFS payment rate was $2,513 for the test.

ADLT

On March 24, 2022, CMS determined TissueCypher meets the criteria for "new ADLT" status. ADLT status exempts TissueCypher from what is called the "14-day rule," which simplifies the billing process for Medicare patients. From April 1, 2022 through December 31, 2022, CMS set the initial period rate equal to the original list price of $2,350. Effective January 1, 2023, the published CLFS rate for TissueCypher is $4,950, which will remain effective through December 31, 2024. This rate is based on the median private payor rates received between April 1, 2022 and August 31, 2022.

IDgenetix

Our IDgenetix test was processed in our San Diego laboratory until the lab's closure in December 2022. We intend to process future tests in our Arizona laboratory. As previously discussed, Noridian is the MAC responsible for administering claims for laboratory services performed in Arizona and California laboratories.

IDgenetix is currently covered under an LCD policy through MolDX and an accompanying billing and coding article through Noridian. The Medicare coverage includes depression and the following seven additional mental health conditions beyond major depressive disorder: schizophrenia, bipolar disorder, anxiety disorders, social phobia, obsessive-compulsive personality disorder, post-traumatic stress disorder and attention deficit hyperactivity disorder. The IDgenetix multi-gene panel is currently reimbursed by Medicare at approximately $1,500 per test. IDgenetix has historically been billed to Medicare using a multi-test unspecified CPT code along with the IDgenetix test-specific MolDX Z-code (the "IDgenetix Z-Code"). In February 2023, MolDX notified us that as part of its annual CPT code updates IDgenetix should shift billing to a different multi-test generic gene sequencing CPT code (the "New CPT Code") and continue using the IDgenetix Z-Code beginning in March 2023. The New CPT Code is currently contractor priced at $917 while it goes through CMS's Gapfill pricing process in 2023. The New CPT Code does not describe all of the components of the IDgenetix test. We, therefore, do not believe the New CPT Code, in conjunction with the IDgenetix Z-Code, provides additional specificity and thus we believe the New CPT Code is not appropriate for IDgenetix.

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 insurance 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.

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. Our revenue from patients covered by Medicare as a percentage of total revenue, was 53% for the year ended December 31, 2022. Additionally, there is a commercial payor from which 12% of our revenue from patients was derived for the year ended December 31, 2022.

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 clinicians 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 clinician 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 clinicians 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. In the future, we may face competition from SkylineDx who has been working to develop a diagnostic test.

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 Test 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 tests for patients diagnosed with BE, and these could compete with TissueCypher in the future.

With respect to IDgenetix, our competition arises from other parties using the same or similar methods as well as alternative methods of PGx testing. IDgenetix competes with Myriad Genetics's GeneSight test, Genomind's PGx test, and test from numerous small commercial and academic laboratories.

Laboratory Operations

In 2022, we operated laboratory facilities in Phoenix, Arizona; Pittsburgh, Pennsylvania; and San Diego, California. All of our facilities are Clinical Laboratory Improvement Amendments of 1988 ("CLIA") certified, College of American Pathologists ("CAP") accredited labs, most recently the Pittsburgh facility. We manage these laboratories to produce the volume of testing required to cover our portfolio of products while maintaining efficiencies, redundant capabilities, and business continuity. Our facilities are positioned to operate in all 50 states, including those requiring additional licenses or certifications such as California, Pennsylvania, Rhode Island, Maryland and New York. As of December 2022, we have folded operations from our San Diego lab into the Phoenix facility and permanently closed our California location.

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 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 likely 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 the 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 ("PMA") 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 the Products and (ii) a percentage in the low-single digits of our and any of our affiliates' or sub-licensees' revenue from the 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, the treatment of cutaneous SCC, BE and gastroenterology, and PGx for mental illness. 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, 2022, is comprised as follows:

	Number of Applications and Patents		
Commercial Focus	**United States**	**International**	**Total**
Owned Patent Families			
Methods for predicting risk of metastasis in cutaneous melanoma	3	16	19
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	13	15
Determining Prognosis and Treatment based on Clinical-Pathologic Factors and Continuous Multigene-Expression Profile Scores	1	1	2
Genes and gene signatures for diagnosis and treatment of melanoma	5	30	35
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	23	25
Expression profiling using microarrays	1	—	1
Strategies for gene expression analysis	1	—	1
Licensed Portfolio from WUSTL			
Method for predicting risk of metastasis	2	—	2
Compositions and methods for detecting cancer metastasis	2	2	4
Total	25	102	127

Included in the table above are 15 issued U.S. patents and 69 issued international patents. This global patent portfolio has filing dates ranging from 2004 to 2022, and therefore are projected to expire between 2024 and 2042, 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 (the "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 16 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

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, 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 and 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 (the "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 the 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, MyPath Melanoma, DiffDx-Melanoma and IDgenetix. Additionally, we have submitted and are working through the NYSDOH approval process for our Pennsylvania laboratory and TissueCypher. We are able, under an allowed process, to offer the test service to New York patients while undergoing review.

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 (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 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.

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 Laboratory Developed Tests ("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 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 the 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 payors.

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 and other companies with LDTs are considered healthcare providers rather than device manufacturers, and LDTs do not require approval or clearance from the FDA, we believe that we are exempt from these reporting requirements. We cannot assure you, however, that the government will agree with our determination. Despite maintaining it has clear regulatory authority over LDTs, the FDA generally has not regulated them and has traditionally exercised enforcement discretion, choosing not to enforce applicable statutory and regulatory requirements. Therefore, most of these tests have neither undergone premarket review nor received FDA clearance, authorization or approval for marketing. We will continue to monitor the FDA's position as changes in this respect could materially 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 ("UK") 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 CPT Editorial Panel. 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 now issues PLA codes in support of this section of PAMA. These PLA 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. Our MyPath Melanoma test was granted a PLA CPT code prior to our May 2021 acquisition of the Myriad MyPath Laboratory. Our TissueCypher test was granted a PLA CPT code prior to our December 2021 acquisition of Cernostics. Our DecisionDx-SCC and DiffDx-Melanoma tests were granted PLA CPT codes effective April 1, 2022.

Healthcare Reform

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. 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. Further, there have been a number of health reform measures by the Biden administration that have impacted the ACA. For example, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 ("IRA"), into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any additional 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. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester.

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, the coverage of or the amounts of reimbursement available for our products from third-party payors, including government and commercial payors.

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, 2022, we had 543 employees, of whom 542 were full-time employees. During the year ended December 31, 2022, we added 198 employees to our team, a 57.4% increase from 2021. 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, 2022:

	Number of Employees
Laboratory Testing Operations	122
Research & Development	100
Sales & Marketing	187
Administrative & General	134
Total as of December 31, 2022	543

	Number of Employees
Friendswood, Texas	92
Phoenix, Arizona	171
Pittsburgh, Pennsylvania	31
Home-based	249
Total as of December 31, 2022	543

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 are committed to fostering, cultivating and preserving a culture of diversity, equity and inclusion (“DEI”). We are a company whose mission is improving health through innovative tests that guide patient care. Keeping people first —patients, clinicians, employees and investors—highlights a critical part of the patient-centric work we do.

Our DEI initiatives are applicable—but not limited—to our practices and policies on recruitment and selection; compensation and benefits; professional development and training; promotions; transfers; social and recreational programs; layoffs; terminations; and the ongoing cultivation of a work environment built on the premise of equity and belonging for employees of all backgrounds. We are committed to maintaining:

- Respectful communication and cooperation between all employees

- Teamwork and employee participation that enables the representation of all groups and employee perspectives
- Employer and employee contributions to the communities we serve to promote a greater understanding and respect for diversity
- Equitable policies, processes and practices

All of our employees have a responsibility to treat others with dignity and respect at all times. All employees are expected to exhibit conduct that promotes inclusion and belonging in the workplace, at work functions on or off the work site, and at all other company-sponsored events. Our DEI strategy and programs hinge upon three core pillars:

1. Recruiting a diverse workforce
2. Building a culture of inclusion
3. Promoting transparency

To ensure we are cultivating an authentic company culture, we will take the following actions:

- Conduct annual diversity awareness/unconscious bias training
- Monitor diversity data, including compensation data
- Offer mentorship programs or networking groups
- Support employee resource groups

As of December 31, 2022, our employees were 65.7% female and 34.3% male. Our overall employee population as of December 31, 2022 was 74.2% White, 11.6% Hispanic or Latino, 7.2% Asian, 2.9% Black or African-American and 4.1% 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, 2022 was 80.6% White, 6.5% Hispanic or Latino and 12.9% other (not Hispanic or Latino). Females represented 35.5% of employees in executive positions.

Affirmative Action

Our DEI practices reaffirm our belief in and commitment to equal employment opportunity ("EEO") for all employees and applicants in all aspects of employment.

We have developed and maintained a written Affirmative Action Program ("AAP"). Our President and Chief Executive Officer supports the AAP and urges each employee to commit to carrying out the intent of the AAP and this statement. We maintain an audit and reporting system to determine overall compliance with its EEO mandates. The EEO Administrator oversees the AAP development, modification, implementation, effectiveness and reporting requirements, and conducts management updates.

We will strive to ensure all aspects of employment, including recruitment, selection, job assignment, training, compensation, benefits, discipline, promotion, transfer, layoff and termination processes remain free of illegal or unethical discrimination based upon race, color, religion, sex (including pregnancy, sexual orientation, gender identity or transgender status), age, national origin, genetic information, marital status, political affiliation, disability, status as a parent, protected veteran status, or a person's relationship or association with a protected veteran. Regular review helps ensure compliance with this policy.

Employee Engagement

We value the unique perspective our employees bring to the organization and encourage open channels of communication. In June 2022, we conducted our second annual employee engagement survey to understand what was working well at Castle and what opportunities we had for improvement. We received feedback from over 89% of our employees and achieved an engagement score of 81%, meaning that 81% of our employees are engaged or enthusiastically engaged in the culture at Castle. Our engagement score was considerably higher than the healthcare benchmark average of 53% for other healthcare companies who conducted the same employee engagement survey in 2022.

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 ("RSUs") 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, 2022.

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

A significant portion of our revenue comes from a small number of third-party payors.

Our revenue for our test reports provided for patients covered by Medicare as a percentage of total revenue, was 53% and 57% for the years ended December 31, 2022 and 2021, respectively. Additionally, there is a commercial payor from which 12% of our revenue from patients were derived for the year ended December 31, 2022. 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 and annual 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 (''ASC'') 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 Medicare, including those claims undergoing appeal, is deemed to be fully constrained due to factors outside our influence (e.g., 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, 2022, we had a net loss of $67.1 million, and as of December 31, 2022, we had an accumulated deficit of $160.9 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 due to additional awards outstanding, attributable to increased headcount. Additionally, our performance could be affected by the impacts of the ongoing COVID-19 pandemic, the invasion of Ukraine by Russia, economic slowdowns, labor shortages, recessions or market corrections, inflation and monetary policy shifts, rising interest rates and tightening of credit markets resulting from the conflict or other evolving macroeconomic developments. Due to the requirements associated with being a public company, including those associated with no longer qualifying as an emerging growth company, we expect to continue incurring 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 or generate positive cash flows. 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 laboratory testing operations, 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. 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 (“U.S. GAAP”) is subject to interpretation by the Financial Accounting Standards Board (‘‘FASB’’), 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.

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, marketable investment securities 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, marketable investment securities 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 the DecisionDx-Melanoma, DecisionDx-SCC, MyPath Melanoma, DiffDx-Melanoma, DecisionDx-UM, TissueCypher and IDgenetix tests 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, gastrointestinal or mental health 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 duration and effects of elevated inflation;
- the effects on our operations of general political and economic conditions and evolving macroeconomic developments, including the COVID-19 pandemic, the invasion of Ukraine by Russia, economic slowdowns, labor shortages, recessions or market corrections, the duration and effects of elevated inflation and monetary policy shifts, rising interest rates and tightening of credit markets resulting from the conflict or other evolving macroeconomic developments; 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

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.

Our revenue in 2022 and 2021 was primarily derived from the sale of our lead product, DecisionDx-Melanoma. While we also derive revenue from our other tests, we expect that the majority of our revenue for at least the next several years will be derived from sales of DecisionDx-Melanoma.

We believe that our long-term commercial success, and ability to generate revenue, will depend on our ability to develop and market additional products, on our ability to increase market penetration for our existing and potential future products and on our ability to obtain 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 and our other tests, 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.

Unfavorable U.S. and global economic conditions could adversely affect our business, financial condition, results of operations or cash flows.

Our results of operations could be adversely affected by general conditions in the U.S. and global economies, the U.S. and global financial markets and adverse macroeconomic developments. U.S. and global market and economic conditions have been, and continue to be, disrupted and volatile due to many factors, including the ongoing COVID-19 pandemic, material shortages and related supply chain challenges, geopolitical developments such as the conflict between Ukraine and Russia, and increasing inflation rates and the responses by central banking authorities to control such inflation, among others. General business and economic conditions that could affect our business, financial condition or results of operations include fluctuations in economic growth, debt and equity capital markets, liquidity of the global financial markets, the availability and cost of credit, investor and consumer confidence, and the strength of the economies in which we, our collaborators, our manufacturers and our suppliers operate.

A severe or prolonged global economic downturn could result in a variety of risks to our business. For example, inflation rates, particularly in the United States, have increased recently to levels not seen in years, and increased inflation may result in increases in our operating costs (including our labor costs), reduced liquidity and limits on our ability to access credit or otherwise raise capital on acceptable terms, if at all. In addition, the U.S. Federal Reserve has raised, and may again raise, interest rates in response to concerns about inflation, which coupled with reduced government spending and volatility in financial markets may have the effect of further increasing economic uncertainty and heightening these risks. Risks of a prolonged global economic downturn are particularly true in Europe, which is undergoing a continued severe economic crisis. A weak or declining economy could also strain our suppliers and manufacturers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Additionally, financial markets around the world experienced volatility following the invasion of Ukraine by Russia in February 2022. In response to the invasion, the United States, UK and European Union (“EU”), along with others, imposed significant new sanctions and export controls against Russia, Russian banks and certain Russian individuals and may implement additional sanctions or take further punitive actions in the future. The full economic and social impact of the sanctions imposed on Russia (as well as possible future punitive measures that may be implemented), as well as the counter measures imposed by Russia, in addition to the ongoing military conflict between Ukraine and Russia, which could conceivably expand into the surrounding region, remains uncertain; however, both the conflict and related sanctions have resulted and could continue to result in disruptions to trade, commerce, pricing stability, credit availability and/or supply chain continuity in both Europe and globally, and has introduced significant uncertainty into global markets. In particular, the Russia-Ukraine conflict has contributed to rapidly rising costs of living (driven largely by higher energy prices) in Europe and other advanced economies. Further, a weak or declining economy could strain our suppliers, manufacturers and collaborators, possibly resulting in additional supply disruption for our product candidates. As a result, our business and results of operations may be adversely affected by the ongoing conflict between Ukraine and Russia, particularly to the extent it escalates to involve additional countries, further economic sanctions or wider military conflict. If economic conditions in Europe and other key markets for our business and the business of our suppliers, manufacturers and collaborators remain uncertain or deteriorate further, including as a result of the COVID-19 pandemic or otherwise, we could experience adverse effects on our business, financial condition, results of operations or cash flows.

Public health crises, such as pandemics or similar outbreaks, could adversely impact our business.

The COVID-19 pandemic, and federal, state and local government responses to these events, adversely impacted our business. Adverse impacts included reduced demand for our test reports, as well as disruptions to 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.

Following the onset of the COVID-19 pandemic, we experienced declines in orders and test report volume in certain periods. 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. 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 calls during the COVID-19 pandemic.

Similar future events, and responses to such events, could also adversely impact and disrupt our business, including, but not limited to:

- decreased test report volume due to a decline in orders of our 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 clinicians as a result of travel restrictions and hindered means of communicating with clinicians;
- delays or disruptions by third parties in the collection, preparation or delivery of the 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 a 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.

