



# Transforming Disease Management



January 9, 2023

# Disclaimers

## Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the “safe harbor” created by those sections. These forward-looking statements include, but are not limited to, statements concerning: our expectation that we will meet or exceed the top end of our range for total revenue guidance for our fiscal year ended December 31, 2022; our preliminary financial and operational results for our fourth quarter and fiscal year ended December 31, 2022, including our expected cash and cash equivalents and short-term investments as of December 31, 2022 and our expected number of total test reports during 2022; estimated sizes of the total addressable markets of our current and future commercial and pipeline products within our dermatologic, gastrointestinal and mental health franchises, and our anticipated actions to further the growth of these franchises and products in 2023 and beyond, and any resulting financial or operational metrics or related expectations with respect to future performance; our expectations regarding timelines and milestones for our dermatologic, gastrointestinal and mental health franchises; our three-year projections for revenue, adjusted gross margins, other operating expenses and net operating cash flow; the potential of DecisionDx-Melanoma to aid in risk-aligned treatment plans for improved patient outcomes and survival rates; the potential of TissueCypher testing to change clinical practice when incorporated into patient management plans; our expectation that we will achieve net operating cash flow positivity by 2025; our expectation that our focused growth investments will contribute to long-term profitability; our milestone expectations regarding the Palmetto/MolDx draft LCD for DecisionDx-SCC, finalization of a Palmetto/Noridian LCD for DiffDx-Melanoma by the end of Q2 2023, publication of a collaborative NCI study showing higher melanoma specific survival for patients tested with DecisionDx-Melanoma, new GI and MyPath/DiffDx commercial team expansion reaching optimal productivity in Q2 2023, expected closure of our San Diego lab by the end of 2022; components and drivers of our near-to mid-term growth and mid-to long-term growth; the impact, accuracy and effectiveness of our commercial and pipeline tests on physicians, patients and their treatment plans, and their individual or collective impact on our prospects and plans, including any objectives of management related thereto; the ability of our tests to provide valuable, clinically actionable information to clinicians and patients, improve health and guide patient care; expected expansion of outside sales territories; our progress roadmaps for our tests; expected launch dates for tests in our pipeline expansion and estimates regarding their total addressable markets or future success; expectations regarding LCD effective timeframes and reimbursement capabilities; the ability of our risk stratification tests to classify risk of metastasis in ways that better support risk-appropriate treatment than reliance on traditional clinicopathologic risk factors alone; integration timelines, growth expectations and strategic opportunities for our TissueCypher test and GI franchise, and our IDgenetix test and our mental health franchise; and our ability to integrate our recent acquisitions into our existing business and the ability of such acquisitions to complement our existing business.

The words “anticipates,” “believes,” “can,” “estimates,” “expects,” “plans,” “potential,” “preliminary,” “will” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. These forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from those in the forward-looking statements, including, without limitation: adjustments to our preliminary financial results resulting from, among other things, the completion of our end-of-period reporting processes and related activities, including the audit by our independent registered public accounting firm of our financial statements; the timing and amount of revenue we are able to recognize in a given fiscal period; the accuracy of our assumptions and expectations underlying our three-year revenue and other financial targets (including, without limitation, our assumptions or expectations regarding: (i) continued reimbursement for our DecisionDx-SCC test at the current rate and reimbursement for our other products and subsequent coverage decisions, (ii) our estimated total addressable markets for our products and product candidates and the related expenses, capital requirements and potential needs for additional financing, (iii) the anticipated cost, timing and success of our product candidates, and our plans to research, develop and commercialize new tests and (iv) our ability to successfully integrate new businesses, assets, products or technologies acquired through previously completed acquisitions); the effects of the COVID-19 pandemic on our business and our efforts to address its impact on our business; subsequent study or trial results and findings may contradict earlier study or trial results and findings or may not support the results discussed in this presentation, including with respect to the diagnostic and prognostic tests discussed in this presentation; actual application of our tests may not provide the aforementioned benefits to patients; and the risks set forth under the heading “Risk Factors” in our Quarterly Report on Form 10-Q for the three months ended September 30, 2022, and in our other filings with the SEC. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements, except as may be required by law.



# Preliminary Q4 2022 Information



January 9, 2023

# Castle Is Focused on Improving Health through Innovative Tests That Guide Patient Care



## Dermatology

Decision Dx  
► Melanoma

Decision Dx  
► SCC

MyPath | DiffDx  
► Melanoma



## Uveal Melanoma

Decision Dx  
► UM



## Gastroenterology

TissueCypher  
► Barrett's Esophagus



## Mental Health

IDgenetiX

Answering clinical questions to guide care along the patient journey

# Preliminary Fourth Quarter and Year-end 2022 Performance Results<sup>1,2</sup> (unaudited)

Expect to meet or exceed top end of guided range of \$132–\$137M<sup>3</sup> for 2022 total revenue

	4Q22	4Q21	2022	2021
Revenue	<b>To be announced</b>	\$25.0M	<b>Expected to meet or exceed top end of guided range<sup>2</sup></b>	\$94.1M
Total test reports	<b>12,563</b>	8,242	<b>44,338</b>	28,118
DecisionDx-Melanoma	<b>7,295</b>	5,635	<b>27,797</b>	20,328
DecisionDx-SCC	<b>1,844</b>	1,265	<b>5,966</b>	3,510
DGEP(MyPath/Diff-Dx)	<b>822</b>	904	<b>3,561</b>	2,662
DecisionDx-UM	<b>432</b>	438	<b>1,711</b>	1,618
TissueCypher	<b>996</b>		<b>2,094</b>	
IDgenetix	<b>1,174</b>		<b>3,209</b>	

## 2022 Year-end Cash, Cash Equivalents & Marketable Investment Securities Expected To Be Approximately \$259 million<sup>1</sup>

Cash, Cash Equivalents and Marketable Investment Securities			
As of 3/31/22 \$309M	As of 6/30/22 \$273M	As of 9/30/22 \$266M	<b>As of 12/31/22 ~\$259M (expected)</b>



# Transforming Disease Management



Third Quarter 2022

November 2, 2022

# Financial Performance Summary Q3 2022

	3Q21	3Q22	Nine Months Ended September 30, 2022
Total test reports	7,727	12,114	31,775
Total Derm test reports	7,352	9,824	27,363
Revenue	\$23.5M	\$37.0M	\$98.7M
Adj. Revenue <sup>1</sup>	\$23.6M	\$37.3M	\$100.6M
Gross Margin	77.9%	69.8%	71.1%
Adj. Gross Margin <sup>1</sup>	80.9%	76.2%	77.6%
Operating Cash Flow	\$(6.1)M	\$(5.2)M	\$(35.7)M
Adj. Operating Cash Flow <sup>1</sup>	\$(3.0)M	\$(5.2)M	\$(35.7)M
Cash, Cash Equivalents & Marketable Investment Securities	as of end of period \$363M	\$266M <sup>2</sup>	



## Mission

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Improving health through innovative tests that guide patient care



## Vision

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



## Values

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ExCIITE: Excitement, Collaboration, Integrity, Innovation, Trust and Excellence

# Three Strategic Guideposts That Create Value for Customers, Patients and Stockholders

## 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*



## Continuous Evolution & Improvement

*We are an industry leader by challenging the status quo with deep scientific expertise, unique value insight, and robust data development*