The receipt of government payments or other assistance during a public crisis or pandemic could generate negative publicity or other adverse impacts for our Company.

Under legislation enacted (or that may be enacted) by the United States federal government in response to public health crises or pandemics, we could receive cash payments or other forms of assistance allocated to healthcare and other companies, the receipt of which could generate negative publicity, harm our reputation, trigger a review or audit by applicable government agencies and/or adversely impact our stock price. For example, during the COVID-19 pandemic we received $1.9 million of government payments in the form of provider relief funds from HHS. Although we do not believe the receipt of these funds was perceived negatively by the public, we can provide no assurance regarding future public reactions to similar events. Further, the terms and conditions of 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 governments 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.

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 Health 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 CPT billing 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. Any significant disruption in our billing operations or the discovery of a 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 billing process or 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 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 affect our ability to deliver test reports in a timely manner or at all, which could significantly harm our business.

The samples that we test are biopsied (if applicable), 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 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 operational problems, natural disasters and public health epidemics. Any errors in any part of the sample collection or preparation process could render us unable to process tests, or deliver test reports, or cause us to deliver incorrect test reports, potentially resulting in harm to patients whose clinicians implement a change in treatment decisions based upon our test report. If we are unable to timely deliver test reports, clinicians may be less likely to recommend and order our products and our revenues could be adversely affected. 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 some of 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 additional laboratory facilities to not only support our growth but to 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 clinician;
- 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, such as Medicare, which accounted for 53% and 57% of our revenue from test reports for the years ended December 31, 2022 and 2021, respectively, with an additional third-party payor accounting for 12% of our revenue from test reports for the year ended December 31, 2022;
- 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 our IDENTITY Study, a 4,800 patient, prospective, multi-center clinical study to develop and validate this inflammatory skin disease pipeline test with the expectation of having initial validation and development data in 2023 and in 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 returned to more normal levels, 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, SLNB surgery is the most widely used pathology staging tool by clinicians 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 laboratories located in Phoenix, Arizona; and Pittsburgh, Pennsylvania, 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 up test volume, or encounter additional disruptions to trade, commerce, pricing stability, credit availability and global supply chain continuity as a result of the invasion of Ukraine by Russia, particularly if we contract with suppliers with operations or commercial relationships in Eastern Europe or to the extent the conflict escalates to involve additional countries, further economic sanctions or wider military conflict. 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 clinicians and patients, our operating results, reputation and business could suffer.

Our success depends on clinician 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 clinicians 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 TAM for our current and future products have not been established with precision and may be smaller than we estimate.

Our estimates of the TAM for the DecisionDx-Melanoma, DecisionDx-UM, DecisionDx-SCC, MyPath Melanoma, DiffDx-Melanoma, TissueCypher and IDgenetix tests are based on a number of internal and third-party estimates, including, without limitation, the annual rate of patients with the applicable indications, 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. 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 TAM 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 TAM 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 clinicians 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 generally have limited reimbursement coverage for our products, 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 clinician. 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 Medicare, including those claims undergoing appeal, is deemed to be fully constrained due to factors outside our influence (e.g., 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. 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 MolDX, 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 clinicians for assessment of appropriate treatment plans, regardless of the decision to undergo or avoid the SLNB surgery. In the second quarter of 2021, Palmetto and the other MACs that participate in the MolDX program each released a revised draft LCD for DecisionDx-Melanoma. The draft LCD included commentary about two publications regarding the clinical utility of GEP tests and included an assessment stating that the new data is not sufficient to change the coverage criteria. There was an open public comment period, and we submitted comments in support of Medicare coverage. The comment period ended on August 8, 2021. Palmetto issued a final LCD on May 19, 2022 with Noridian issuing the same on June 16, 2022. The final LCDs did not result in any change in coverage.

Separately, 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 UM 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.

Separately, we also have received Medicare coverage for our MyPath Melanoma, DecisionDx-SCC, TissueCypher and IDgenetix tests.

The process to obtain Medicare coverage 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 Medicare coverage for those products or in maintaining our current Medicare coverage. 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 MolDX 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. Medicare reimbursement rates for our tests are subject to change and may decrease from those currently in effect. For example, in February 2023, MolDX notified us that as part of its annual CPT code updates IDgenetix should shift billing to a different multi-test generic gene sequencing CPT code and continue using the IDgenetix Z-Code beginning in March 2023. The New CPT Code is currently contractor priced at $917 while it goes through CMS's Gapfill pricing process in 2023. The New CPT Code does not describe all of the components of the IDgenetix test. We, therefore, do not believe the New CPT Code, in conjunction with the IDgenetix Z-Code, provides additional specificity and thus we believe the New CPT Code is not appropriate for IDgenetix.

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. The dossier was accepted as complete in the third quarter of 2020. In early 2021, we submitted our technical assessment dossier for DiffDx-Melanoma. The dossier was accepted as complete in the first quarter of 2021. In June 2022, Palmetto and Noridian each posted a draft LCD that would provide coverage criteria for DiffDx-Melanoma, and each of the comment periods closed during the third quarter of 2022. We believe the LCD for DiffDx-Melanoma will be finalized by the end of the second quarter of 2023. However, there is no assurance that any draft or final LCD will match our expectations, be posted in a timeframe consistent with our historical experience or will be posted at all. Regarding DecisionDx-SCC, no draft LCD has been posted by Palmetto or Noridian to date.

In the second quarter of 2022, following the completion of a requested medical review and pricing of our DecisionDx-SCC test by Novitas, we obtained a PLA code and began receiving reimbursement from Novitas for DecisionDx-SCC at a rate of approximately $3,800 per test. In November 2022, CMS set our rate of reimbursement for DecisionDx-SCC at $3,873 per test. DecisionDx-SCC will go through CMS's Gapfill pricing process in 2023, which we expect to conclude in late 2023. We expect our current rate of $3,873 per test to be maintained through the Gapfill process and for the Gapfill rate to go into effect in 2024.

On June 9, 2022, Novitas posted a draft oncology biomarker LCD that proposes to rely upon evidentiary reviews sourced from three databases for all oncology biomarker tests: ClinGen, OncoKB and NCCN. We believe the purpose of the proposals in this draft LCD are to streamline future reviews. Two of the databases do not review GEP tests and NCCN has not yet, to our knowledge, reviewed DecisionDx-SCC. If finalized as proposed, then DecisionDx-SCC would not be included as a covered test in the associated billing and coding article. The comment period for the draft LCD ended on September 6, 2022. We cannot predict whether this draft LCD will be finalized as proposed or what the timing of any final LCD might be.

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 the 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 including those established by CMS 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 health 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.

CLIA Certifications

We are 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.

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.

We have a current CLIA accreditation under the CAP program to conduct our tests at our clinical reference laboratories in Phoenix, Arizona. The most recent CAP inspection of our Phoenix, Arizona laboratories occurred in October 2022.

We currently have a CLIA certificate of registration for our Pittsburgh, Pennsylvania laboratories which expires in February 2024. In November 2022, our Pittsburgh, Pennsylvania passed CAP inspection and received CAP accreditation. We have since applied for, and are currently waiting to receive, our updated CLIA accreditation for our Pittsburgh, Pennsylvania laboratories.

In addition, certain states require our laboratories to be licensed in specific states in order to test specimens from those states. Accordingly, our laboratories are licensed by California, Maryland, Pennsylvania, Rhode Island and New York. Other states do not currently require additional licensure they 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 the NYSDOH on a test-by-test basis before they are offered. Our laboratory director and laboratory operations must also be separately qualified and approved through the state of New York. DecisionDx-Melanoma, DecisionDx-CMSeq, DecisionDx-UM, DecisionDx-PRAME, DecisionDx-UMSeq, DecisionDx-SCC, MyPath Melanoma, DiffDx-Melanoma and IDgenetix have each been approved. In July 2022, we submitted TissueCypher for review by the NYSDOH and expect a response in the first quarter of 2023. Our laboratory director has been qualified by the NYSDOH. We are subject to periodic inspection by the NYSDOH and are required to demonstrate ongoing compliance with the NYSDOH regulations and standards. Our most recent inspection was in October 2022 and we were deemed to be compliant with the NYSDOH regulations and standards. To the extent the NYSDOH had identified any instances of non-compliance, and we were unable to remedy such non-compliance, the State of New York could withdraw approval for our products to test samples from New York state. We will need to seek the 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 entered into, and may enter into in the future, contracts 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. For example, we have a U.S. Federal Supply Schedule contract with the Veterans Health Administration covering our skin cancer tests. Government contracts normally contain additional requirements that may increase our costs of doing business, reduce our profits (or increase our losses) 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. 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. Further, there have been a number of health reform measures by the Biden administration that have impacted the ACA. For example, on August 16, 2022, President Biden signed the IRA into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any additional 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 until 2031, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester.

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, 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 FCA ‘‘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 FCA, 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;
- the 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 AKS 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, which 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, local 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 laws, regulations, rules, contractual obligations, policies and other 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 may 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, federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws (e.g., wiretapping laws). 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, the California Rights Privacy Act of 2020 ("CPRA"), effective January 1, 2023, which will expand the CCPA, including by applying to personal information of business representatives and employees and establishing a new regulatory agency to implement and enforce the law; and the California Confidentiality of Medical Information Act, which restricts the use and disclosure of health information and other personal information. Although the CCPA and the CPRA exempt some personal information processed in the context of clinical trials, the CCPA and CPRA, 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 U.S. 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 EU's General Data Protection Regulation (EU) 2016/679 ("GDPR") and the UK's GDPR.

In addition, we may be unable to transfer personal data from Europe and other jurisdictions to the United States or other countries due to data localization requirements or limitations on cross-border data flows. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area ("EEA") and the UK have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and the UK to the United States in compliance with law, such as the EEA and the UK's standard contractual clauses, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK, or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data out of Europe for allegedly violating the GDPR's cross-border data transfer limitations.

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. In addition to data privacy and security laws, we are contractually subject to industry standards adopted by industry groups and may become subject to such obligations in the future. For example, we are subject to the Payment Card Industry Data Security Standard ("PCI DSS"). The PCI DSS requires companies to adopt certain measures to ensure the security of cardholder information, including using and maintaining firewalls, adopting proper password protections for certain devices and software, and

restricting data access. Noncompliance with PCI-DSS can result in penalties ranging from $5,000 to $100,000 per month by credit card companies, litigation, damage to our reputation, and revenue losses. We rely on vendors to process payment card data, and those vendors may be subject to PCI DSS, and our business may be negatively affected if our vendors are fined or suffer other consequences as a result of PCI DSS noncompliance.

More generally, we are also bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. For example, certain privacy laws, such as the GDPR, the CCPA, and the CPRA, may require our customers to impose specific contractual restrictions on their service providers. Additionally, we publish privacy policies and other statements regarding data privacy and security, and, if these policies or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we could experience adverse consequences.

Obligations related to data privacy and security are quickly changing in an increasingly stringent fashion, creating regulatory uncertainty as to the effective future legal framework. These obligations may be subject to varying applications and interpretations, which may be inconsistent or conflicting among jurisdictions, 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 on 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 as of December 31, 2022 includes 15 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 System, including test validation, specimen tracking and quality control, our bioinformatics analytical software systems, our test report generating systems and billing systems. 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 2022, we provided over 1,700 test reports for DecisionDx-UM. If the 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, 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, TissueCypher and IDgenetix 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 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; 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. This competition has become exacerbated by the increase in employee resignations currently taking place throughout the United States as a result of the COVID-19 pandemic, which is commonly referred to as the "great resignation." We may also experience employee turnover as a result of the ongoing "great resignation." In response to competition, rising inflation rates and labor shortages, we may need to adjust employee cash compensation, which would affect our operating costs and our margins, or equity compensation, which would affect our outstanding share count and cause dilution to existing stockholders. All of our employees are at-will, which means that either we or the employee may terminate their employment at any time.

With respect to equity compensation, as of December 31, 2022, we have granted awards in excess of the number of shares authorized for issuance under our 2019 Equity Incentive Plan (the "2019 Plan"). Although the 2019 Plan provides for automatic increases in the number of shares authorized for issuance annually through January 1, 2029, there can be no assurances that these increases will be adequate to support our requirements for future equity awards or that we will be able to obtain approval from our stockholders in the future should we require authorization for the issuance of additional shares. In December 2022, our board of directors adopted a separate equity plan, the 2022 Inducement Plan (the "Inducement Plan"), to be used exclusively for grants of awards as an inducement material to new employees entering into employment with us. However, the Inducement Plan cannot be used to grant ongoing equity awards to existing employees. If we are unable to provide adequate or competitive equity compensation, we may have to adjust other elements of our compensation packages and may encounter difficulties attracting and retaining personnel.

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, human resources, 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. For example, since May 2021, we have completed the acquisitions of Myriad MyPath Laboratory, Cernostics and AltheaDx, each of which we expect will contribute to our future growth. These acquisitions and other 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 effectively 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, automate or otherwise improve the efficiency of our operational processes 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 have engaged in, 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.

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, December 2021 and April 2022, we completed the acquisitions of the Myriad MyPath Laboratory, Cernostics and AltheaDx, respectively. These and any other strategic acquisition 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;
- difficulties in scaling and growing the operations of acquired businesses in a cost-efficient manner;
- 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 and losses on the remeasurement of contingent consideration;

- incurrence of substantial debt or dilutive issuances of equity securities, the assumption of additional liabilities, exposure to unknown liabilities and being subject to disputes with the former owners of an acquired businesses;
- 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, Cernostics and AltheaDx, 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, TissueCypher and IDgenetix tests into our commercial offerings and the ability of the combined strengths of Castle, the Myriad MyPath Laboratory, Cernostics or AltheaDx to position us for continued growth and success as a leader in the diagnostics space. Further, there are inherent execution and business risks associated with managing the integration and growth objectives of more than one acquisition at the same time and such circumstances may have the effect of heightening the operational and financial risks related to acquisitions noted above and the other risks described in this "Risk Factors" section.

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 cannot be assured given our limited historical experience with such transactions.

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

As of December 31, 2022, we had federal net operating loss ("NOL") carryforwards of approximately $207.2 million, of which $106.1 million will begin to expire in 2029 if not utilized to offset taxable income, and $101.1 million may be carried forward indefinitely. Also, as of December 31, 2022, we had state NOL carryforwards of $114.0 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 Coronavirus Aid, Relief, and Economic Security Act ("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 is limited to 80% of taxable income.

In addition, under Sections 382 and 383 of the IRC, 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 (such as research tax credits) to offset its post-change income or taxes may be limited. For example, with respect to the NOLs we obtained in our acquisitions of Cernostics and AltheaDx, $36,347,000 of NOLs are expected to expire unused as a result of Section 382 limitations. 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.

Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the TCJA, the CARES Act and the IRA enacted many significant changes to the U.S. tax laws. Further guidance from the Internal Revenue Service and other tax authorities with respect to such legislation may affect us, and certain aspects of such legislation could be repealed or modified in future legislation. In addition, it is uncertain if and to what extent various states will conform to federal tax laws. Future tax reform legislation could have a material impact on the value of our deferred tax assets and could increase our future U.S. tax expense.

Effective January 1, 2022, the TCJA eliminated the option to deduct research and development expenses for tax purposes in the year incurred and requires taxpayers to capitalize and subsequently amortize such expenses over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. Unless the United States Department of the Treasury issues regulations that narrow the application of this provision to a smaller subset of our research and development expenses or the provision is deferred, modified, or repealed by Congress, it could harm our future operating results by effectively increasing our future tax obligations. The actual impact of this provision will depend on multiple factors, including the amount of research and development expenses we will incur, whether we achieve sufficient income to fully utilize such deductions and whether we conduct our research and development activities inside or outside the United States.

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 and the third parties upon which we rely (such as contractors and consultants) Process proprietary, confidential, and sensitive information (including but not limited to intellectual property, proprietary business information and personal information).