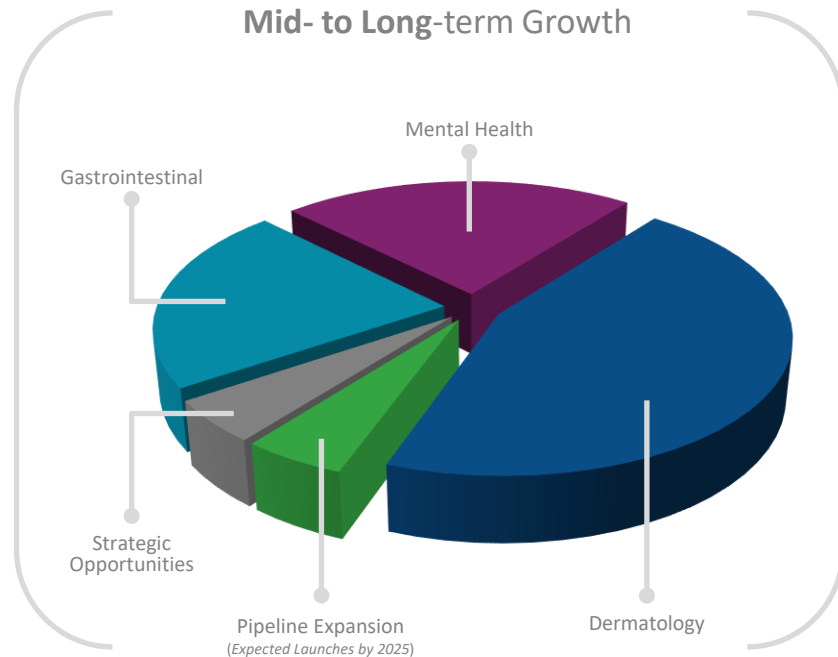
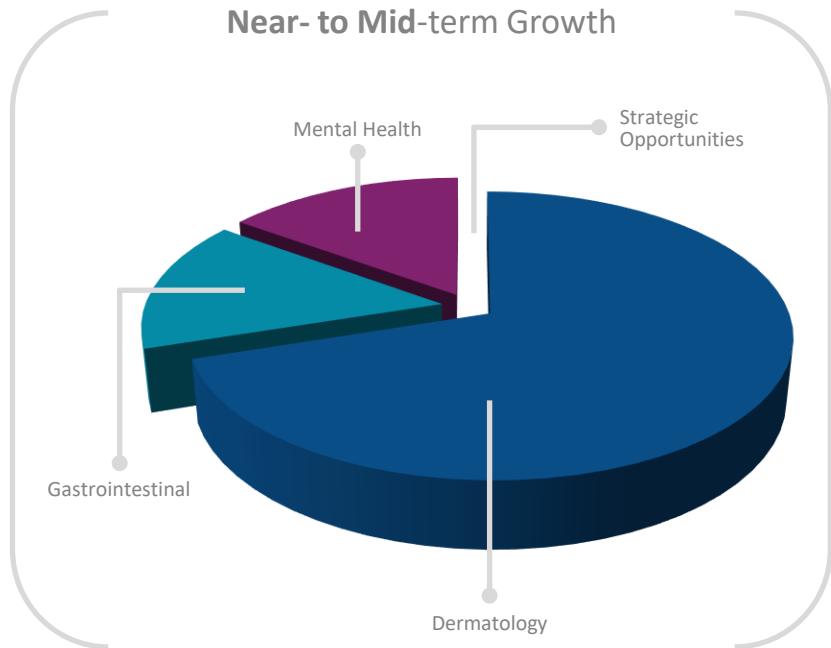
## Exceptional Employees

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



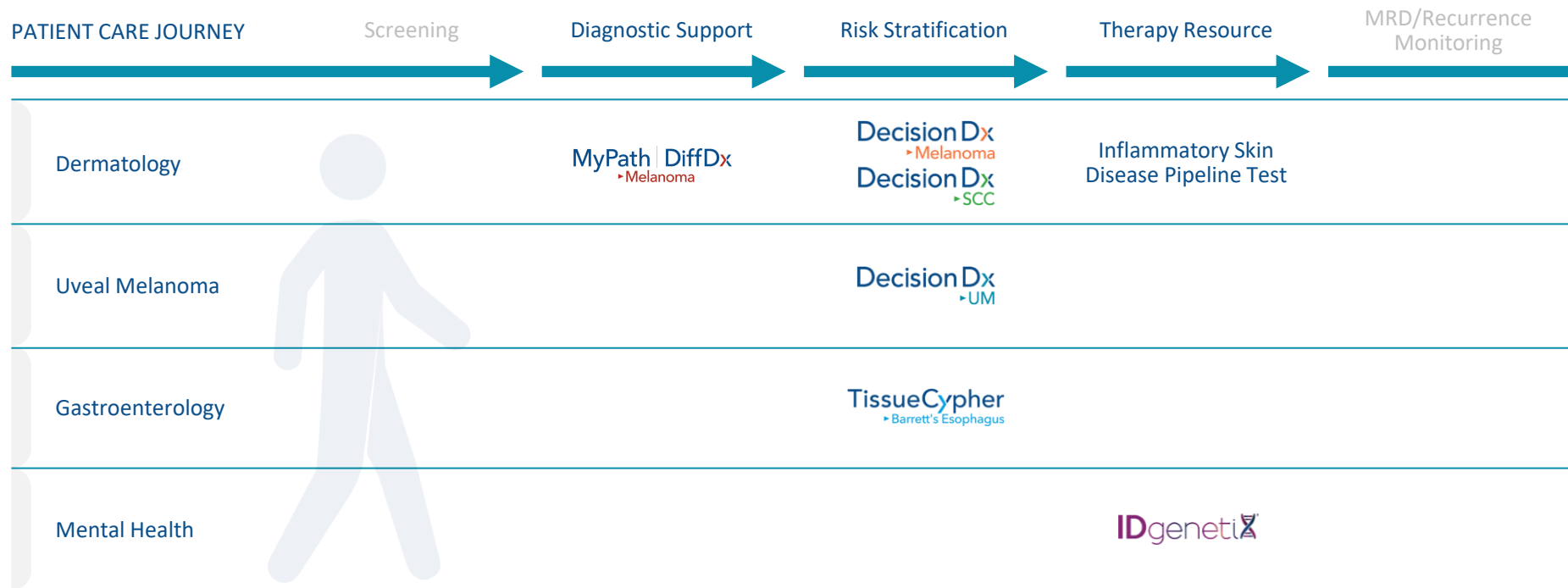
# Driving Long-Term Growth through Strong Execution and our Operational Guideposts

Exceptional Employees, Continuous Evolution & Improvement and Customer & Solution Centric



# Answering Clinical Questions to Guide Care along the Patient Journey

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



# Estimated ~\$8B U.S. Total Addressable Market<sup>1</sup> for Commercially Available Tests

	Dermatology		Gastroenterology	Mental Health
Cutaneous melanoma/ risk of metastasis, SLNB positivity risk	Cutaneous squamous cell carcinoma/risk of metastasis	Suspicious pigmented lesions/melanoma status	Barrett's esophagus/risk of progression to esophageal cancer	Mental health therapy response
~130K Patients classified as Stage I, II or III <sup>2</sup>	~200K Patients w/high-risk features <sup>2</sup>	~300K Patients w/ diagnostically ambiguous lesions	~415K Patients receiving upper GI endoscopies/year who meet the intended use criteria for TissueCypher <sup>3</sup>	Based on indicated use of IDgenetix for patients diagnosed with depression, anxiety and other mental health conditions
<b>~\$540M</b>	<b>~\$820M</b>	<b>~\$600M</b>	<b>~\$1B</b>	<b>~\$5B</b>

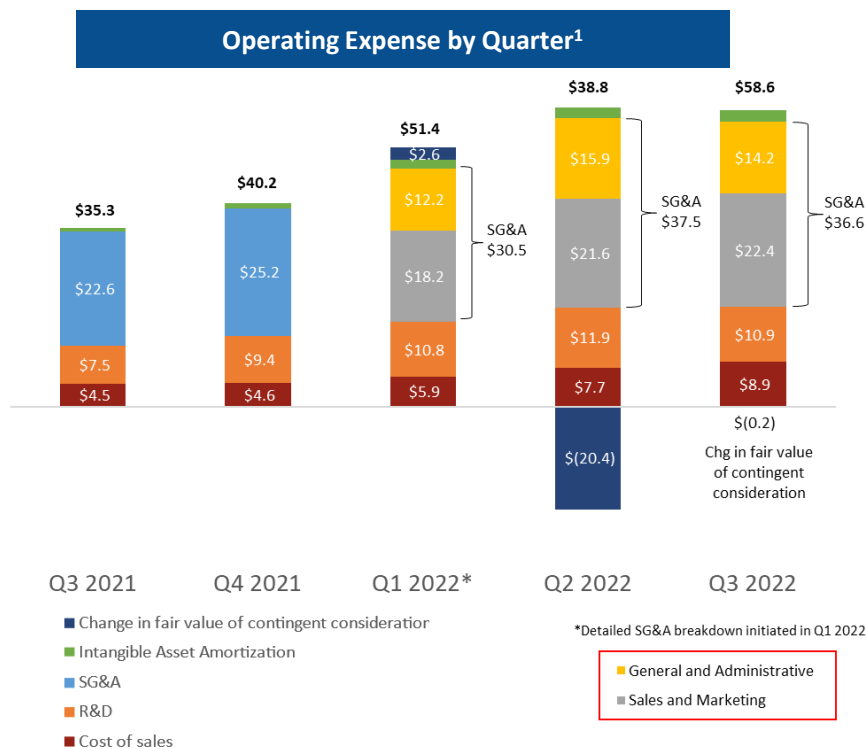
Tests in pipeline add an additional estimated ~\$3.6B to our U.S. TAM  
(\$1.9B for inflammatory skin disease pipeline test and ~1.7B for additional dermatology pipeline tests)

# Committed to Delivering Long-term Growth with Net Operating Cash Flow Positivity by 2025

	Three-year plan (2025)
<b>Revenue</b>	25-35% year-over-year growth <sup>1</sup> ; Total revenue in 2025 of \$255m-\$330m
<b>Adjusted Gross Margins</b>	80%-85% by 2025
<b>Other Operating Expenses<sup>2</sup></b>	75%-85% of revenue by 2025
<b>Net Operating Cash Flow</b>	Positive <sup>3</sup>

# Q3 2022 Operating Expenses

Executed planned investments to support our growth initiatives for long-term value creation



## Key Drivers for Q3 2022 OpEx

- **Cost of Sales** – Higher personnel costs due to headcount additions, particularly in our laboratories related to recent acquisitions. Higher laboratory activity, which is attributable to higher test volumes, also increased costs of supplies and services.
- **R&D** – Higher personnel costs associated with our increased headcount to manage and run our clinical studies, which include expenses related to salaries, wages and stock-based compensation as well as higher inventory usage to support R&D activities and higher costs for clinical studies.
- **SG&A** – Higher personnel costs associated with headcount expansion in our dermatology, GI and mental health commercial teams, which include expenses related to salaries, stock-based compensation and bonuses.
- **Amortization of Acquired Intangible Assets** – Related to MyPath Melanoma, TissueCypher and IDgenetix tests.

# Key Q3 and Recent 2022 Accomplishments



Achieved strong growth over Q3 2021 in total revenue (+58%) and achieved a new record in total test report volume (12,114, +57% compared to Q3 2021)



Presented three-year financial targets and strategic guideposts at 2022 Investor Day



AGA Clinical Practice Update released with best practice advice for the potential utilization of TissueCypher to risk stratify patients with non-dysplastic Barrett's esophagus



Expanded evidence supporting Dermatology and Uveal Melanoma tests through the publication of four new peer-reviewed studies<sup>1</sup>



Received AZBio Fast Lane Award from the Arizona Bioindustry Association (AZBio), recognizing Castle's achievement of outstanding milestones in the last 18 months

# Expected Upcoming Milestones



Expected publication of collaborative NCI study showing higher melanoma specific survival for patients tested with DecisionDx-Melanoma



Expected finalization of Palmetto/Noridian LCD for DiffDx-Melanoma by end of Q2 2023; MyPath Melanoma is already covered by full reimbursement by Medicare



Expect new GI and MyPath/DiffDx commercial team expansion to reach optimal productivity in Q2 2023



Expected closure of San Diego lab by end of 2022, folding operations into our Phoenix location



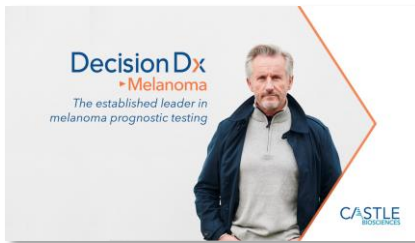
Two-year TissueCypher ADLT rate beginning Jan. 1, 2023

# First-to-Market Dermatologic Franchise, Additional Growth Opportunities

## Diagnostic Support



## Risk Stratification



## Therapy Response<sup>1</sup>



*Strong provider growth and continued adoption with ~2,335 new ordering clinicians and ~9,155 unique ordering clinicians for our dermatologic tests over the last 12 months<sup>2</sup>*

# Decision Dx

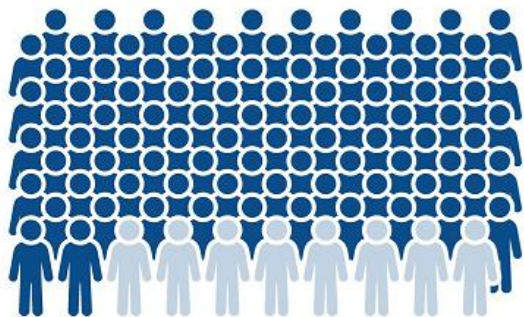
▶ Melanoma

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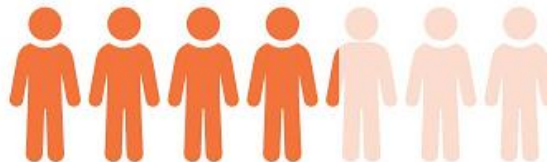
# Traditional Approaches to Staging Melanoma Miss Patients with Aggressive Tumor Biology

**Greater than 90%** of patients are considered lower risk (Stage I and II) at the time of diagnosis



\*Excludes stage IV

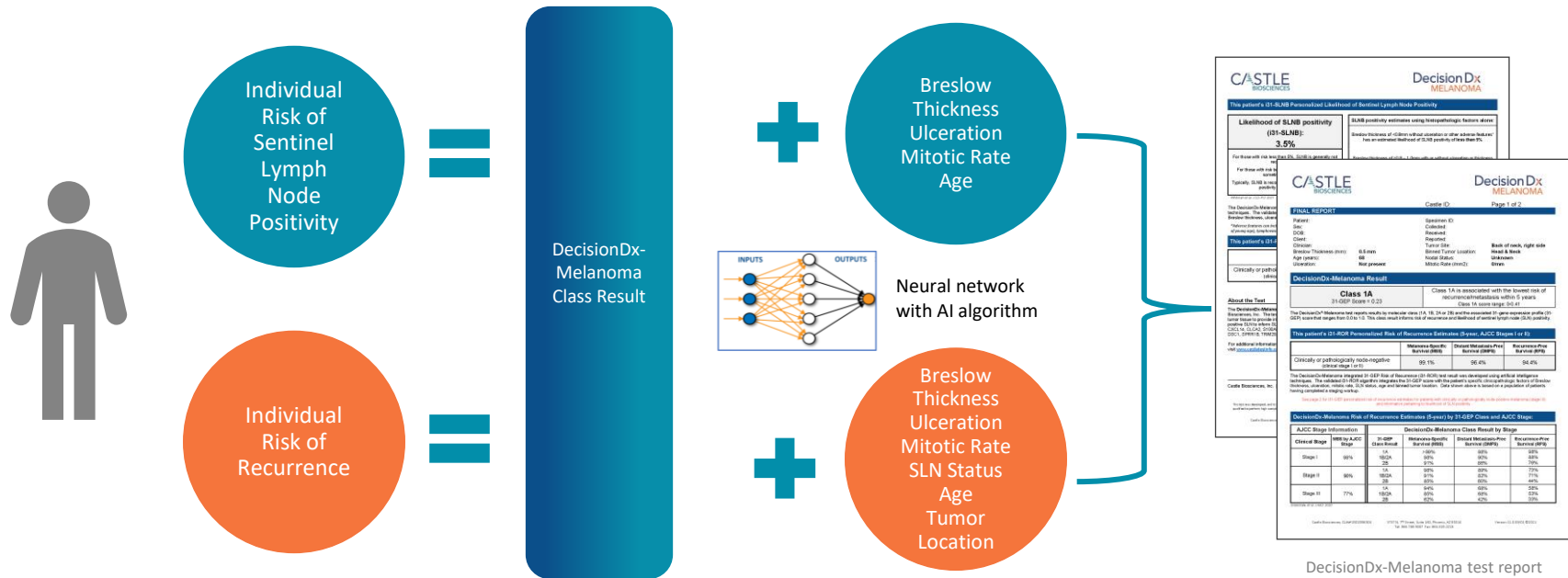
**More than half** of the deaths caused by melanoma (excluding Stage IV) occur in patients who were originally diagnosed as lower risk (Stage I or II)