Cyber-attacks, malicious internet-based activity, online and offline fraud and other similar activities threaten the confidentiality, integrity and availability of our proprietary, confidential, and sensitive information and information technology systems, and those of the third parties upon which we rely. Such threats are prevalent, continue to increase, and are becoming increasingly difficult to detect. These threats come from a variety of sources, including threat actors, traditional computer “hackers,” organized criminal threat actors, personnel (such as through theft or misuse), hacktivists, sophisticated nation-states, and nation-state-supported actors. Some 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 retaliatory 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 the third parties upon which we rely (such as 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, credential harvesting, 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 our proprietary, confidential and sensitive information. In particular, 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. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities’ systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. 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. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. Additionally, 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. We take steps to detect and remediate vulnerabilities but we may not be able to detect and remediate all vulnerabilities because the threats and techniques used to exploit the vulnerability change frequently and are often sophisticated in nature. Therefore, such vulnerabilities could be exploited but may not be detected until after a security incident has occurred. These vulnerabilities pose material risks to our business. 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 upon 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. Additionally, while we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. 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.

In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position.

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.

Additionally, financial markets around the world experienced volatility following the invasion of Ukraine by Russia in February 2022. In response to the invasion, the United States, UK and EU, along with others, imposed significant new sanctions and export controls against Russia, Russian banks and certain Russian individuals and may implement additional sanctions or take further punitive actions in the future. The full economic and social impact of the sanctions imposed on Russia (as well as possible future punitive measures that may be implemented), as well as the counter measures imposed by Russia, in addition to the ongoing military conflict between Ukraine and Russia, which could conceivably expand into the surrounding region, remains uncertain; however, both the conflict and related sanctions have resulted and could continue to result in disruptions to trade, commerce, pricing stability, credit availability, and/or supply chain continuity, in both Europe and globally, and has introduced significant uncertainty into global markets. While we do not operate in Russia or Ukraine, as the adverse effects of this conflict continue to develop and potentially spread, both in Europe and throughout the rest of the world, our business and results of operations may be adversely affected, particularly to the extent this conflict escalates to involve additional countries, further economic sanctions or wider military conflict. 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 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. 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. For example, during 2022, the SEC adopted new rules covering pay versus performance disclosures, "clawback" policies and insider trading plans. Future changes in regulations and disclosure obligations 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 will continue to increase our legal and financial compliance costs and to make some activities more time-consuming and costly. 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.

In 2021, the rate of inflation in the United States began to increase and then rose to levels not experienced in over 40 years, but began subsiding in the second half of 2022. We are experiencing inflationary pressures, primarily in personnel costs and with certain lab supplies. We anticipate inflationary impacts on other cost areas in the future. 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 the extent to which the rate of inflation were to further increase, if at all, 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 and marketable investment securities may be further diminished, 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. As such, the effects of inflation may adversely impact our results of operations, financial condition and cash flows.

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 Russia's invasion of Ukraine in February 2022, 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 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 on our operations of general political and economic conditions, including the COVID-19 pandemic, the invasion of Ukraine by Russia, economic slowdowns, recessions or market corrections, the duration and effects of elevated inflation, rising interest rates and tightening of credit markets resulting from the conflict or other evolving macroeconomic developments;
- trading activity by a limited number of stockholders who together beneficially own a significant percentage of our outstanding common stock;
- general investor interest in emerging growth stocks;
- 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 of other companies 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.

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 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 acquisitions and the 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 appearance 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. Additionally, Derek J. Maetzold and Daniel M. Bradbury, the chairperson of our board of directors, each served on the board of directors of AltheaDx, a commercial-stage molecular diagnostics company that we acquired in April 2022. Further, each of the following individuals was a direct or indirect beneficial owner of AltheaDx securities and received consideration in the transaction: Mr. Bradbury; Mr. Maetzold; Thomas Sullivan, John Maetzold and Peter Maetzold, immediate family members of Mr. Maetzold; Frank Stokes, our Chief Financial Officer; Tobin Juvenal, our Chief Commercial Officer; Kristen Oelschlager, our Chief Operating Officer; and Joshua Albers and Allysa Topel, immediate family members of Ms. Oelschlager.

These types of related party arrangements are required to be disclosed in our public filings 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 are a smaller reporting company and we cannot be certain if the scaled disclosure requirements applicable to smaller reporting companies will make our common stock less attractive to investors.

Effective as of June 30, 2022, we requalified as a smaller reporting company as defined in the Exchange Act. We began to take advantage of certain of the scaled disclosures available to smaller reporting companies beginning our Quarterly Report on Form 10-Q for our second quarter ended June 30, 2022 and will be able to take advantage of these scaled disclosures for so long as the market value of our voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

We cannot predict if investors will find our common stock less attractive because we will rely on these scaled disclosures. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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, 2022, our executive officers, directors and the known holders of more than 5% of our outstanding common stock, in the aggregate, beneficially owned approximately 32% 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 meetings 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 chairperson 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 acquirers 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 26,700 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, expiring in November 2025, with an option to renew for one additional five-year period. We also lease approximately 35,600 square feet of laboratory and office space in Phoenix, Arizona under two agreements, expiring in April 2033 and July 2033. For both leases, there are options to renew for two additional five-year terms.

In April 2022, we entered into a lease agreement for 20,856 square feet of laboratory and office space in Pittsburgh, Pennsylvania, with a 10.5-year term and an option to renew for one additional five-year period. Starting in early 2026, the total square footage under this lease will increase to approximately 44,677. We expect to commence operations in this new facility in the second quarter of 2023.

In connection with our acquisition of Cernostics in December 2021, we occupy 8,100 square feet of office and laboratory space in Pittsburgh, Pennsylvania under a lease which we renewed in September 2022, expiring in May 2023.

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, trades on the Nasdaq Global Market under the symbol "CSTL".

Holders of Record

As of February 21, 2023, there were approximately 127 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.

Recent Sales of Unregistered Equity Securities

None.

Use of Proceeds from the 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, 2022, 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 under the heading "Special Note Regarding Forward-Looking Statements" and "Risk Factors."

Overview

Castle Biosciences is applying innovative diagnostics to inform disease management and improve patient outcomes. 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.

Our Test Portfolio

We currently market five proprietary MAAA tests for use in the dermatologic, ocular and gastroenterology fields. We also offer a proprietary PGx test to guide optimal drug treatment for patients suffering from depression, anxiety and other mental health conditions following our acquisition of AltheaDx in April 2022, as discussed below. Currently, our revenue is primarily generated by our DecisionDx-Melanoma risk stratification test for cutaneous melanoma, our DecisionDx-SCC risk stratification test for SCC and our DecisionDx-UM risk stratification test for UM.

Test Overview

Our Dermatologic Tests

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. In a typical year, we estimate approximately 130,000 patients are diagnosed with invasive cutaneous melanoma in the United States, representing an estimated U.S. TAM of approximately $540 million. We launched DecisionDx-Melanoma in May 2013.

DecisionDx-SCC is our proprietary GEP test for use in patients with SCC, with one or more risk factors (also referred to as “high-risk” SCC). We estimate 20% of SCC patients, or 200,000 annually in the United States, are classified as high risk, representing an estimated U.S. TAM of approximately $820 million. We launched DecisionDx-SCC in August 2020.

Initially, we offered both our MyPath Melanoma test and our DiffDx-Melanoma test under an offering that we referred to as our Diagnostic GEP offering for use in patients with a melanocytic lesion and uncertainty related to the malignancy of the lesion. Of the two million suspicious pigmented lesions biopsied annually in the United States, we estimate approximately 300,000 of those present a difficult-to-diagnose melanocytic lesion, representing an estimated U.S. TAM of approximately $600 million associated with these two tests. We launched DiffDx-Melanoma in November 2020 and began to offer MyPath Melanoma following our acquisition of the Myriad MyPath Laboratory from Myriad Genetics, Inc. in 2021. Our internal data indicates that we have improved the technical performance of MyPath Melanoma such that it is now comparable to the technical performance of DiffDx-Melanoma. As such, following an internal assessment of the clinical value of offering both tests, we made the decision to suspend the clinical offering of DiffDx-Melanoma in February 2023.

Our Uveal Melanoma Test

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 estimate approximately 2,000 patients in the United States are diagnosed annually with UM, representing an estimated U.S. TAM of approximately $9.3 million. We launched DecisionDx-UM in January 2010.

Our Gastroenterology Test

The TissueCypher Barrett’s Esophagus Test is the world’s first precision medicine test designed to predict future development of HGD and/or esophageal cancer in patients with ND, IND or LGD BE. We estimate approximately 415,000 patients annually undergo an endoscopic biopsy with a subsequent diagnosis of non-dysplastic, indefinite or low-grade dysplastic BE, representing an estimated U.S. TAM of approximately $1 billion. We began offering the TissueCypher Barrett’s Esophagus Test following our acquisition of Cernostics in December 2021.

Our Mental Health Test

IDgenetix is a PGx test for depression, anxiety and other mental health conditions. IDgenetix is designed to provide important genetic information to clinicians to help guide personalized treatment plans for their patients, with the potential to help patients achieve a faster therapeutic response and improve their chances of remission by identifying appropriate medications more efficiently than the standard of care trial-and-error approach. We estimate a U.S. TAM of approximately $5 billion associated with this test. We began offering the IDgenetix test following our acquisition of AltheaDx in April 2022.

Commercial Expansion Efforts

During the first half of 2021, we expanded our dermatologic commercial team, bringing our dermatologic sales force to the mid-60s. In September 2022, we established a new commercial sales team dedicated to our Diagnostic GEP

offering, with the current dermatologic commercial team shifting to focus primarily on DecisionDx-Melanoma and DecisionDx-SCC.

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 Test. This dedicated team focuses on gastroenterology specialists that diagnose and manage patients with BE. In September 2022, we added additional outside territories for our TissueCypher Barrett's Esophagus Test. AltheaDx, which we acquired in late April 2022, has a commercial team covering approximately 20 outside sales territories.

We will continue to assess market response in determining further commercial expansions.

Reimbursement

The primary source of revenue for our products is reimbursement from third-party payors, which includes government payors, such as Medicare, 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.

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 Medicare coverage for our DecisionDx-Melanoma, DecisionDx-SCC, MyPath Melanoma, DecisionDx-UM, TissueCypher and IDgenetix tests which meet certain criteria for Medicare and Medicare Advantage beneficiaries, representing approximately 60 million covered lives. A ‘‘covered life’’ means a subscriber, or a dependent of a subscriber, who is insured under an insurance carrier's policy.

The Medicare rates discussed below are prior to giving effect to applicable sequestration in effect from time to time as described in further detail under "Government Regulation and Product Approval—Healthcare Reform" included in Item 1, Business, of this Annual Report on Form 10-K.

DecisionDx-Melanoma

LCD

Palmetto, the MAC responsible for administering MolDX, 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.

In the second quarter of 2021, Palmetto and the other MACs that participate in the MolDX program posted a revised draft LCD for DecisionDx-Melanoma. The draft LCD included commentary about two publications regarding the clinical utility of GEP tests and included an assessment stating that the new data is not sufficient to change the coverage criteria. There was an open public comment period, and we submitted comments in support of Medicare coverage. The comment period ended on August 8, 2021. Palmetto issued a final LCD on May 19, 2022 with Noridian issuing the same on June 16, 2022. The final LCDs did not result in any change in coverage.

ADLT

On May 17, 2019, CMS determined that DecisionDx-Melanoma meets the criteria for “new ADLT” status. From July 1, 2019 through March 31, 2020, the Medicare reimbursement rate was equal to the initial list price of $7,193 per test. 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.

Beginning in 2022, the rate for DecisionDx-Melanoma has been 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 was set using median private payor rate data from January 1, 2021 to June 30, 2021. Our rate for 2022 was $7,193 per test and will continue to be $7,193 per test for 2023.

DecisionDx-UM

LCD

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 UM and to guide surveillance and referral to medical oncology for those patients. Similar to cutaneous melanoma, the median age at diagnosis for UM is estimated at 58-62 years old. The Medicare eligible population represents close to 45% of the addressable market.

ADLT

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. For example, the rate for 2023 was set using median private payor rate data from January 1, 2021 to June 30, 2021. Our rate for 2021 was $7,776 per test. Our rate remained at $7,776 for 2022 and will remain at $7,776 per test for 2023.

Diagnostic GEP Offering

MyPath Melanoma

MyPath Melanoma is currently covered under a MolDX LCD policy through Noridian that became effective in June 2019. MyPath Melanoma was approved as a new ADLT in September 2019. The rate for 2022 was $1,950 per test. Our 2023 rate will be set at $1,755 per test, based on data submitted by the predecessor owner of the Myriad MyPath Laboratory relating to the first half of 2021. Rates for our MyPath Melanoma test will continue to be set annually based upon the median private payor rate for the first half of the second preceding calendar year.

DiffDx-Melanoma

In early 2021, we submitted our technical assessment dossier for DiffDx-Melanoma. The dossier was accepted as complete in the first quarter of 2021. In June 2022, Palmetto and Noridian each posted a draft LCD that would provide coverage criteria for DiffDx-Melanoma, and each of the comment periods closed during the third quarter of 2022. We believe the LCD for DiffDx-Melanoma will be finalized by the end of the second quarter of 2023. However, there is no assurance that any draft or final LCD will match our expectations, be posted in a timeframe consistent with our historical experience or will be posted at all.

In the second quarter of 2022, we obtained a PLA code for DiffDx-Melanoma. DiffDx-Melanoma will go through CMS's Gapfill pricing process in 2023, which we expect to conclude in late 2023.

DecisionDx-SCC

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. To date, neither Palmetto nor Noridian has posted a draft LCD for DecisionDx-SCC.

On June 9, 2022, Novitas posted a draft oncology biomarker LCD that proposes to rely upon evidentiary reviews sourced from three databases for all oncology biomarker tests: ClinGen, OncoKB and NCCN. We believe the purpose of the proposals in this draft LCD are to streamline future reviews. Two of the databases do not review GEP tests and NCCN has not yet, to our knowledge, reviewed DecisionDx-SCC. If finalized as proposed, then DecisionDx-SCC would not be included as a covered test in the associated billing and coding article. The comment period for the draft LCD ended on September 6, 2022. We cannot predict whether this draft LCD will be finalized as proposed or what the timing of any final LCD might be.

In the second quarter of 2022, following the completion of a requested medical review and pricing of our DecisionDx-SCC test by Novitas, we obtained a PLA code and began receiving reimbursement from Novitas for DecisionDx-SCC at a rate of approximately $3,800 per test. In November 2022, CMS set our rate of reimbursement for DecisionDx-SCC at $3,873 per test. DecisionDx-SCC will go through CMS's Gapfill pricing process in 2023,

which we expect to conclude in late 2023. We expect our current rate of $3,873 per test to be maintained through the Gapfill process and for the Gapfill rate to go into effect in 2024.

TissueCypher

TissueCypher is processed in our Pittsburgh, Pennsylvania laboratory and falls under the Medicare jurisdiction managed by Novitas which previously reviewed TissueCypher. We receive payments for claims according to the published CLFS rate. For 2022, the published CLFS payment rate was $2,513 for the test.

On March 24, 2022, CMS determined that TissueCypher meets the criteria for “new ADLT” status. From April 1, 2022 through December 31, 2022, CMS has set the initial period rate equal to the original list price of $2,350. Effective January 1, 2023, the published CLFS rate for TissueCypher is $4,950, which will remain effective through December 31, 2024. This rate is based on the median private payor rates received between April 1, 2022 and August 31, 2022.

IDgenetix

Our IDgenetix test was processed in our San Diego laboratory until the lab’s closure in December 2022. We intend to process future tests in our Arizona laboratory. As previously discussed, Noridian is the MAC responsible for administering claims for laboratory services performed in Arizona and California laboratories.