**2x**  
as likely  
to survive

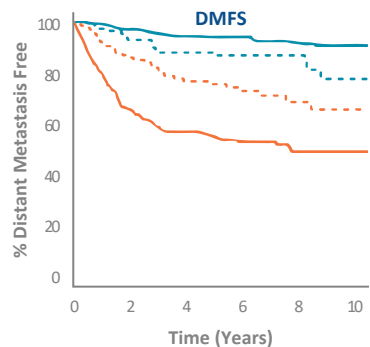
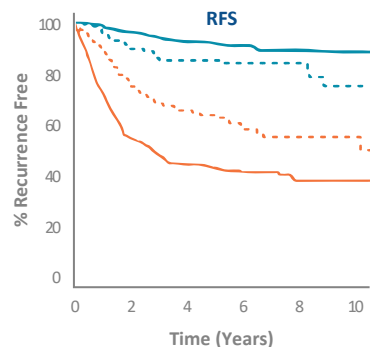
Based on a recent study, patients were found to be twice as likely to survive if they had asymptomatic recurrence detected, compared to those who had symptoms at the time their recurrence was detected.

# DecisionDx-Melanoma Provides Answers for Two Critical Clinical Questions



DecisionDx-Melanoma test results predict a patient's individual risk of recurrence and individual risk of sentinel lymph node positivity using two proprietary algorithms

# DecisionDx-Melanoma GEP Has Consistent and Independent Evidence of Prognostic Value across Studies



FEATURE	HR RFS (95% CI) p-value	HR DMFS (95% CI) p-value
Breslow thickness (per mm)	1.12 (1.03-1.22), p=0.01	1.14 (1.02-1.26), p=0.02
Ulceration	1.63 (1.18-2.25), p=0.003	2.03 (1.48-2.78), p<0.001
Age (per year)	1.01 (0.99-1.03), p=0.60	1.00 (0.98-1.03), p=0.65
SLNB	2.42 (1.88-3.10), p<0.001	2.80 (2.07-3.77), p<0.001
<b>31-GEP test</b>	<b>2.90 (2.01-4.19), p&lt;0.001</b>	<b>2.75 (1.76-4.32), p&lt;0.001</b>



# Decision Dx

▶ Melanoma

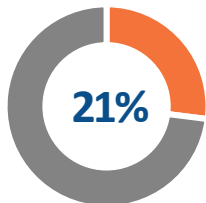
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## Collaboration with the National Cancer Institute

Linking DecisionDx-Melanoma clinical testing with patients  
captured in the NCI-SEER Registry

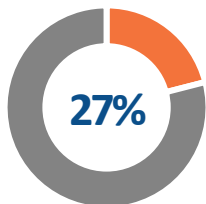
# NCI/SEER Data Linked with DecisionDx-Melanoma Test Results

Data analysis of a cohort of real-world, unselected, prospectively tested patients with cutaneous melanoma



Benefit in Overall Survival (OS) in patients who were tested at 3 years over those who were not tested

	3-year OS (95% CI)	Deaths, % (n/N)
31-GEP Tested	93.1% (92.0-94.2%)	4.8% (174/3,621)
Matched Untested	91.2% (90.4-91.9%)	6.1% (658/10,863)
<b>Hazard Ratio<sup>‡</sup></b>	<b>0.79 (0.67-0.93)</b>	<b>P=0.006</b>



Benefit in Melanoma Specific Survival (MSS) in patients who were tested at 3 years over those who were not tested

	3-year MSS (95% CI)	Deaths, % (n/N)
31-GEP Tested	97.7% (97-98.4%)	1.6% (58/3,621)
Matched Untested	96.6% (96.2-97.1%)	2.2% (238/10,863)
<b>Hazard Ratio<sup>‡</sup></b>	<b>0.73 (0.54-0.97)</b>	<b>P=0.03</b>

Data provides direct evidence that patients tested with DecisionDx-Melanoma have better survival rates than untested patients and suggests that testing can aid in risk-aligned treatment plans for improved patient outcomes and survival rates

# DecisionDx-Melanoma Disease Specific Survival Outcomes are Favorable Relative to Other Tests

## Sentinel lymph node biopsy (SLNB)

- SLNB is a risk-stratification surgical procedure “test” in melanoma
- MSLT-1 found that SLNB had no impact on 10-year melanoma-specific survival<sup>1</sup>

Tumor size	P-value	10-yr MSS
Thin (<1.2mm)	Not reported	Not impacted
Intermediate (1.2-3.5mm)	not significant (p=.18)	Not impacted
Thick (>3.5)	not significant (p=.56)	Not impacted

## Breast Cancer Test

Breast Cancer Test <sup>2</sup>	3-yr BCSS*
Breast Cancer Test	99.6%
Matched Untested	99.1%
Absolute Mortality Difference	<b>0.50% (p&lt;0.05)</b>

BCSS mortality difference of **0.50% at 3 years** when comparing tested and untested populations

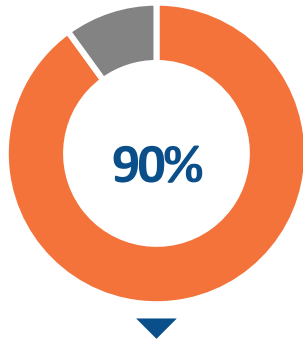
## Decision Dx ► Melanoma

Decision Dx ► Melanoma	3-yr MSS <sup>3</sup>
DecisionDx-Melanoma	97.7%
Matched Untested	96.6%
Absolute Mortality Difference	<b>1.1% (p&lt;0.05)</b>

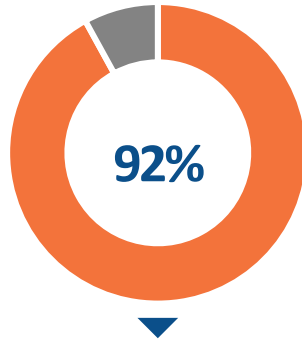
MSS mortality difference of **1.1% at 3 years** when comparing tested and untested populations

# Patients with Melanoma Desire Testing with DecisionDx-Melanoma

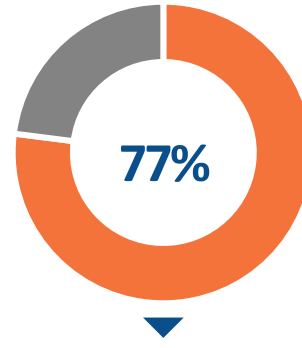
Data from a patient study conducted in collaboration with the Melanoma Research Foundation



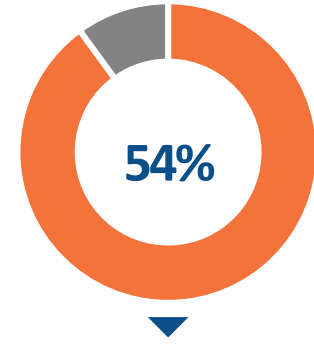
Wanted prognostic information about their melanoma tumors at diagnosis



Felt the testing was useful



Wanted testing to obtain all of the information they could about their melanoma



Of the patients who did not receive 31-GEP testing, 54% wished they had been offered the option

**None of the patients surveyed indicated decision regret regarding their decision to obtain DecisionDx-Melanoma testing, even patients who received a poor prognosis/high-risk (Class 2) DecisionDx-Melanoma test result**

## DecisionDx-Melanoma Is Supported by Significant Scientific Evidence

**9,000+**

Total patients included in studies including *independent validation*

**36+**

Peer-reviewed, published studies including *prospective studies and 2 meta-analyses*

**112,820+**

Patients with a clinical *DecisionDx-Melanoma* order from *10,750+ clinicians*

**1A**

Level 1A evidence\*

**50%**

*Demonstrated change* in management for 1 of 2 patients tested

**Medicare+**

Covered by Medicare and multiple private insurers with an *industry-leading* patient assistance program

# Decision Dx

▶ SCC

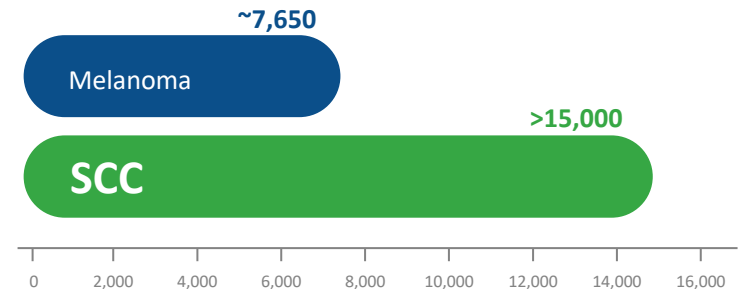
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# Cutaneous Squamous Cell Carcinoma Is an Emerging Problem in the U.S.

- Managing SCC is a significant clinical issue as deaths from SCC are now estimated to exceed those from melanoma
- Because cancer treatment plans and their outcomes are guided by risk for metastasis, prognostic accuracy has direct implications on patient management
- Traditional staging fails to identify >30% of SCC cases who go on to metastasize, and >75% of SCC cases are over-called by staging
- Unlike melanoma, breast and other common cancers, SCC patient care has not been personalized with risk predicting gene expression profile (GEP) tests

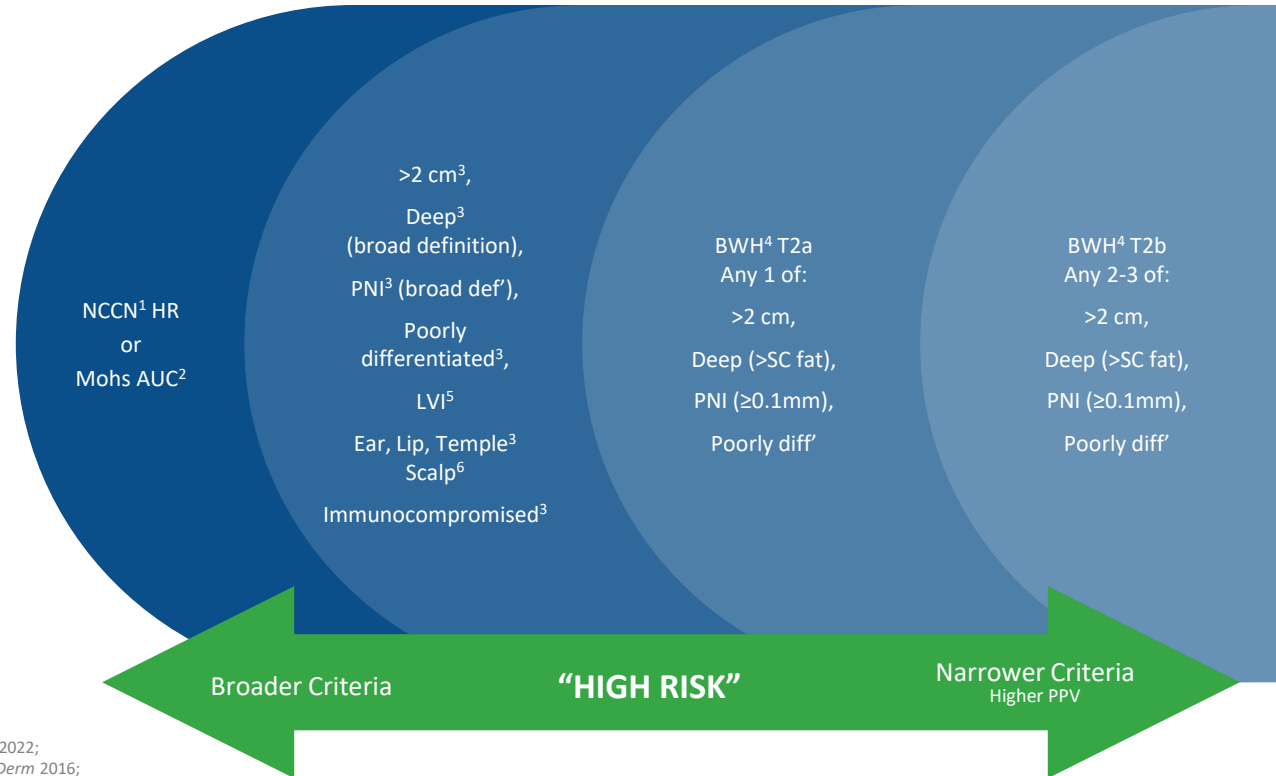
DEATHS PER YEAR IN THE U.S.



**Utility of traditional clinicopathologic risk factors is limited by their low positive predictive value**

# How is Risk Assessment Traditionally Done for SCC Patients?

- The SCC community uses the term “high-risk” SCC to describe different patient populations
- Current SCC staging fails to identify >30% of cases who will go on to experience metastasis



*Additional Risk Factors from NCCN and Mohs AUC:  
Rapidly growing tumor, neurologic symptoms, LVI, site  
of prior RT or chronic inflammatory process,  
and select histologic subtypes (also see template for SCC  
testing criteria)*

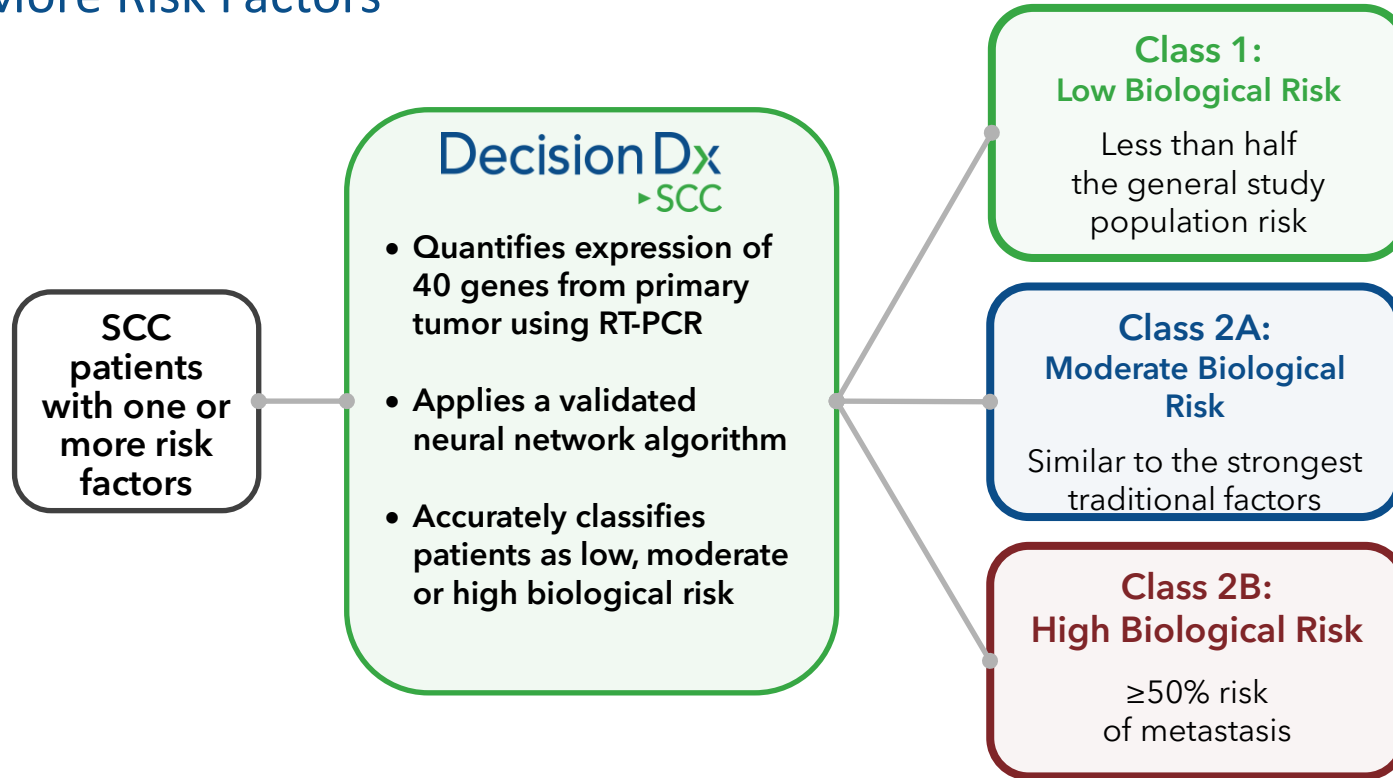
<sup>1</sup> NCCN Guidelines for Squamous Cell Skin Cancer v2.2022;