IDgenetix is currently covered under an LCD policy through MolDX and an accompanying billing and coding article through Noridian. The Medicare coverage includes depression and the following seven additional mental health conditions beyond major depressive disorder: schizophrenia, bipolar disorder, anxiety disorders, social phobia, obsessive-compulsive personality disorder, post-traumatic stress disorder and attention deficit hyperactivity disorder. The IDgenetix multi-gene panel is currently reimbursed by Medicare at approximately $1,500 per test. IDgenetix has historically been billed to Medicare using a multi-test unspecified CPT code along with the IDgenetix test-specific MolDX Z-code. In February 2023, MolDX notified us that as part of its annual CPT code updates IDgenetix should shift billing to a different multi-test generic gene sequencing CPT code and continue using the IDgenetix Z-Code beginning in March 2023. The New CPT Code is currently contractor priced at $917 while it goes through CMS’s Gapfill pricing process in 2023. The New CPT Code does not describe all of the components of the IDgenetix test. We, therefore, do not believe the New CPT Code, in conjunction with the IDgenetix Z-code, provides additional specificity and thus we believe the New CPT Code is not appropriate for IDgenetix.

Delivered Test Reports

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 test reports delivered by us during the years ended December 31, 2022 and 2021 are presented in the table below:

	Proprietary Dermatologic GEP Tests							
	DecisionDx-Melanoma	DecisionDx-SCC	Diagnostic GEP offering [1]	Dermatologic Total	DecisionDx-UM	TissueCypher Barrett's Esophagus Test[2]	IDgenetix[3]	Grand Total
Q1 2022	6,023	1,142	950	8,115	456	56	—	8,627
Q2 2022	7,125	1,344	955	9,424	431	352	827	11,034
Q3 2022	7,354	1,636	834	9,824	392	690	1,208	12,114
Q4 2022	7,301	1,845	822	9,968	432	1,030	1,214	12,644
For the year ended December 31, 2022	27,803	5,967	3,561	37,331	1,711	2,128	3,249	44,419
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	27	—	8,269
For the year ended December 31, 2021	20,328	3,510	2,662	26,500	1,618	27	—	28,145

(1) Includes MyPath Melanoma and DiffDx-Melanoma. We began offering MyPath Melanoma following our acquisition of the Myriad MyPath Laboratory on May 28, 2021. We offered both MyPath Melanoma and DiffDx-Melanoma under our Diagnostic GEP offering until February 2023 when we suspended the offering of DiffDx-Melanoma, as discussed above.

(2) We began offering the TissueCypher Barrett's Esophagus Test on December 3, 2021, following the completion of our acquisition of Cernostics.

(3) We began offering the IDgenetix test on April 26, 2022, following our acquisition of AltheaDx. Includes both single-gene and multi-gene tests.

For the years ended December 31, 2022 and 2021, our dermatologic test report volume increased by 40.9% and 57.8%, respectively, largely driven by continued growth from our DecisionDx-Melanoma and DecisionDx-SCC tests. For a discussion of how we recognize revenue derived from our tests, refer to "Net Revenues" under "Components of Results of Operations" below.

We continue to see new clinicians order our dermatologic tests for the first time. For the year ended December 31, 2022, we saw approximately 2,312 new ordering clinicians for our dermatologic tests compared to 1,938 during the same period of 2021. Total ordering clinicians for our dermatologic tests were approximately 7,670 for the year ended December 31, 2022.

In developing our DecisionDx-SCC and 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 our DecisionDx-SCC test. For example, we found that for the year ended December 31, 2022, approximately 79% of all clinicians ordering DecisionDx-SCC had also ordered our DecisionDx-Melanoma test during that same period.

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 Operations.

Test Reports Delivered

Test reports delivered for DecisionDx-Melanoma, DecisionDx-SCC, MyPath Melanoma and DiffDx-Melanoma, DecisionDx-UM, TissueCypher Barrett's Esophagus Test and IDgenetix 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.

New Ordering Clinicians

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, MyPath Melanoma and DiffDx-Melanoma. 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.

Other Events

Impact of Macroeconomic Developments

Global economic and business activities continue to face widespread macroeconomic uncertainties, including labor shortages, inflation and monetary supply shifts, recession risks and potential disruptions from the Russia-Ukraine conflict. We continue to actively monitor the impact of these macroeconomic factors on our results of operations, financial condition and cash flows. The extent of the impact of these factors on our operational and financial performance, including our ability to execute our business strategies and initiatives in the expected timeframe, will depend on future developments, which are uncertain and cannot be predicted; however, any continued or renewed disruption resulting from these factors could negatively impact our business.

Impact of COVID-19 Pandemic

We are continuing to monitor our compliance with state and local government mandates to protect the health and safety of our workforce. Although state and local government restrictions put in place to slow the spread of the virus have been eased in most 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, which could negatively impact our results of operations, financial condition and cash flows. We believe the volumes of in-person sales calls have returned to our pre-COVID-19 levels and we expect to continue to maintain uninterrupted business operations.

Our Financial Results

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.

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 clinicians 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 clinicians, as well as attract new clinicians. Our report volume could be negatively impacted by developments related to the COVID-19 pandemic or other evolving macroeconomic developments, 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.
- **Expansion of our sales force and marketing programs.** We believe the expansion of our direct sales force and marketing organization to educate clinicians and pathologists on the value of our molecular diagnostic testing products will significantly impact our performance.
- **Integrating acquisitions.** Revenue growth, operational results and advances to our business strategy depends on our ability to integrate any acquisitions into our existing business and effectively scale their operations. The integration of acquired assets may impact our revenue growth, increase the cost of operations or may require management resources that otherwise would be available for ongoing development of our existing business.
- **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 clinician adoption of new products and driving favorable coverage decisions by payors for such products.

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, DecisionDx-SCC 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 clinicians. 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 Medicare, including those claims undergoing appeal, is deemed to be fully constrained due to factors outside our influence (e.g., 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. Our ability to recognize revenue for a test is dependent on the development of reimbursement experience and obtaining coverage decisions. For tests with limited reimbursement experience or no coverage, we recognize revenues 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, including through acquisitions, 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 and tests acquired through acquisitions. For example, we expect to commence operations in a new expanded laboratory facility in Pittsburgh, Pennsylvania in the second quarter of 2023.

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, 2022 and 2021" for details.

Research and Development

Research and development expenses include costs incurred to develop our diagnostic and prognostic 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 and marketable investment securities to further support and accelerate our research and development activities, including two important studies that are underway to support our DecisionDx-Melanoma test. The first is the CONNECTION study, which is collecting long-term outcomes for up to 10,000 patients who have been tested with DecisionDx-Melanoma. The second 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, in 2021, we initiated our IDENTITY Study, 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. As of February 2, 2023, we have 54 committed sites and 507 patients enrolled in our IDENTITY study. We have also initiated two additional disease studies for pipeline tests for new indications.

We previously funded the PERSONALize study, which was evaluating the use of DecisionDx-Melanoma in patients eligible for adjuvant therapy. Other of our sponsored studies are designed to provide risk stratification analyses within various subgroups. These studies have shown statistically and clinically significant risk stratification separation. Based upon this currently available and anticipated future data, we have decided to close the PERSONALize study.

Selling, General and Administrative

Selling, general and administrative ("SG&A") expenses include executive, selling and marketing, legal, finance and accounting, human resources and billing. These expenses consist of personnel costs (including salaries, bonuses, benefits and stock-based compensation expense), direct marketing expenses, audit and legal expenses, consulting costs, payor outreach programs and allocated overhead, including rent, information technology, equipment depreciation, and utilities. 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 obtained through acquisitions, such as our acquisitions of the Myriad MyPath Laboratory in May 2021, Cernostics in December 2021 and AltheaDx in April 2022.

Change in Fair Value of Contingent Consideration

Change in fair value of contingent consideration is associated with our acquisitions of Cernostics and AltheaDx and the related additional contingent consideration of up to $50.0 million and $75.0 million, respectively, payable based on the achievement of certain commercial milestones relating to the year ending December 31, 2022 in the case of Cernostics, and the years ending December 31, 2022, 2023 and 2024, in the case of AltheaDx. No amounts were paid relating to the year ended December 31, 2022 for Cernostics and AltheaDx since the applicable commercial milestones were not achieved.

Interest Income

Interest income consists primarily of earnings on cash and cash equivalents, primarily money market funds, and marketable investment securities, primarily short-term U.S. government obligations.

Interest Expense

Interest expense is primarily attributable to finance leases.

Income Tax (Benefit) Expense

In connection with our acquisitions of AltheaDx in April 2022 and Cernostics in December 2021, and taking into consideration the additional deferred tax liabilities resulting from such acquisitions, we determined that a portion of our valuation allowance should be reduced, which was reflected in our income tax benefit for the years ended December 31, 2022 and 2021, respectively. Our consolidated financial statements do not reflect any federal or state income tax benefits attributable to the pre-tax losses we have incurred, due to the uncertainty of realizing a benefit from those items. As of December 31, 2022, we had federal NOL carryforwards of $207.2 million, of which $106.1 million will begin to expire in 2029 if not utilized to offset federal taxable income, and $101.1 million may be carried forward indefinitely. Also, as of December 31, 2022, we had state NOL carryforwards of $114.0 million, which begin to expire in 2028 if not utilized to offset state taxable income.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

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

	Years Ended December 31,			
	2022	2021	Change	
Net revenues	$ 137,039	$ 94,085	$ 42,954	45.7 %
Operating expenses and other operating income:				
Cost of sales (exclusive of amortization of acquired intangible assets)	32,009	15,822	16,187	102.3 %
Research and development	44,903	29,646	15,257	51.5 %
Selling, general and administrative	143,003	86,738	56,265	64.9 %
Amortization of acquired intangible assets	8,266	1,958	6,308	322.2 %
Change in fair value of contingent consideration	(18,287)	—	(18,287)	NA
Total operating expenses, net	209,894	134,164	75,730	56.4 %
Operating loss	(72,855)	(40,079)	(32,776)	(81.8)%
Interest income	3,968	68	3,900	NM
Interest expense	(17)	(1)	(16)	NM
Loss before income taxes	(68,904)	(40,012)	(28,892)	(72.2)%
Income tax benefit	(1,766)	(8,720)	6,954	79.7 %
Net loss	$ (67,138)	$ (31,292)	$ (35,846)	(114.6)%

(1) NA = Not applicable
(2) NM = Not meaningful

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

	Years Ended December 31,		
	2022	2021	Change
Dermatologic[(1)]	$ 124,809	$ 85,753	$ 39,056
Other[(2)]	12,230	8,332	3,898
Total net revenues	$ 137,039	$ 94,085	$ 42,954

(1) Consists of DecisionDx-Melanoma, DecisionDx-SCC and Diagnostic GEP offering.
(2) Consists primarily of DecisionDx-UM. Also includes TissueCypher and IDgenetix.

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

	Years Ended December 31,		
	2022	2021	Change
Net revenues	$ 137,039	$ 94,085	$ 42,954
Less: Cost of sales (exclusive of amortization of acquired intangible assets)	32,009	15,822	16,187
Less: Amortization of acquired intangible assets	8,266	1,958	6,308
Gross margin	$ 96,764	$ 76,305	$ 20,459
Gross margin percentage	70.6 %	81.1 %	(10.5)%

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

	Years Ended December 31,		
	2022	2021	Change
Cost of sales (exclusive of amortization of acquired intangible assets)	$ 3,755	$ 2,058	$ 1,697
Research and development	7,635	4,522	3,113
Selling, general and administrative	24,931	15,160	9,771
Total stock-based compensation expense	$ 36,321	$ 21,740	$ 14,581

Net Revenues

Net revenues for the year ended December 31, 2022 increased by $43.0 million, or 45.7%, to $137.0 million compared to the year ended December 31, 2021 due to a $39.1 million increase in revenue from our dermatologic tests and a $3.9 million increase in revenue from our other tests (non-dermatologic).

The increase from our dermatologic tests was primarily attributable to a 36.8% increase in DecisionDx-Melanoma test report volumes, due to a combination of the effects of our dermatologic sales force expansion during the second quarter of 2021 and increased patient flow potentially attributable to the easing of COVID-19 restrictions. The higher dermatologic revenues also reflect an increase in DecisionDx-SCC revenues primarily due to the Medicare payments discussed above, representing approximately 35.6% of the increase in dermatologic revenue.

The increase in revenue from our other tests (non-dermatologic) of $3.9 million was primarily attributable to TissueCypher, acquired with Cernostics in December 2021 and IDgenetix, acquired with AltheaDx in April 2022. See Note 6 to the consolidated financial statements for additional information on recent acquisitions.

The increases in total revenue were partially offset by the effect of variations in revenue adjustments related to tests delivered in previous periods, associated with changes in estimated variable consideration, which were $2.0 million of net negative revenue adjustments for the year ended December 31, 2022 compared to $3.3 million of net positive revenue adjustments for the year ended December 31, 2021. The year-over-year decrease is primarily attributable to the effect of favorable adjustments related to the settlement and collection during the year ended December 31, 2021 of certain groups of receivables from prior years that did not recur during the year ended December 31, 2022.

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, 2022 increased by $16.2 million, or 102.3%, compared to the year ended December 31, 2021, primarily due to higher personnel costs, increased expenditures on supplies and third-party services. Personnel costs increased in 2022 along with headcount in our laboratory testing operations, including headcount increases attributable to our acquisitions of Cernostics and AltheaDx. The increased personnel costs also reflect higher salaries and wages for existing employees. Supply and service expenses have increased due to higher laboratory activity, which is attributable to higher test volumes. Due to the nature of our business, a significant portion of our cost of sales expenses represents 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 expenses (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, gastrointestinal, mental health and pipeline tests.

Gross Margin

Our gross margin percentage was 70.6% for the year ended December 31, 2022, compared to 81.1% for the same period in 2021. The decrease was primarily due to higher personnel costs attributable to investments in laboratory headcount as well as higher rates of pay, higher amortization expense associated with our acquired intangible assets, and variations in revenue adjustments related to tests delivered in previous periods. In the near term, we expect that our gross margin percentage will be lower, compared to prior periods, 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 continue to be negatively impacted by amortization of intangible assets associated with recent acquisitions.

Research and Development

Research and development expenses increased by $15.3 million, or 51.5%, for the year ended December 31, 2022, compared to the year ended December 31, 2021. Approximately 65.6% of the increase is attributable to higher personnel costs, primarily due to expansions in headcount in support of our growth, higher pay rates and higher stock-based compensation expense, and approximately 9.7% is attributable to higher costs for clinical studies, including costs related to our IDENTITY and CONNECTION studies. The remainder of the increase is primarily associated with meeting costs, travel expenses, and materials and supplies. We expect to continue to increase our research and development expenses as we fund ongoing evidence development related to our existing products as well as additional pipeline programs.

Selling, General and Administrative

The following table provides a breakdown of SG&A expenses (in thousands):

	Years Ended December 31,		
	2022	2021	Change
Sales and marketing	$ 86,607	$ 48,965	$ 37,642
General and administrative	56,396	37,773	18,623
Total selling, general and administrative expense	$ 143,003	$ 86,738	$ 56,265

Sales and marketing expense increased by $37.6 million, or 76.9%, for the year ended December 31, 2022 compared to the year ended December 31, 2021. Approximately $23.1 million, or 61.4% of the increase is attributable to higher personnel costs including salaries, stock-based compensation and bonuses. Personnel costs have increased through the expansion of our dermatology-facing commercial team headcount to the mid-60s during the second quarter of 2021, through our acquisitions of Cernostics in December 2021 and AltheaDx in April 2022, and through the expansion of our outside sales territories and sales force in September 2022, as discussed under “Commercial Expansion Efforts” above. In addition to increases through sales force expansion, higher personnel costs also reflect salary increases for members of our existing sales force. The remainder of the increase in sales and marketing expenses was primarily associated with travel, training events and conferences fees. The higher expenses for training events and travel reflect an increase in our sales and commercial operations related to our expanded headcount and expanded test offerings, as well a return to more in-person activities resulting from the continued easing of COVID-19 restrictions. Stock-based compensation expense included in sales and marketing was $12.3 million for the year ended December 31, 2022 compared to $7.2 million for the year ended December 31, 2021.