<sup>2</sup> Connolly et al. *JAAD* 2012; <sup>3</sup> Thompson et al. *JAMA Derm* 2016;

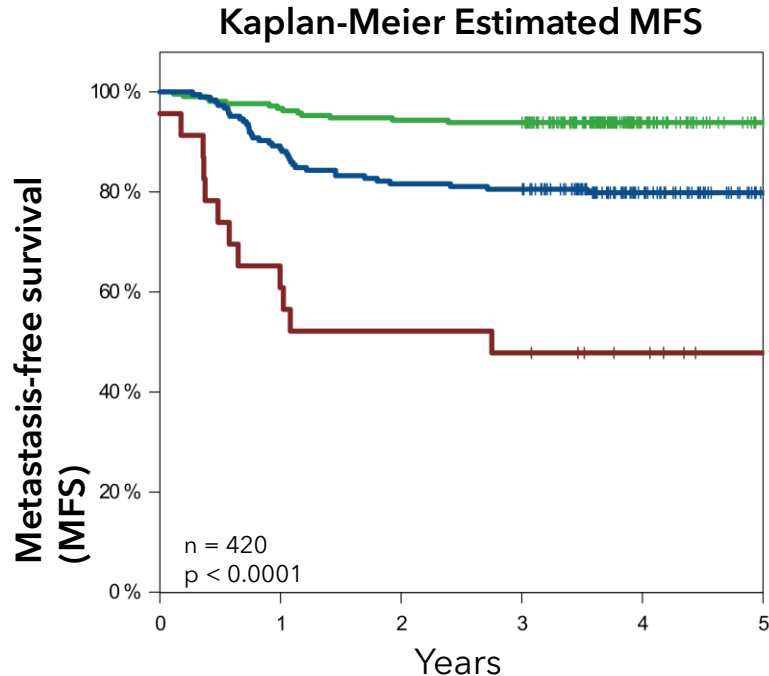
<sup>4</sup> Jambusaria-Pahlajani et al. *JAMA Derm* 2013;

<sup>5</sup> Skulsky et al. *Head & Neck* 2016; <sup>6</sup> Mo et al. *JAMA Derm* 2020

# DecisionDx-SCC Predicts Metastatic Risk For SCC Patients With One Or More Risk Factors



# Decisiondx-scc Is Validated To Predict Metastatic Risk For Individual SCC Patients With One Or More Risk Factors



## Class 1 - Low Biological Risk

<7% risk of metastasis;  
Less than half the general study population risk

## Class 2A - Moderate Biological Risk

20% risk of metastasis;  
Similar to the strongest traditional factors

## Class 2B - High Biological Risk

≥50% risk of metastasis

**Cohort  
Distribution:**

Class 1  
Class 2A  
Class 2B



# MyPath | DiffDx

► Melanoma

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# Unmet Need in Patients with a Difficult-to-Diagnose Pigmented Lesion

## The Clinical Problem

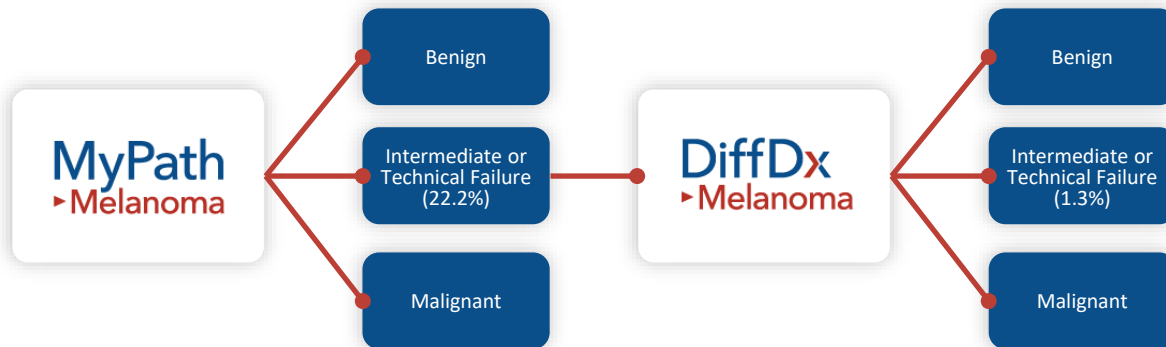
A clinical hurdle for dermatopathology is the accurate diagnosis of difficult-to-diagnose melanocytic neoplasms

Of the estimated two million suspicious pigmented lesions biopsied annually in the U.S., approximately 300,000 of those cannot be classified with confidence as either benign tissue or melanoma through traditional histopathology methods

These difficult-to-diagnose lesions are commonly sent for second opinions to expert dermatopathologists who have more experience with challenging cases; however, the nature of many lesions remains ambiguous with discordant rates of lesions in this category of 25-43% (Elmore et al. 2017)

Diagnostic ambiguity can lead to clinical management uncertainty and overtreatment, leading to unnecessary excisions and increased patient morbidity, and undertreatment, with the potential for missing diagnoses of malignant melanoma

## Diagnostic GEP is Designed to Provide Clinically Actionable, Objective Results for Nearly All Patients



>98%

By leveraging our second GEP test, >98% of patients with ambiguous melanocytic lesions received a clinically actionable result<sup>1,2</sup>

# TissueCypher

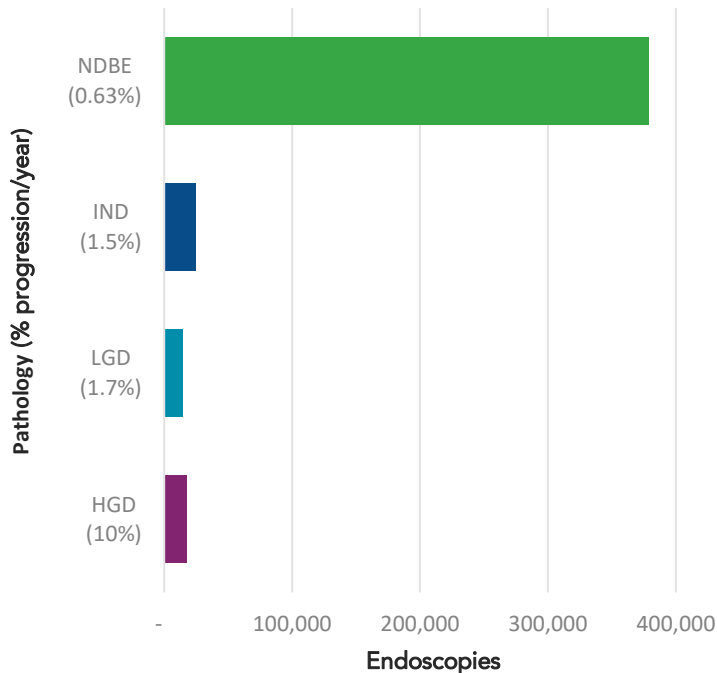
▶ Barrett's Esophagus

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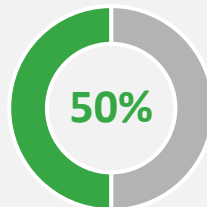