General and administrative expenses increased by $18.6 million, or 49.3%, for the year ended December 31, 2022, compared to the year ended December 31, 2021. The increase is primarily attributable to $12.2 million in higher personnel costs including salaries, stock-based compensation and bonuses. The higher personnel costs reflect expanded headcount in our administrative support functions, including that related to the acquisitions of Cernostics and AltheaDx, as well as higher rates of salaries and wages. Stock-based compensation expense included in general and administrative expense was $12.7 million for the year ended December 31, 2022, compared to $7.9 million for the year ended December 31, 2021. Furthermore, professional fees increased by $3.9 million, partially due to $1.7 million related to the transaction costs associated with our acquisition of AltheaDx during the year ended December 31, 2022. The remainder of the increase in general and administrative expenses was primarily associated with other general increases.

Amortization of Acquired Intangible Assets

Amortization of acquired intangible assets increased by $6.3 million for the year ended December 31, 2022, compared to the year ended December 31, 2021. The increase is primarily associated with amortization of developed technology attributable to the acquisitions of Myriad MyPath Laboratory, Cernostics and AltheaDx in May 2021, December 2021 and April 2022, respectively. Amortization of acquired intangible assets is projected to be approximately $9.0 million for the year ending December 31, 2023.

Change in Fair Value of Contingent Consideration

The change in fair value of contingent consideration for the year ended December 31, 2022 of $18.3 million, a net gain, compared to the year ended December 31, 2021, is related to the final remeasurement of the contingent consideration associated with our acquisition of Cernostics.

Interest Income

Interest income increased by $3.9 million for the year ended December 31, 2022, compared to the year ended December 31, 2021, primarily as a result of higher interest rates and our purchases of marketable investment securities.

Income Tax Benefit

Income tax benefit was $1.8 million for the year ended December 31, 2022 compared to $8.7 million for the year ended December 31, 2021.

Substantially all of the income tax benefit in the year ended December 31, 2022 was primarily attributable to a reduction of $1.6 million in our valuation allowance on net deferred tax assets resulting from our acquisition of AltheaDx in April 2022. 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.

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, we recorded minimal amounts in income tax benefit because in both the year ended December 31, 2022 and 2021, the income tax benefit of the pre-tax 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 $36.3 million for the year ended December 31, 2022 compared to $21.7 million for the year ended December 31, 2021. We expect material increases in stock-based compensation expense in future periods, reflecting mainly higher awards outstanding due to growth in our headcount. As of December 31, 2022, we had 543 employees compared to 345 as of December 31, 2021. As of December 31, 2022, the total unrecognized stock-based compensation cost related to outstanding awards was $131.6 million, which is expected to be recognized on a straight-line basis over a weighted-average period of 3.0 years. We expect to continue granting stock-based compensation awards, which we expect to further contribute to increases in stock-based compensation expense in future periods.

Liquidity and Capital Resources

Sources of Liquidity

Our principal sources of liquidity are our cash and cash equivalents, marketable investment securities and cash generated from the sale of our products. All of our marketable investment securities are considered investment grade, are readily available for use in current operations and have contractual maturities of one year or less. As of December 31, 2022, we had marketable investment securities of $135.7 million, and we had no such balance as of December 31, 2021. As of December 31, 2022 and 2021, we had cash and cash equivalents of $122.9 million and $329.6 million, respectively.

Since becoming a public company, our liquidity has been primarily derived from 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, marketable investment securities and anticipated cash generated from sales of our products will be sufficient to fund our operations for at least the next 12 months and for the foreseeable future. However, we have based these estimates on assumptions that may prove to be wrong, and could result in us depleting our capital resources sooner than expected.

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 allowed 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. Upon filing of this Annual Report Form 10-K, we will no longer qualify as a well-known seasoned issuer as our non-affiliate market capitalization will be less than $700 million during the 60-day period prior to the filing of this Annual Report, and as a result this registration statement is no longer effective. We intend on filing a new shelf registration statement later in 2023.

As mentioned above, we expect to use a portion of our cash and cash equivalents and marketable investment securities to further support and accelerate our research and development activities, including the clinical studies noted above in “Components of the Results of Operations—Research and Development.”

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. On December 18, 2020, we issued and sold 4,600,000 shares of our common stock 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. 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 December 2021, we acquired Cernostics for $30.7 million in cash and in April 2022, we acquired AltheaDx, for $30.5 million in cash and $17.1 million in shares of our common stock. Under the definitive agreement to acquire Cernostics, we also agreed to pay up to an additional $50.0 million of additional contingent consideration based on the achievement of certain commercial milestones relating to the year ending December 31, 2022. However, based on the actual outcome of the commercial milestones for the year ended December 31, 2022, none of the $50.0 million in additional contingent consideration was earned, and therefore we have no further obligation to make any such payments. With respect to AltheaDx, we agreed to pay additional contingent consideration of up $75.0 million, 50% in cash and 50% in common stock, based on the achievement of certain commercial milestones relating to the years ending December 31, 2022, 2023 and 2024. The portion associated with the commercial milestones for the year ended December 31, 2022 will not be paid since the applicable commercial milestones were not met. This portion represented $35.0 million of the $75.0 million total potential payment obligation, exclusive of a potential catch-up payment in 2023 of $17.5 million which will become payable if all 2023 commercial milestones are fully met. Therefore, a potential payment obligation of up to $57.5 million with respect to the remaining commercial milestones for 2023 and 2024 remains as of December 31, 2022. In each case, the number of shares of our common stock that may be issued in connection with the commercial milestone payments is subject to limitations, as discussed in Notes 6 and 11 to the consolidated financial statements. Our actual liability with respect to these commercial milestone payments from our acquisitions will depend, in part, on our ability to successfully integrate IDgenetix (acquired from AltheaDx) into our suite of commercial product offerings and the timing thereof. See Note 6 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, 2022 we had a net loss of $67.1 million and an accumulated deficit of $160.9 million as of December 31, 2022. 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, marketable investment securities and anticipated cash generated from the sale of our commercial

products will be sufficient to fund our operations for at least the next 12 months and for the foreseeable future. We believe we will meet longer-term expected cash requirements and obligations through a combination of existing cash and cash equivalents, marketable investment securities and anticipated cash generated from sales of our products and issuances of equity securities or debt offerings. 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 clinicians, 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 Part 1, Item 1A., “Risk Factors” in this Annual Report on Form 10-K.

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, 2022 totaled approximately $23.5 million, of which $2.0 million is payable in 2023 and $21.6 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 may increase in the future 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 10 of 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,	
	2022	2021
Net cash used in operating activities	$ (41,655)	$ (18,983)
Net cash used in investing activities	(166,545)	(66,657)
Net cash provided by financing activities	1,515	5,421
Net change in cash and cash equivalents	(206,685)	(80,219)
Cash and cash equivalents, beginning of year	329,633	409,852
Cash and cash equivalents, end of year	$ 122,948	$ 329,633

Operating Activities

Net cash used in operating activities was $41.7 million for the year ended December 31, 2022, and was primarily attributable to the net loss of $67.1 million, the change in fair value of contingent consideration of $18.3 million, increases in accounts receivable of $6.2 million, deferred income taxes of $1.9 million, increases in inventory of $1.7 million and increases in accretion of discounts on marketable investment securities of $1.4 million, partially offset by non-cash stock-based compensation expense of $36.3 million, depreciation and amortization of $10.5 million and increases in accrued compensation of $8.5 million.

Net cash used in operating activities was $19.0 million for the year ended December 31, 2021, and 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.

Investing Activities

Net cash used in investing activities was $166.5 million for the year ended December 31, 2022 and consisted primarily of purchases of marketable investment securities of $134.7 million, the cash portion of the AltheaDx purchase consideration of $27.0 million (net of cash and cash equivalents acquired) and purchases of property and equipment of $5.6 million.

Net cash used in investing activities was $66.7 million for the year ended December 31, 2021 was primarily attributable to our asset acquisitions of Myriad MyPath Laboratory and Cernostics (which collectively totaled $63.2 million) and purchases of property and equipment of $3.5 million.

Financing Activities

Net cash provided by financing activities was $1.5 million for the year ended December 31, 2022, and consisted primarily of $2.5 million of proceeds from contributions to our 2019 Employee Stock Purchase Plan (the “ESPP”) and $0.8 million of proceeds from exercise of common stock options, partially offset by payment of employees’ taxes on vested RSUs of $1.7 million.

Net cash provided by financing activities was $5.4 million for the year ended December 31, 2021, and consisted primarily of $4.2 million of proceeds from exercise of common stock options and $2.3 million of proceeds from contributions to the ESPP, partially offset by payment of employees’ taxes on vested RSUs 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.

Inflation

In 2021, the rate of inflation in the United States began to increase and then rose to levels not experienced in over 40 years, but began subsiding in the second half of 2022. We are experiencing inflationary pressures, primarily in personnel costs and with certain lab supplies. We anticipate inflationary impacts on other cost areas in the future. 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 the extent to which the rate of inflation further increases, if at all, 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 and marketable investment securities may be further diminished, 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. As such, the effects of inflation may adversely impact our results of operations, financial condition and cash flows.

Critical Accounting Estimates

Our consolidated financial statements are prepared in accordance with U.S. GAAP. 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 clinician, 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. Our revenues are primarily 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, 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. We also provide a test for UM, DecisionDx-UM. We began offering the TissueCypher Barrett's Esophagus Test for patients with BE following an asset acquisition completed in December 2021. We began offering a proprietary PGx test service focused on mental health IDgenetix®, following a business combination completed in April 2022.

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. The payments for our services are primarily 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 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, 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 Medicare 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, 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, 2022 and 2021 were $1,987,000 of net negative revenue adjustments and $3,324,000 of net positive revenue adjustments, respectively, 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.

Stock-Based Compensation

Stock-based compensation expense for equity instruments issued to employees and non-employees, including stock options, RSUs, performance-based restricted stock units ("PSUs") and purchase rights issued under the 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 and PSUs, 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 awards with only service conditions, which is generally the awards' vesting period, typically four years for options and RSUs and the two-year offering period for the ESPP. PSUs vest upon the achievement of certain performance conditions and the provision of service with us through a specified period. Accruals of compensation cost for PSUs are based on the probable outcome of the performance conditions and are reassessed each reporting period. We recognize compensation cost for PSUs separately for each vesting tranche on a ratable basis over the requisite service period. The requisite service period for PSUs is based on an analysis of vesting requirements and performance conditions for the particular award. 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 the 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 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 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,	
	2022	2021
Average expected term (years)	5.8	6.1
Expected stock price volatility	68.34% - 75.02%	66.50% - 68.83%
Risk-free interest rate	1.54% - 4.21%	0.51% - 1.48%
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,	
	2022	2021
Average expected term (years)	1.3	1.2
Expected stock price volatility	62.98% - 91.78%	61.13% - 86.50%
Risk-free interest rate	0.60% - 3.45%	0.06% - 0.20%
Dividend yield	—%	—%

Intangible Assets and Goodwill

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.

Goodwill

Our goodwill is not amortized but is tested for impairment on an annual basis or whenever events or changes in circumstances indicate that it may be impaired. We perform annual impairment reviews of our goodwill balance during the fourth quarter of each year. We may perform a qualitative assessment to determine if it is necessary to perform a quantitative impairment test. If we determine that a quantitative impairment test is necessary, we apply the guidance in Accounting Standards Update ("ASU") No. 2017-04, *Intangibles—Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment*, by comparing the fair value of the reporting unit to its carrying value, including the goodwill. If the carrying value exceeds the fair value, we recognize an impairment loss for the amount by which the carrying value exceeds fair value, up to the total amount of goodwill allocated to the reporting unit. We did not incur any goodwill impairment losses in any of the periods presented. We have concluded that our business is comprised of a single reporting unit. For our annual impairment test for the year ended December 31, 2022, we elected to bypass the qualitative assessment and proceeded directly to the quantitative assessment by comparing our reporting unit's fair value to its carrying value. Since we have a single reporting unit, fair value of the reporting unit was measured at our total market capitalization on the impairment test date based on the closing price of our common stock. Our impairment test indicated that the fair value of our reporting unit substantially exceeded its carrying value. Factors that could result in an impairment of goodwill in the future include declines in the price of our common stock, increased competition, changes in macroeconomic developments and unfavorable government or regulatory developments.

Contingent Consideration

Under the terms of business combinations or asset acquisitions, we may be required to pay additional contingent consideration if specified future events occur or if certain conditions are met.

In a business combination, in accordance with ASC Topic 805, *Business Combinations*, contingent consideration is recorded at fair value as of the acquisition date and classified as liabilities or equity based on applicable U.S. GAAP. For contingent consideration classified as liabilities, we remeasure the contingent consideration at fair value each period with changes in fair value recorded in the statements of operations each period.

For contingent consideration in transactions that are not business combinations, we apply applicable U.S. GAAP. With respect to the additional contingent consideration that may be payable in connection with the acquisition of Cernostics, an asset acquisition we completed on December 3, 2021, we account for the contingent consideration as liability in accordance with ASC 480, *Distinguishing Liabilities from Equ*ity ("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 consolidated statements of operations each period.

Liabilities for contingent consideration are classified as a "Level 3" fair value measurements (as defined in Note 11 to our consolidated financial statements included in this Annual Report on Form 10-K) 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. For example, during the year ended December 31, 2022, as a result of a change in management's projections regarding the outcome of certain commercial milestones associated with our acquisition of Cernostics, the fair value of the related contingent consideration liability decreased by $18.3 million.

Recent Accounting Pronouncements

We have evaluated recently issued, but not yet effective, accounting pronouncements and do not believe that these accounting pronouncements will have any material impact on our consolidated financial statements or disclosures upon adoption.

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, 2022. Based upon the evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2022, 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 U.S. GAAP.

As of December 31, 2022, 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, 2022, our internal control over financial reporting was effective based on those criteria.

Our independent registered public accounting firm, KPMG LLP, has audited the effectiveness of our internal control over financial reporting as of December 31, 2022, 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 2022 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 2023 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 delinquent reports under Section 16(a) of the Exchange Act is to be included in the section entitled "Delinquent Section 16(a) Reports."

Such information is to 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 ever were to amend or waive any provision that applies to our principal executive officer, principal financial officer, principal accounting officer or any person performing similar functions, we intend to satisfy our disclosure obligations, if any, with respect to any such waiver or amendment by posting such information on our website, rather than by filing a Current Report on Form 8-K.

Item 11. Executive Compensation.

The information required by this item is to be included in the 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 the 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 the 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 the 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 the 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.
2.2^†	Agreement and Plan of Merger, dated April 4, 2022, by and among the Registrant, AltheaDx, Inc., Acorn Merger Sub, Inc. and Fortis Advisors LLC, incorporated by reference to Exhibit 2.1 of the Registrant's Current Report on Form 8-K filed with the SEC on April 4, 2022.
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.

Exhibit Number	Description of document
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.
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*+	Castle Biosciences, Inc. 2022 Inducement Plan.
10.12*+	Forms of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the Castle Biosciences, Inc. 2022 Inducement Plan.
10.13*+	Forms of Stock Option Grant Notice, Option Agreement and Notice of Exercise under the Castle Biosciences, Inc. 2022 Inducement Plan.
10.14*+	Non-Employee Director Compensation Policy, as amended effective January 31, 2023.
10.15+	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.
10.16*+	Castle Biosciences, Inc. Retirement Policy Approved January 13, 2023
10.17+	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.
10.18+	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.
10.19+	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.
10.20	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.
10.21	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.
10.22	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.
10.23	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.
10.24†	Fourth Amendment to Standard Office Lease, dated March 11, 2022, by and between the Registrant and Alturas Siete I, LLC, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed with the SEC on March 17, 2022.
10.25*†	Fifth Amendment to Standard Office Lease, dated October 24, 2022, by and between the Registrant and Alturas Siete I, LLC.
10.26	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.
10.27	First Amendment to Standard Office Lease, dated February 16, 2021, by and between the Registrant and Alturas Siete II, 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 February 9, 2023, by and between the Registrant and Alturas Siete, II, LLC.
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*	Second Amendment to Commercial Lease, executed December 15, 2022, by and between the Registrant and Tannos Land Holdings III, LLC.
10.33†	Lease Agreement, dated April 1, 2022, by and between the Registrant and ACA Concourse East Unit 3 LLC, incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q filed with the SEC on May 9, 2022.
10.34#	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.