# 435,000 Barrett's Esophagus Related Endoscopies Per Year

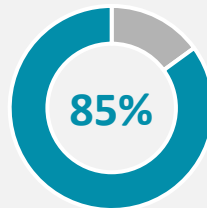
## Expert Pathology



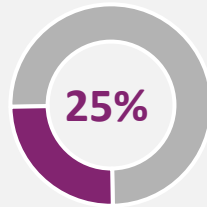
## Need for additional risk stratification tools



50% of annual progressors are initially diagnosed as non-dysplastic<sup>1</sup>



Up to 85% of low-grade patients are downgraded upon expert GI pathology review<sup>2,3</sup>



25% of high-grade/cancer diagnoses occur within 1 year of endoscopy<sup>4</sup>

# TissueCypher is a Risk Stratification Tool for Patients with Barrett's Esophagus

## Biomarkers and Spatial Biology

Molecular biomarkers to detect changes in the context of tissue structure prior to morphologic changes

## Digital Microscopy

Vision systems that objectively and reproducibly analyze and interpret tissue structures and features



## Clinical Validation

Peer-reviewed publications that demonstrate the effectiveness of the test

## Artificial Intelligence

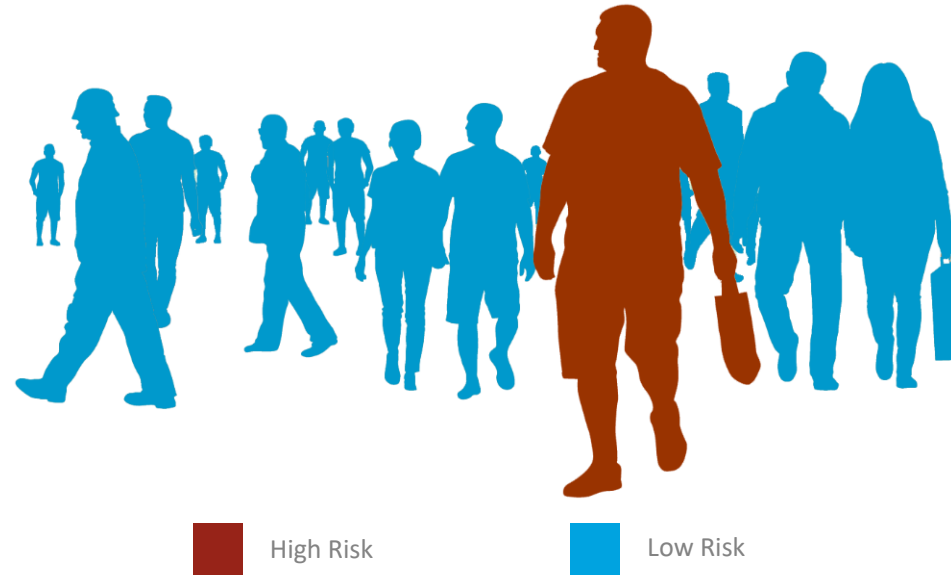
A risk classifier trained on a large data set to recognize progressor vs non-progressor tissue samples

# The World's First Prognostic AI-driven Precision Medicine Test for Barrett's Esophagus

## Individualize 5-year risk of progression to HGD or EAC

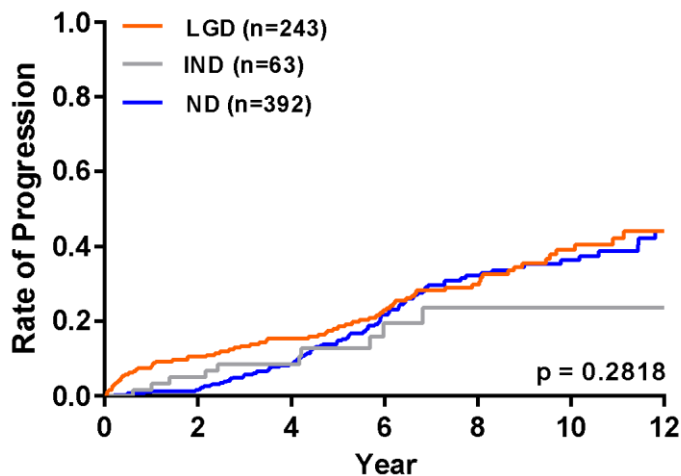
- Indicated for NDBE, IND, and LGD
- High Risk score enables increased surveillance or early intervention to prevent cancer
- Low Risk score minimizes over treatment and supports extension of surveillance intervals to guideline recommendations