\# 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.

† Certain schedules or exhibits have been omitted pursuant to Item 601(a)(5) of Regulation S-K. A copy of any omitted schedule or exhibit will be furnished to the SEC upon request; provided, however, that we may request confidential treatment pursuant to Rule 24b-2 of the Exchange Act for any schedule or exhibit so furnished.

^ Pursuant to Item 601(b)(2) 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, 2023

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
/s/ Derek J. Maetzold **(Derek J. Maetzold)**	President, Chief Executive Officer and Director (*Principal Executive Officer*)	February 28, 2023
/s/ Frank Stokes **(Frank Stokes)**	Chief Financial Officer (*Principal Financial and Accounting Officer*)	February 28, 2023
/s/ Daniel M. Bradbury **(Daniel M. Bradbury)**	Chairperson of the Board of Directors	February 28, 2023
/s/ Mara G. Aspinall **(Mara G. Aspinall)**	Member of the Board of Directors	February 28, 2023
/s/ Kimberlee S. Caple **(Kimberlee S. Caple)**	Member of the Board of Directors	February 28, 2023
/s/ G. Bradley Cole **(G. Bradley Cole)**	Member of the Board of Directors	February 28, 2023
/s/ Ellen Goldberg **(Ellen Goldberg)**	Member of the Board of Directors	February 28, 2023
/s/ Miles D. Harrison **(Miles D. Harrison)**	Member of the Board of Directors	February 28, 2023
/s/ Tiffany P. Olson **(Tiffany P. Olson)**	Member of the Board of Directors	February 28, 2023

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

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

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Castle Biosciences, Inc. and subsidiaries (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2022, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2022, 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 consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022 based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

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

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

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

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (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.

Critical Audit Matters

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

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 $137.0 million for the year ended December 31, 2022, 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.

Valuation of developed technology acquired in business combination

As discussed in Note 6 to the consolidated financial statements, on April 26, 2022, the Company acquired 100% of the equity interests in AltheaDx, Inc. for total consideration transferred of $47.6 million. As a result of the acquisition, the Company recorded an intangible asset comprised of developed technology in the amount of $35.0 million, based on the estimated acquisition-date fair value. The transaction was accounted for as a business combination.

We identified the assessment of the acquisition-date fair value of the developed technology intangible asset as a critical audit matter. Key assumptions used to estimate the fair value of the developed technology included the projected revenues, projected EBITDA and the discount rate. Evaluating the key assumptions involved challenging auditor judgment as they represent subjective determinations of future performance, as well as future market and economic conditions. Additionally, the audit effort associated with evaluating the fair value of the developed technology required specialized skills and knowledge.

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 Company's determination of the acquisition-date fair value of the developed technology intangible asset, including controls related to the development of the projected revenues, projected EBITDA and discount rate assumptions. We

assessed the reasonableness of the Company's projected revenues and EBITDA by comparing them to relevant industry data and other third-party information. In addition, we involved valuation professionals with specialized skills and knowledge who:

- assisted in evaluating the discount rate used in the valuation by comparing the inputs to publicly available data for comparable entities
- tested the estimate of the fair value of the developed technology using the Company's cash flow forecasts and the discount rate
- compared the result to the Company's fair value estimate.

/s/ KPMG LLP

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

San Diego, California
February 28, 2023

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

	December 31,	
	2022	2021
ASSETS		
Current Assets		
Cash and cash equivalents	$ 122,948	$ 329,633
Marketable investment securities	135,677	—
Accounts receivable, net	23,476	17,282
Inventory	3,980	2,021
Prepaid expenses and other current assets	6,207	4,807
Total current assets	292,288	353,743
Long-term accounts receivable, net	1,087	1,308
Property and equipment, net	14,315	9,501
Operating lease assets	12,181	7,383
Goodwill and other intangible assets, net	126,348	88,922
Other assets – long-term	1,110	1,715
Total assets	$ 447,329	$ 462,572
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities		
Accounts payable	$ 4,731	$ 2,546
Accrued compensation	24,358	15,483
Operating lease liabilities	1,777	1,179
Other accrued and current liabilities	5,262	5,678
Total current liabilities	36,128	24,886
Noncurrent portion of contingent consideration	—	18,287
Noncurrent operating lease liabilities	11,533	6,900
Deferred tax liability	428	635
Other liabilities	90	124
Total liabilities	48,179	50,832
Commitments and Contingencies (Note 12)		
Stockholders' Equity		
Preferred stock, $0.001 par value; 10,000,000 shares authorized as of December 31, 2022 and 2021; no shares issued and outstanding as of December 31, 2022 and 2021.	—	—
Common stock, $0.001 par value; 200,000,000 authorized as of December 31, 2022 and 2021; 26,553,681 and 25,378,520 shares issued and outstanding as of December 31, 2022 and 2021, respectively.	27	25
Additional paid-in capital	560,409	505,482
Accumulated deficit	(160,905)	(93,767)
Accumulated other comprehensive loss	(381)	—
Total stockholders' equity	399,150	411,740
Total liabilities and stockholders' equity	$ 447,329	$ 462,572

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

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

	Years Ended December 31,	
	2022	**2021**
NET REVENUES	$ 137,039	$ 94,085
OPERATING EXPENSES AND OTHER OPERATING INCOME		
Cost of sales (exclusive of amortization of acquired intangible assets)	32,009	15,822
Research and development	44,903	29,646
Selling, general and administrative	143,003	86,738
Amortization of acquired intangible assets	8,266	1,958
Change in fair value of contingent consideration	(18,287)	—
Total operating expenses, net	209,894	134,164
Operating loss	(72,855)	(40,079)
Interest income	3,968	68
Interest expense	(17)	(1)
Loss before income taxes	(68,904)	(40,012)
Income tax benefit	(1,766)	(8,720)
Net loss	$ (67,138)	$ (31,292)
Loss per share, basic and diluted	$ (2.58)	$ (1.24)
Weighted-average shares outstanding, basic and diluted	26,054	25,137

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

CASTLE BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)

	Years Ended December 31,	
	2022	**2021**
Net loss	$ (67,138)	$ (31,292)
Other comprehensive loss:		
Net unrealized loss on available-for-sale securities	(381)	—
Comprehensive loss	$ (67,519)	$ (31,292)

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	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
BALANCE, JANUARY 1, 2021	—	$ —	24,812,487	$ 25	$ 478,162	$ (62,496)	$ —	$ 415,691
Adoption of ASC 842	—	—	—	—	—	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
Stock-based compensation expense	—	—	—	—	36,321	—	—	36,321
Exercise of common stock options	—	—	148,735	1	832	—	—	833
Issuance of common stock from vested restricted stock units and payment of employees' taxes	—	—	183,887	—	(1,688)	—	—	(1,688)
Issuance of common stock under the employee stock purchase plan	—	—	78,652	—	2,352	—	—	2,352
Issuance of common stock in acquisition of business	—	—	763,887	1	17,110	—	—	17,111
Net unrealized loss on marketable investment securities	—	—	—	—	—	—	(381)	(381)
Net loss	—	—	—	—	—	(67,138)	—	(67,138)
BALANCE, DECEMBER 31, 2022	—	$ —	26,553,681	$ 27	$ 560,409	$ (160,905)	$ (381)	$ 399,150

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,	
	2022	2021
OPERATING ACTIVITIES		
Net loss	$ (67,138)	$ (31,292)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	10,543	3,407
Stock-based compensation expense	36,321	21,740
Change in fair value of contingent consideration	(18,287)	—
Deferred income taxes	(1,877)	(8,736)
Accretion of discounts on marketable investment securities	(1,368)	—
Other	158	—
Change in operating assets and liabilities:		
Accounts receivable	(6,218)	(4,631)
Prepaid expenses and other current assets	(1,224)	617
Inventory	(1,680)	327
Operating lease assets	991	931
Other assets	618	(180)
Accounts payable	582	(182)
Operating lease liabilities	(608)	(852)
Accrued compensation	8,495	6,208
Medicare advance payment	—	(8,350)
Other accrued and current liabilities	(963)	2,286
Other liabilities	—	(276)
Net cash used in operating activities	(41,655)	(18,983)
INVESTING ACTIVITIES		
Purchases of property and equipment	(5,632)	(3,483)
Asset acquisitions, net of cash and cash equivalents acquired	547	(63,184)
Acquisition of business, net of cash and cash equivalents acquired	(26,966)	—
Proceeds from sale of property and equipment	195	10
Purchases of marketable investment securities	(134,689)	—
Net cash used in investing activities	(166,545)	(66,657)
FINANCING ACTIVITIES		
Payment of common stock offering costs	—	(336)
Proceeds from exercise of common stock options	833	4,234
Payment of employees' taxes on vested restricted stock units	(1,688)	(781)
Proceeds from contributions to the employee stock purchase plan	2,492	2,312
Repayment of principal portion of finance lease liabilities	(122)	(8)
Net cash provided by financing activities	1,515	5,421

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

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

	Years Ended December 31,	
	2022	**2021**
NET CHANGE IN CASH AND CASH EQUIVALENTS	(206,685)	(80,219)
Beginning of year	329,633	409,852
End of year	$ 122,948	$ 329,633
SUPPLEMENTAL DISCLOSURE OF CASH PAID FOR:		
Interest	$ 16	$ 1
Income taxes	$ 120	$ 16
DISCLOSURE OF NON-CASH INVESTING AND FINANCING ACTIVITIES:		
Accrued purchases of property and equipment	$ 1,396	$ 33
Common stock issued in acquisition of business	$ 17,111	$ —
Operating lease assets obtained in exchange for lease obligations	$ 6,075	$ 2,892
Asset acquisition, liability for contingent consideration	$ —	$ 18,287
Property and equipment acquired with tenant improvement allowance	$ 51	$ 54
Asset acquisition, receivable for purchase price adjustment	$ —	$ 519

The accompanying notes are an integral part of these 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 clinicians and their patients with personalized, clinically actionable information to inform treatment decisions and improve health outcomes. We are based in Friendswood, Texas (a suburb of Houston, Texas) and our laboratory operations are conducted at our facilities located in Phoenix, Arizona and Pittsburgh, Pennsylvania.

We have a history of recurring net losses and negative cash flows and as of December 31, 2022, we had an accumulated deficit of $160.9 million. We believe our marketable investment securities of $135.7 million, cash and cash equivalents of $122.9 million as of December 31, 2022 and revenue from our test reports will be sufficient to meet our anticipated cash requirements through at least the 12-month period following the date that these consolidated financial statements were issued.

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.

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 goodwill impairment test, 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.

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.

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.

Marketable Investment Securities

All debt securities are recognized in accordance with Financial Accounting Standards Board (‘‘FASB’’) Accounting Standards Codification (‘‘ASC’’) Topic 320, *Investments-Debt Securities* (‘‘ASC 320’’). Management determines the appropriate classification of securities at the time of purchase and re-evaluates such determination at each balance sheet date. All debt securities are classified as available-for-sale and are recorded at fair value in accordance with ASC 320. We recognize the unrealized gains and losses related to changes in fair value as a separate component

of accumulated other comprehensive loss within total stockholders' equity, net of related deferred income tax effects on our consolidated balance sheets. Premiums or discounts from par value are amortized to interest income over the life of the underlying investment. Realized gains and losses on available-for-sale securities are calculated at the individual security level and included in interest income in the consolidated statements of operations. Impairments on available-for-sale debt securities, if any, are recorded in consolidated statements of operations. See Notes 5 and 11 for further details.

Revenue Recognition

In accordance with ASC Topic 606, *Revenue from Contracts with Customers* ("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 clinician, 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 noncurrent assets. The estimated timing of payment utilized as a basis for classification as noncurrent 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, 2022 and 2021. 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, Phoenix, Arizona and Pittsburgh, Pennsylvania, 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 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.

Goodwill

Goodwill represents the excess of the purchase price over the fair value of the net tangible and intangible assets acquired in a business combination. In accordance with ASC Topic 350, *Intangibles—Goodwill and Other*, our goodwill is not amortized but is tested for impairment on an annual basis or whenever events or changes in circumstances indicate that it may be impaired. We perform annual impairment reviews of our goodwill balance

during the fourth quarter of each year. We may perform a qualitative assessment to determine if it is necessary to perform a quantitative impairment test. If we determine that a quantitative impairment test is necessary, we apply the guidance in Accounting Standards Update ("ASU") No. 2017-04, *Intangibles—Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment*, by comparing the fair value of the reporting unit to its carrying value, including the goodwill. If the carrying value exceeds the fair value, we recognize an impairment loss for the amount by which the carrying value exceeds fair value, up to the total amount of goodwill allocated to the reporting unit. We did not incur any goodwill impairment losses in any of the periods presented. We have concluded that our business is comprised of a single reporting unit. For our annual impairment test for the year ended December 31, 2022, we elected to bypass the qualitative assessment and proceeded directly to the quantitative assessment by comparing our reporting unit's fair value to its carrying value. Since we have a single reporting unit, fair value of the reporting unit was measured at our total market capitalization on the impairment test date based on the closing price of our common stock. Our impairment test indicated that the fair value of our reporting unit substantially exceeded its carrying value. Factors that could result in an impairment of goodwill in the future include declines in the price of our common stock, increased competition, changes in macroeconomic developments and unfavorable government or regulatory developments.

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 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, 2022 and 2021.

Acquisitions

We assess acquisitions under ASC Topic 805, *Business Combinations* ("ASC 805"), 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 contingent consideration if specified future events occur or if certain conditions are met.

In a business combination, in accordance with ASC 805, contingent consideration is recorded at fair value as of the acquisition date and classified as liabilities or equity based on applicable U.S. GAAP. For contingent consideration classified as liabilities, we remeasure the contingent consideration at fair value each period with changes in fair value recorded in the statements of operations each period.

For contingent consideration in transactions that are not business combinations, we apply U.S. GAAP. With respect to additional contingent consideration that must or may be settled by issuance of a variable number of shares, we account for the contingent consideration as a liability in accordance with ASC Topic 480, *Distinguishing Liabilities from Equity* ("ASC 480"). 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 each period.

Contingent consideration is classified as current or noncurrent in our consolidated balance sheets based on the contractual timing of future settlement. For additional information on the contingent consideration, see Notes 6 and 11.

Leases

Effective January 1, 2021, we account for leases in accordance with ASC Topic 842, *Leases (*"ASC 842"). 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. Upon adoption of ASC 842, effective January 1, 2021, we recognized operating lease ROU 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 10 for details on our leases.

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 ("R&D") costs are charged to operations as incurred. Advance payments for goods and services that will be used in future R&D 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 R&D services on behalf of us will be expensed as services are rendered or when the milestone is achieved.

R&D 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. Our 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. Our board of directors reviews and evaluates the performance against these objectives and ultimately determines the actual achievement levels attained. 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, 2022 and 2021, we accrued approximately $18,209,000 and $12,071,000, 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, 2022 and 2021, we provided a discretionary matching contribution of $3,525,000 and $2,036,000, respectively. The higher amount for the year ended December 31, 2022 primarily reflects an increase in the number of employees compared to the year ended December 31, 2021.

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, 2022 and 2021.

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") and performance-based restricted stock units ("PSUs"), the fair value is equal to the closing price of our common stock on the date of grant. For awards with only service conditions, we recognize compensation costs on a straight-line basis 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. PSUs vest upon the achievement of certain performance conditions and the provision of service with us through a specified period. Accruals of compensation cost for PSUs are based on the probable outcome of the performance conditions and are reassessed each reporting period. We recognize compensation cost for PSUs separately for each vesting tranche on a ratable basis over the requisite service period. The requisite service period for PSUs is based on an analysis of vesting requirements and performance conditions for the particular award. 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. Comprehensive loss is made up of net loss plus other comprehensive loss, if any.

CARES Act Payroll Tax Deferral

The CARES Act permitted 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% were 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 and the remaining $276,000 of such taxes were repaid during the year ended December 31, 2022.

3. Revenue

All of our revenues from contracts with customers are associated with the provision of diagnostic and prognostic testing services. Our revenues are primarily attributable to our DecisionDx®-Melanoma test for cutaneous melanoma. We also provide a test for patients with cutaneous squamous cell carcinoma, DecisionDx®-SCC, two tests for use in patients with suspicious pigmented lesions, MyPath® Melanoma and DiffDx®-Melanoma, a test for uveal melanoma ("UM"), DecisionDx®-UM, and a test for patients diagnosed with Barrett's esophagus ("BE"), the TissueCypher® Barrett's Esophagus Test. We also began offering a pharmacogenomics ("PGx") testing service focused on mental health, IDgenetix®, following a business combination completed in April 2022. 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. The payments for our services are primarily 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 Medicare are generally paid at a rate established on Medicare's Clinical Laboratory Fee Schedule or by the respective Medicare contractor within 30 days from receipt. Medicare claims that were either submitted to Medicare prior to the local coverage determination ("LCD") or other coverage commencement date or are not covered 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). A successful appeal at any of these levels may result in prompt payment.

In the absence of Medicare coverage, contractually established reimbursements rates or other coverage, 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 Medicare, including those claims undergoing appeal, is deemed to be fully constrained due to factors outside our influence (e.g., 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, 2022 and 2021 were $1,987,000 of net negative revenue adjustments and $3,324,000 of net positive revenue adjustments, respectively, 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.

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 solely of accounts receivable (both current and noncurrent) as of December 31, 2022 and 2021.

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.

Disaggregation of revenues

The table below provides the disaggregation of revenue by type (in thousands):

	Years Ended December 31,	
	2022	2021
Dermatologic	$ 124,809	$ 85,753
Other	12,230	8,332
Total net revenues	$ 137,039	$ 94,085

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 and prognostic 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 (noncurrent)	
	Year Ended December 31,		As of December 31,		As of December 31,	
	2022	2021	2022	2021	2022	2021
Medicare	53 %	57 %	28 %	24 %	*	*
Payor A	12 %	*	14 %	12 %	16 %	15 %
Payor B	*	*	*	10 %	*	*

* Less than 10%

There were no other third-party payors that individually accounted for more than 10% of the Company's total revenue or accounts receivable for the periods shown in the table above.

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, vesting of RSUs and PSUs or purchases under the ESPP. The treasury stock method is used to calculate the potential dilutive effect of these common stock equivalents. Contingently issuable PSU awards are included in the computation of diluted loss per share when the applicable performance criteria would be met and the common shares would be issuable if the end of the reporting period were the end of the contingency period. However, potentially dilutive shares are excluded from the computation of diluted loss per share when their effect is antidilutive.

Because we reported 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, 2022 and 2021

because to do so would be antidilutive or, in the case of PSUs, the applicable performance conditions have not yet been met (in thousands):

	Years Ended December 31,	
	2022	2021
Stock options	3,521	3,209
RSUs and PSUs	1,650	250
ESPP	146	62
Total	5,317	3,521

In addition, in connection with the acquisition of AltheaDx, Inc. ("AltheaDx"), we may be required to issue shares of our common stock to satisfy the contingent consideration obligations, pending the outcome of certain commercial and regulatory milestones, as required by the definitive agreement to acquire AltheaDx. For purposes of calculating diluted loss per share, no such shares were assumed to have been issued because none of the applicable conditions have been met to date. See Notes 6 and 11 for additional information.

5. Marketable Investment Securities

The following table presents our available-for-sale debt securities (in thousands):

	December 31, 2022			
		Unrealized		Estimated Fair Value
	Amortized Cost	Gains	Losses	
U.S. government securities	$ 136,058	$ —	$ (381)	$ 135,677
Total	$ 136,058	$ —	$ (381)	$ 135,677

We had no available-for-sale debt securities as of December 31, 2021.

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. We classify all investments as current assets, as these are readily available for use in current operations. The cost of securities sold is determined based on the specific identification method for purposes of recording gains and losses.

There were no realized gains or losses on sales of investments for the years ended December 31, 2022 and 2021.

We evaluated our investment portfolio under the available-for-sale debt securities impairment model guidance and determined our investment portfolio is comprised of low-risk, investment grade securities. As of December 31, 2022, unrealized losses on available-for-sale investments are not attributed to credit risk. We believe that an allowance for credit losses is unnecessary because the unrealized losses on certain of our marketable investment securities are due to market factors. No credit-related or noncredit-related impairment losses were recorded for the years ended December 31, 2022 and 2021. The allowance for credit losses was zero as of December 31, 2022 and 2021.

As of December 31, 2022, all of our available-for-sale debt securities had contractual maturities of one year or less. Accrued interest receivable is included in prepaid expenses and other current assets in our consolidated balance sheets. As of December 31, 2022 and 2021 the accrued interest receivable balance was immaterial and zero, respectively.

Additional information relating to the fair value of marketable investment securities can be found in Note 11.

6. 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. ("Cernostics"), which offers the TissueCypher Barrett's Esophagus Test 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 indemnification claims, if any. Our consolidated balance sheet at December 31, 2021 reflected a receivable for the post-closing purchase price adjustment, representing the difference between actual and estimated cash and working capital at closing, among other things. During the year ended December 31, 2022, we received cash of $547,000 in settlement of this receivable.

We 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 ended December 31, 2022 ("Cernostics Earnout Payments"). The portion of any Cernostics Earnout Payments that could have been settled in shares of our common stock was subject to certain limitations and the aggregate number of shares that could have been issued for the Cernostics Earnout Payments may not have exceeded 5,034,653 shares. Any Cernostics Earnout Payments in shares of our common stock would have been based on the volume weighted-average price of our common stock for the 15 trading days ending December 30, 2022. The Cernostics Earnout Payments represent contingent consideration. ASC 480 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 represented the fair value of the obligation as of the acquisition date. Our consolidated balance sheet at December 31, 2022 reflected a liability of zero for the Cernostics Earnout Payments since the applicable commercial milestones were not met. 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.

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 an assembled workforce of $563,000, with an estimated useful life of five years, and each is being amortized on a straight-line basis.

AltheaDx, Inc.

On April 26, 2022, we completed the acquisition of 100% of the equity interests in AltheaDx. AltheaDx offers the IDgenetix test, a PGx test focused on mental health. We believe this acquisition enabled us to expand upon our

existing portfolio of testing solutions in support of our growth strategy. We have concluded that the transaction represents a business combination under ASC 805. The financial results of AltheaDx have been included in our consolidated financial statements since the date of the acquisition. The amount of revenue from AltheaDx included in the consolidated statements of operations from the acquisition date through December 31, 2022 was $912,000. The loss attributable to AltheaDx included in the consolidated statements of operations from the acquisition date through December 31, 2022 was approximately $12,372,000. This amount does not reflect transaction costs from the acquisition or the effects of the valuation allowance reduction discussed in Note 15. Transaction costs associated with the acquisition were $1,711,000 for the year ended December 31, 2022 and were recognized as expenses in the consolidated statements of operations.

We have also agreed to pay up to an additional $75.0 million in cash and common stock in connection with the achievement of certain milestones based on 2022, 2023 and 2024 commercial milestones for the IDgenetix test (the "AltheaDx Earnout Payments"). Upon any achievement of each relevant milestone event, the associated payment will be paid 50% in cash and 50% in shares of our common stock based on a price per share equal to the volume-weighted-average price of our common stock for the 20 trading days as of the applicable milestone determination date. In accordance with the terms of the definitive agreement governing the acquisition of AltheaDx, the maximum number of shares of our common stock issuable to former AltheaDx security holders may not exceed 1,271,718 shares. Therefore, taking into consideration the number of shares already issued at closing, a maximum of 507,831 additional shares of our common stock remain issuable with respect to the AltheaDx Earnout Payments. In the event a number of shares in excess of 507,831 would otherwise be issuable in connection with the AltheaDx Earnout Payments, we will issue shares up to the maximum number permitted and pay cash for the remaining portion of the obligation. Contingent consideration liability associated with the AltheaDx Earnout Payments was zero as of the April 26, 2022 date of acquisition.

Our calculations of the consideration transferred and the purchase price allocation for the acquisition of AltheaDx are finalized as of December 31, 2022. During the measurement period, we recorded adjustments to accrued liabilities, income taxes, intangible assets, contingent consideration and the resulting goodwill after finalizing our valuation of these items.

The following table presents the acquisition-date fair value of the consideration transferred, summarizes the final allocation of the fair values of assets acquired and liabilities assumed in the acquisition of AltheaDx, and includes measurement period adjustments recorded during 2022 (in thousands, except for shares):

	April 26, 2022 (as initially reported)	Measurement Period Adjustments	April 26, 2022 (as adjusted)
Consideration Transferred			
Cash	$ 30,510	$ (8)	$ 30,502
Common stock (763,887 shares)	17,111	—	17,111
Contingent consideration	1,528	(1,528)	—
Total consideration transferred	$ 49,149	$ (1,536)	$ 47,613
Fair Value Allocation			
Cash and cash equivalents	$ 3,536	$ —	$ 3,536
Accounts receivable	302	—	302
Inventory	279	—	279
Prepaid expenses and other current assets	262	—	262
Property and equipment	314	—	314
Intangible asset	37,000	(2,000)	35,000
Other assets – long-term	12	—	12
Accounts payable	(231)	—	(231)
Accrued compensation	(380)	—	(380)
Other accrued and current liabilities	(532)	119	(413)
Deferred tax liabilities	(1,819)	147	(1,672)
Other liabilities	(88)	—	(88)
Net identifiable assets acquired	38,655	(1,734)	36,921
Goodwill	10,494	198	10,692
Total fair value of net assets assumed	$ 49,149	$ (1,536)	$ 47,613

The fair value of the common stock issued was measured using the April 26, 2022 closing price of $22.40 per share, as reported by the Nasdaq Global Market. A portion of the upfront cash and stock consideration is being held in escrow for a specified period following closing to secure indemnification claims, if any.

During the fourth quarter of 2022, we reversed losses originally recorded during the second and third quarters of 2022 that were associated with the remeasurement of contingent consideration before finalizing the valuation. Also during the fourth quarter of 2022, we recorded an immaterial adjustment to reduce the amortization expense associated with the intangible asset.

The intangible asset is comprised of developed technology with an estimated useful life of 15 years and is being amortized on a straight-line basis. The goodwill, which is not expected to be deductible for income tax purposes, was primarily attributable to potential future growth opportunities and the organized workforce.

Unaudited Pro Forma Financial Information

The following unaudited pro forma financial information for the years ended December 31, 2022 and 2021 combines our historical financial results and the results of AltheaDx, assuming that the companies were combined as of January 1, 2021, and includes adjustments for amortization expense from the acquired intangible assets and additional stock-based compensation expense. Nonrecurring pro forma adjustments consist of acquisition-related transaction costs of $1,711,000 and an income tax benefit of $1,626,000, both assumed to have been recognized during the year ended December 31, 2021 and therefore removed from the year ended December 31, 2022.

The following unaudited pro forma financial information (in thousands) is for informational purposes only and is not necessarily indicative of (i) the results of operations that would have been achieved if the acquisition had taken place as of January 1, 2021 or (ii) the results of operations that are expected in future periods:

	Pro Forma Data	
	Years Ended December 31,	
	2022	2021
Net revenues	$ 137,591	$ 94,671
Net loss	$ (72,819)	$ (41,764)

Related Parties

Derek J. Maetzold, our President and Chief Executive Officer ("CEO"), and a member of our board of directors, and Daniel M. Bradbury, the Chairperson of our board of directors, each served on the board of directors of AltheaDx until the acquisition of AltheaDx was completed, were direct or indirect beneficial owners of AltheaDx securities and received consideration in the transaction. Further, Frank Stokes, our Chief Financial Officer; Tobin W. Juvenal, our Chief Commercial Officer; Kristen Oelschlager, our Chief Operating Officer and certain immediate family members of Mr. Maetzold and Ms. Oelschlager were direct or indirect beneficial owners of AltheaDx securities and received consideration in the transaction. These individuals may receive additional contingent consideration in the form of the AltheaDx Earnout Payments if the relevant commercial and regulatory milestone events occur. Our entry into the definitive agreement to acquire AltheaDx was approved by our board of directors based upon the unanimous recommendation of a special transaction committee comprised entirely of independent members of our board of directors without any financial interest in AltheaDx or any conflict of interest with respect to the acquisition of AltheaDx.

7. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	As of December 31,	
	2022	2021
Lab equipment[(1)]	$ 9,721	$ 3,727
Leasehold improvements	5,171	5,044
Computer equipment	4,336	2,457
Furniture and fixtures	1,660	1,288
Construction-in-progress	1,275	27
Total	22,163	12,543
Less accumulated depreciation[(1)]	(7,848)	(3,042)
Property and equipment, net	$ 14,315	$ 9,501

(1) Includes lab equipment under a finance lease of $369 thousand and accumulated depreciation of $137 thousand as of December 31, 2022 and $237 thousand and accumulated depreciation of $8 thousand as of December 31, 2021.

Depreciation expense was recorded in the consolidated statements of operations as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Cost of sales (exclusive of amortization of acquired intangible assets)	$ 874	$ 478
Research and development	337	248
Selling, general and administrative	1,067	722
Total	$ 2,278	$ 1,448

8. Goodwill and Other Intangible Assets, Net

Goodwill

Information on the change in carrying value of our goodwill is presented below (in thousands):

	Goodwill
Balance, December 31, 2021	$ —
Acquisition of AltheaDx	10,692
Balance, December 31, 2022	$ 10,692

There were no accumulated impairments of goodwill as of December 31, 2022 or 2021. We had no goodwill as of December 31, 2021.

Other Intangible Assets, Net

Our other intangible assets, net consist of the following (in thousands):

	December 31, 2022			
	Gross carrying value	Accumulated amortization	Net	Weighted-Average Remaining Life (in years)
Developed technology	$ 125,317	$ (10,102)	$ 115,215	12.9
Assembled workforce	563	(122)	441	4.0
Total other intangible assets, net	$ 125,880	$ (10,224)	$ 115,656	

	December 31, 2021			
	Gross carrying value	Accumulated amortization	Net	Weighted-Average Remaining Life (in years)
Developed technology	$ 90,317	$ (1,949)	$ 88,368	13.2
Assembled workforce	563	(9)	554	4.9
Total other intangible assets, net	$ 90,880	$ (1,958)	$ 88,922	

The estimated future aggregate amortization expense as of December 31, 2022 is as follows (in thousands):

Years Ending December 31,	
2023	$ 9,013
2024	9,038
2025	9,013
2026	9,004
2027	8,901
Thereafter	70,687
Total	$ 115,656

Amortization expense of intangible assets was $8.3 million and $2.0 million for the years ended December 31, 2022 and 2021, respectively.

9. Other Accrued and Current Liabilities

Other accrued liabilities consisted of the following (in thousands):

	As of December 31,	
	2022	2021
Accrued service fees	$ 2,125	$ 1,905
Clinical studies	1,822	1,655
Employee stock purchase plan contributions	900	760
Payroll-related liabilities	37	695
Other	378	663
Total	$ 5,262	$ 5,678

10. 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 terms end in 2033 with options to renew for two additional five-year terms.

On April 1, 2022, we entered into a lease agreement for commercial office space in Pittsburgh, Pennsylvania, which provides for a term of 10.5 years, a five-year renewal option, an early termination clause and a lease incentive allowance of $2.5 million to apply toward leasehold improvements. In September 2022, we obtained access to the facilities and initiated leasehold improvement work. Lease payments will commence at a future date upon the completion of leasehold improvements, at which point the facilities will be ready for intended use. We intend to use the additional space for general office and laboratory facilities.

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 acquisitions of AltheaDx in April 2022 and Cernostics in December 2021, we assumed finance leases 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):

		As of December 31,	
Lease Balance	**Classification**	**2022**	**2021**
Lease Assets			
Operating	Operating lease assets	$ 12,181	$ 7,383
Finance	Property and equipment, net	$ 232	$ 229
Lease Liabilities			
Current			
Operating	Operating lease liabilities	$ 1,777	$ 1,179
Finance	Other accrued and current liabilities	$ 148	$ 105
Noncurrent			
Operating	Noncurrent operating lease liabilities	$ 11,533	$ 6,900
Finance	Other liabilities	$ 90	$ 124

Costs associated with our leases were included in the consolidated statement of operations as follows (in thousands):

	Years Ended December 31,	
Lease Cost	**2022**	**2021**
Operating lease cost[(1)]	$ 1,997	$ 1,450
Finance lease cost		
Amortization of lease assets	129	8
Interest on finance lease liabilities	16	1
Short-term lease cost	477	29
Total lease cost	$ 2,619	$ 1,488

(1) Includes variable lease cost of $371 thousand and $187 thousand for the years ended December 31, 2022 and 2021, respectively.

Other Information

Supplemental cash flow information on leases is as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Cash paid for amounts included in the measurement of lease liabilities		
Operating cash flows from operating leases	$ 1,283	$ 1,145
Operating cash flows from interest paid on finance leases	$ 16	$ 1
Financing cash flows from finance leases	$ 122	$ 8

Information regarding the weighted-average lease term and weighted-average discount rate is presented below:

	As of December 31,	
	2022	2021
Weighted-average remaining lease term (years)		
Operating leases	9.4	9.1
Finance leases	1.9	2.3
Weighted-average discount rate		
Operating leases	7.3 %	4.9 %
Finance leases	6.4 %	5.0 %

The following is a maturity analysis of our operating lease and finance lease liabilities as of December 31, 2022 (in thousands):

	Operating leases	Finance leases
Years Ending December 31,		
2023	$ 1,838	$ 153
2024	2,122	72
2025	2,014	30
2026	2,180	—
2027	2,219	—
Thereafter	12,921	—
Total lease payments	23,294	255
Less: Interest component	(9,984)	(17)
Present value of lease payments	$ 13,310	$ 238

As of December 31, 2022, we expect $0.7 million in undiscounted future lease payments for leases that had not yet commenced.

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.

The table below provides information 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, 2022 and 2021 (in thousands):

	As of December 31, 2022			
	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]	$ 108,673	$ —	$ —	$ 108,673
U.S. government securities[2]	$ 135,677	$ —	$ —	$ 135,677
Liabilities				
Contingent consideration[3]	$ —	$ —	$ —	$ —

	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
U.S. government securities[2]	$ —	$ —	$ —	$ —
Liabilities				
Contingent consideration[3]	$ —	$ —	$ 18,287	$ 18,287

(1) Classified as “Cash and cash equivalents” in the consolidated balance sheets.

(2) Classified as “Marketable investment securities” in the consolidated balance sheets.

(3) Current portion, if any, classified as “Other accrued and current liabilities” in the consolidated balance sheets.

Contingent Consideration

In connection with our acquisition of Cernostics, we recorded a contingent consideration liability for the additional contingent consideration of up to $50.0 million that could have been payable based on the achievement of certain commercial milestones relating to the year ending December 31, 2022. The Cernostics Earnout Payments could have been settled in cash or shares of our common stock, at our sole discretion. The portion of any Cernostics Earnout Payments that could have been settled in shares of our common stock were subject to certain limitations and the aggregate number of shares that could have been issued for the Cernostics Earnout Payments could not have exceeded 5,034,653 shares. Any Cernostics Earnout Payments in shares of our common stock could have been based on the volume weighted-average price of our common stock for the 15 trading days ending December 30, 2022. There were no Cernostics Earnout Payments that became payable because the commercial milestones were not achieved during the earnout period.

In connection with our acquisition of AltheaDx, we agreed to pay contingent consideration of up to $75.0 million based on the achievement of certain commercial milestones relating to the 2022, 2023, and 2024 commercial

milestones, as discussed further in Note 6. The portion of the AltheaDx Earnout Payments associated with the commercial milestones for the year ended December 31, 2022 will not be paid since the applicable commercial milestones were not met. This portion represented $35.0 million of the $75.0 million total potential payment obligation, exclusive of the catch-up payment in 2023 of $17.5 million which will become payable if all 2023 commercial milestones are fully met. Therefore, a potential payment obligation of up to $57.5 million with respect to the remaining commercial milestones for 2023 and 2024 remains as of December 31, 2022. If the settlement of the remaining portion of the Althea Earnout Payments were to occur as of December 31, 2022, no amounts would be due based on the achievement of the commercial milestones to date.

The contingent consideration was 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 for the Cernostics Earnout Payments used assumptions for expected volatility of the financial metrics and a risk-adjusted discount rate, which were 20.0% and 16.1%, respectively, as of December 31, 2021. The final valuation for the contingent consideration as of the date of acquisition was assessed to be zero and resulted in a measurement period adjustment. See Note 6 for additional information on the measurement period adjustment. Since the final valuation, there have been no changes in the fair value of the contingent consideration during the year ended December 31, 2022. The contingent consideration liability is remeasured at fair value at each reporting period taking into account any updated assumptions or changes in circumstances. Any changes in the fair value are recorded as gains or losses in our consolidated statement of operations. A measurement period adjustment was recognized in the fourth quarter of 2022 to reverse the preliminary valuation of the contingent consideration and losses recorded during the interim period.

The following table discloses the summary of changes in the contingent consideration liability measured at fair value using Level 3 inputs for the year ended December 31, 2022 (in thousands):

	Cernostics	AltheaDx	Total
Balance, December 31, 2021	$ 18,287	$ —	$ 18,287
Acquisition of AltheaDx	—	—	—
Change in fair value	(18,287)	—	(18,287)
Balance, December 31, 2022	$ —	$ —	$ —

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.

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, 2022 or 2021.

During the year ended December 31, 2021, we paid $336,000 in common stock offering costs related to a public offering of common stock completed in December 2020.

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. On December 22, 2022, our board of directors approved the 2022

Inducement Plan (the "Inducement Plan") to reserve 350,000 shares of our common stock that may be issued pursuant to awards made as an inducement material to the grantee's entering into employment with us to the extent such grantee was not previously an employee of ours or is entering into employment following a bona fide period of non-employment with us.

Options under the plans may be granted as incentive stock options ("ISO") or non-statutory stock options ("NSOs"). ISOs may only be granted to our employees (including directors who are also considered employees). NSOs may be granted to 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, 2022, we have granted awards for 1,473,888 shares in excess of the number of shares authorized for issuance under the 2019 Plan. The 2019 Plan provides for automatic annual increases to the number of shares authorized for issuance, equal to 5% of our common shares outstanding as of the immediately preceding year end, through January 1, 2029. Under this provision, effective January 1, 2023, an additional 1,327,684 shares became available under the 2019 Plan.

Stock Options

Stock option activity under our stock plans for the years ended December 31, 2022 and 2021 is set forth below:

	Stock Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Balance as of January 1, 2021	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	3,586,688	$ 34.75		
Granted	263,645	$ 22.35		
Exercised	(148,735)	$ 5.59		
Forfeited/Cancelled	(281,758)	$ 34.08		
Balance as of December 31, 2022	3,419,840	$ 35.11	7.5	$ 12,643
Exercisable at December 31, 2022	2,032,859	$ 30.09	7.0	$ 11,713

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, 2022 and 2021:

	Restricted Stock Units Outstanding	Weighted-Average Grant Date Fair Value
Balance as of January 1, 2021	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	1,050,174	$ 44.31
Granted	2,988,107	$ 23.15
Vested [(1)]	(257,708)	$ 45.14
Forfeited/Cancelled	(302,651)	$ 27.12
Balance as of December 31, 2022	3,477,922	$ 27.56

(1) The aggregate number of shares withheld upon vesting for employee tax obligations was 73,821 and 16,640 for the years ended December 31, 2022 and 2021, respectively.

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 CEO which we have determined to be outside the ordinary course of business. Under the 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 IRC, when calculating the number of shares of common stock owned, an individual must attribute all shares owned by specified family members. Because 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 RSUs designed to compensate the three children for these differences. The aggregate number of shares underlying the RSUs 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 were recognized as stock-based compensation expense, included in selling, general and administrative expenses, during the year ended December 31, 2021.

Performance-Based Restricted Stock Units

PSUs represent the right to receive shares of our common stock contingent upon the achievement of certain financial performance measures. We issue new shares to satisfy PSUs upon vesting.

The following table summarizes our PSU activity for the year ended December 31, 2022:

	Performance-Based Restricted Stock Units Outstanding	Weighted-Average Grant Date Fair Value
Balance as of December 31, 2021	—	$ —
Granted	196,033	$ 23.23
Vested	—	$ —
Forfeited/Cancelled	—	$ —
Balance as of December 31, 2022	196,033	$ 23.23

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, 2022, 814,599 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 265,536 shares becoming available under the ESPP effective January 1, 2023. We issue new shares to satisfy the 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.

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,	
	2022	2021
Average expected term (years)	5.8	6.1
Expected stock price volatility	68.34% - 75.02%	66.50% - 68.83%
Risk-free interest rate	1.54% - 4.21%	0.51% - 1.48%
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,	
	2022	2021
Average expected term (years)	1.3	1.2
Expected stock price volatility	62.98% - 91.78%	61.13% - 86.50%
Risk-free interest rate	0.60% - 3.45%	0.06% - 0.20%
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 as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Cost of sales (exclusive of amortization of acquired intangible assets)	$ 3,755	$ 2,058
Research and development	7,635	4,522
Selling, general and administrative	24,931	15,160
Total stock-based compensation expense	$ 36,321	$ 21,740

For the years ended December 31, 2022 and 2021, the weighted-average grant date fair value of stock options was $14.34 and $29.89 per option, respectively, and the weighted-average grant date fair value of the purchase rights granted under the ESPP was $16.79 and $27.60 per share, respectively. As of December 31, 2022, the total unrecognized stock-based compensation cost related to outstanding awards was $131,644,000, which is expected to be recognized on a straight-line basis over a weighted-average period of 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, 2022 and 2021 was $3,745,000 and $27,191,000, respectively. The aggregate intrinsic value of shares issued under the ESPP was $534,000 and $6,341,000 during

the years ended December 31, 2022 and 2021, respectively. The aggregate fair value of RSUs that vested during the years ended December 31, 2022 and 2021 was $5,863,000 and $2,698,000, respectively. No tax benefits related to stock-based compensation were recorded in the consolidated statements of operations during the years ended December 31, 2022 and 2021 due to the valuation allowance on net deferred tax assets.

15. Income Taxes

The components of income tax expense (benefit) are as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Current tax expense		
U.S. federal	$ —	$ —
State and local	111	16
Total current	111	16
Deferred tax benefit		
U.S. federal	(1,626)	(8,726)
State and local	(251)	(10)
Total deferred	(1,877)	(8,736)
Total income tax benefit	$ (1,766)	$ (8,720)

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,	
	2022	2021
Pre-tax loss	$ (68,904)	$ (40,012)
U.S. federal taxes at statutory rate	(14,470)	(8,402)
State income taxes	(3,751)	(1,764)
Research and development tax credit	(1,814)	(1,658)
Change in valuation allowance	17,075	2,570
Stock-based compensation	3,323	(880)
Non-deductible officers' compensation	1,326	1,571
Change in fair value of contingent consideration	(3,840)	—
Transaction costs	359	—
Other	26	(157)
Income tax benefit	$ (1,766)	$ (8,720)

Significant components of deferred tax assets and liabilities are as follows (in thousands):

	As of December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss ("NOL") carryforwards	$ 49,253	$ 24,316
Accrued liabilities	6,503	4,168
Capitalized R&D costs	6,738	—
Lease liabilities	3,549	2,114
Stock-based compensation	4,489	2,202
R&D tax credit	5,665	3,670
Other	445	240
Total deferred tax assets	76,642	36,710
Less valuation allowance	(49,953)	(17,774)
Deferred tax assets, net	$ 26,689	$ 18,936
Deferred tax liabilities:		
Prepaid expenses	$ (289)	$ (330)
Property and equipment	(3,269)	(2,285)
Intangible assets	(19,026)	(12,913)
ROU assets	(3,577)	(2,166)
Section 481(a) adjustment (cash to accrual)	(956)	(1,877)
Total deferred tax liabilities	(27,117)	(19,571)
Net deferred tax liability	$ (428)	$ (635)

At December 31, 2022, we had NOL carryforwards for federal income tax purposes of approximately $207,242,000 of which $106,093,000 will begin to expire in 2029 if not utilized to offset taxable income, and $101,149,000 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, 2022, we had state NOL carryforwards of approximately $114,041,000, which begin to expire in 2028 if not utilized to offset state taxable income. Our R&D tax credit carryforwards of $5,665,000 at December 31, 2022 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, 2022 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. We have also performed Section 382 analyses with respect to the NOLs we obtained in our acquisitions of Cernostics and AltheaDx. Based on changes in ownership that have occurred, $36,347,000 of NOLs are expected to expire unused as a result of Section 382 limitations.

During the years ended December 31, 2022 and 2021, in connection with the acquisitions of AltheaDx and Cernostics, we recorded additional net deferred tax liabilities of $1,672,000 and $9,371,000, respectively, primarily due to book-tax differences related to the acquired intangible assets. As a result of these additional deferred tax liabilities, we determined that $1,626,000 and $8,726,000 of our existing valuation allowance should be reduced, which was reflected in our income tax benefit for the years ended December 31, 2022 and 2021, respectively. At December 31, 2022 and 2021, we placed a valuation allowance of $49,953,000 and $17,774,000, 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, 2022 and 2021. We are generally no longer subject to tax examinations for U.S. federal income tax purposes for fiscal years prior to 2019 and fiscal years prior to 2018 for multiple state jurisdictions. However, since we have been in an NOL position since 2008, our 2008 to 2018 federal tax returns and our 2008 to 2017 state tax returns are potentially subject to examination adjustments to the extent of those NOL carryforwards.

CORPORATE OFFICES
Castle Biosciences, Inc.
505 S. Friendswood Drive, Suite 401
Friendswood, Texas 77546
866.788.9007

2023 ANNUAL MEETING
May 25, 2023, at 10:00 a.m. Eastern Time
Omni William Penn Hotel
530 William Penn Place
Pittsburgh, Pennsylvania 15219

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."

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 2022 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.

BOARD OF DIRECTORS

Daniel M. Bradbury
Chairman, Castle Biosciences, Inc.,
Executive Chairman, Equillium, Inc.,
Founder and Managing Member, BioBrit, LLC

Mara G. Aspinall
Managing Director, BlueStone Venture Partners,
Managing Member, Health Catalysts Group

Kimberlee S. Caple
Division President, Genetic Analysis Division,
Thermo Fisher Scientific

G. Bradley Cole
Former General Manager, Precision Oncology,
Exact Sciences Corporation

Ellen Goldberg
Founder & President, CHORD Consulting

Miles Harrison
Former President & General Manager for
North America, Galderma Laboratories L.P.

Tiffany P. Olson
Former President, Nuclear & Precision
Health Solutions, Cardinal Health

Derek J. Maetzold
Founder, President, CEO and Director,
Castle Biosciences, Inc.

EXECUTIVE OFFICERS

Derek J. Maetzold
Founder, President, CEO and Director

Tobin W. Juvenal
Chief Commercial Officer

Kristen M. Oelschlager
Chief Operating Officer

Frank Stokes
Chief Financial Officer

CASTLE BIOSCIENCES

505 S. Friendswood Drive, Suite 401
Friendswood, Texas 77546
866.788.9007

For more information, please visit **www.castlebiosciences.com**