TissueCypher  
► Barrett's Esophagus

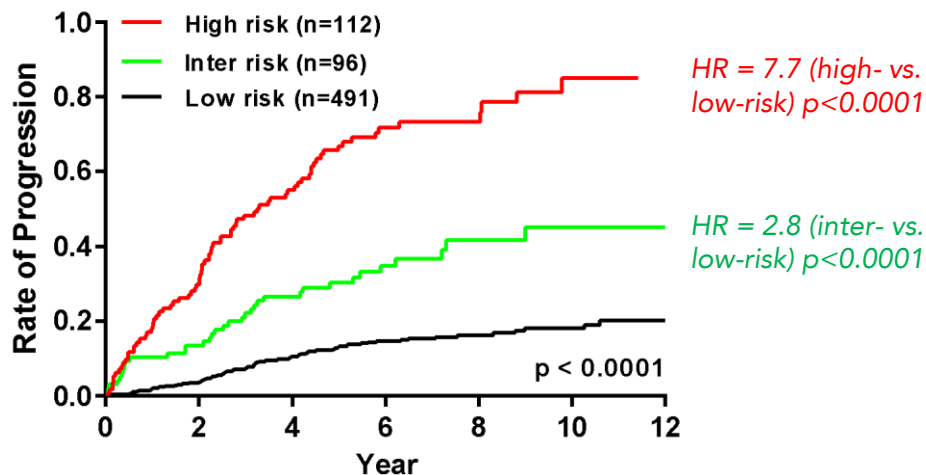


# TissueCypher Is the Strongest Independent Predictor of Progression

Original Pathologic Diagnosis

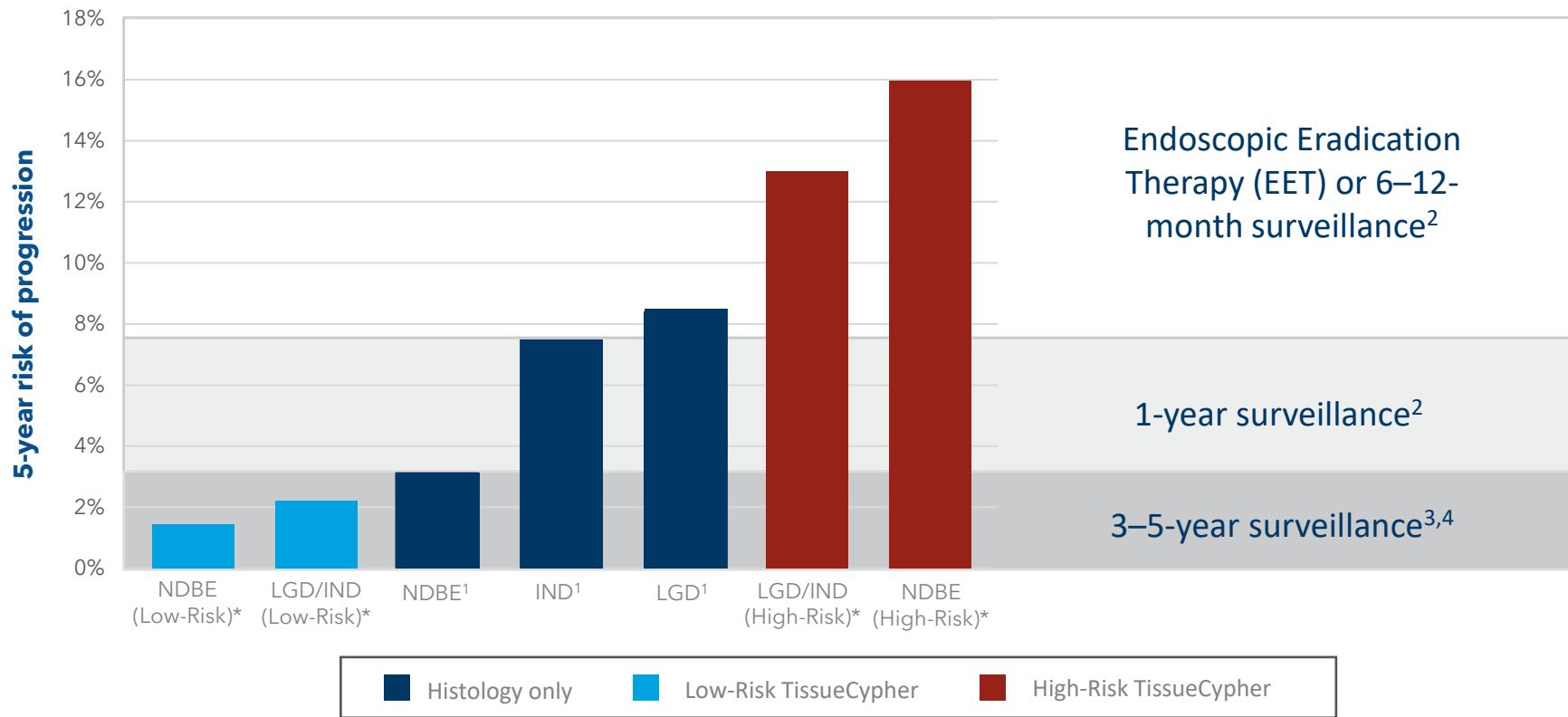


TissueCypher



n=699 patients<sup>1-5</sup> (ND n=567, IND n=50, LGD n=82)  
 152 incident progressors, 38 prevalent cases, 509 non-progressors

# Consideration of Patient Management Based on Risk of Progression



# How Incorporation of TissueCypher Testing Can Change Clinical Practice

## Clinical guideline based on histology and segment length

NDBE	IND	LGD
Surveillance in 3 to 5 years <sup>1,2,3</sup> 3 years if segment length $\geq 3$ cm <sup>2</sup> 5 years if segment length $< 3$ cm <sup>2</sup>	Surveillance in 3 to 6 months following PPI Rx, Surveillance in 12 months for persistent IND <sup>1,2</sup>	EET or Surveillance in 6-12 months <sup>1,2</sup>

## TissueCypher ► Barrett's Esophagus

**LOW  
Risk Class**

**HIGH/INT  
Risk Class**

NDBE	IND/LGD BE
Consider surveillance in 3 to 5 years	Consider surveillance in 12 months and PPIs as needed

NDBE	IND/LGD BE
Rule out prevalent HGD/EAC and consider EET or surveillance in 1 year	Rule out prevalent HGD/EAC and consider EET and PPIs as needed

CASTLE  
BIOSCIENCES

IDgenetiX<sup>®</sup>

---



# Medication Selection for Mental Illness Is Challenging

## Inadequate Therapy Response

~53% of patients with major depressive disorder (MDD) have an inadequate response to first-line treatment<sup>1</sup>

## Low Remission Rates

72% of patients with MDD do not achieve remission using current standard of care treatment approaches<sup>2</sup>

## High Prevalence of Adverse Drug Events

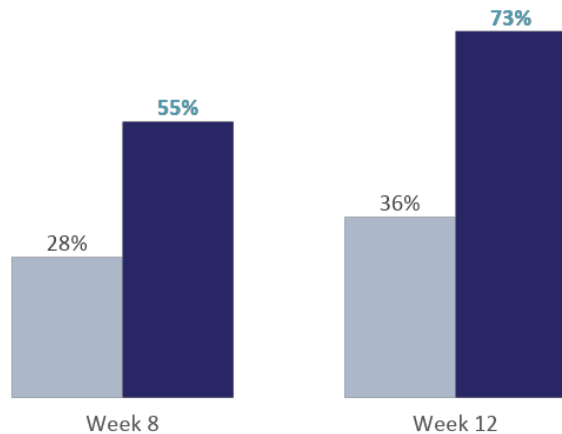
The likelihood of discontinuation rises from 8.6% with first-line medication treatment to 41.4% with fourth-line treatment<sup>3</sup>

*"...finding an effective antidepressant can take years"*  
- Mental Health America

## 2.5x Increase in Remission Rates for Severe Depression Demonstrated Enhanced Clinical Outcomes vs. Standard of Care

### Response Rate

≥ 50% Reduction from Baseline

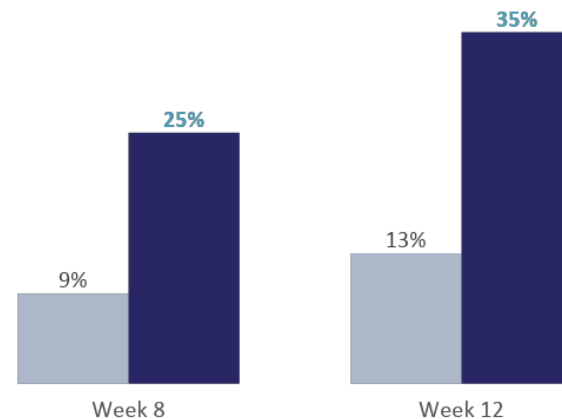


*p*-value 0.01

*p*-value 0.001

### Remission Rate

Patients Achieving Remission



*p*-value 0.05

*p*-value 0.02

2x

increase in response rate  
vs. control

>2.5x

increase in remission rate vs.  
control



Control  
IDgenetix

# Precision Medicine Designed to Streamline Medication Selection for Mental Health

IDgenetix is redefining the standards of next generation PGx

	IDgenetix	PGx Original	Trial & Error
Multi-Gene Test	✓	✓	
RCT/Clinical Utility	✓	✓	
Medicare Coverage	✓	✓	
Comorbidity (MDD & Anxiety)	✓		
Drug-Drug Interactions	✓		
Lifestyle Factors	✓		

# Decision Dx ▶UM

---



# DecisionDx-UM: the Standard of Care in the Management of Newly Diagnosed Uveal Melanoma

## Strong Evidence Base

- 24 peer-reviewed publications, **3,100+ patients**
- 

## Widespread Adoption

- Nearly **8 in 10 patients** diagnosed with uveal melanoma in the U.S. receive the DecisionDx-UM test as part of their diagnostic workup
  - **1,618 reports** issued in 2021
- 

## Broad Reimbursement

- In 2021, received payment on ~93% of claims
  - Medicare LCD **covers patients** with a confirmed diagnosis and no evidence of metastatic disease
  - 2022 Medicare rate of \$7,776
- 

## AJCC and NCCN Guideline Inclusion

## Facts About Uveal Melanoma

- **~2,000** patients diagnosed in the U.S. annually
  - **~97%** of patients – no evidence of metastatic disease at the time of diagnosis
  - **~30%** will develop metastases within 5 years
- 

## Decision Dx -UM

15-Gene Expression Profile (GEP) Test

Low-risk: **~67%**  
Low Intensity Management

High-risk: **~33%**  
High Intensity Management

CASTLE  
BIOSCIENCES

Thank you



## Use Of Non-GAAP Financial Measures (Unaudited)

In this presentation, we use the metrics of Adjusted Revenue, Adjusted Gross Margin and Adjusted Operating Cash Flow, which are non-GAAP financial measures and are not calculated in accordance with generally accepted accounting principles in the United States (GAAP). Adjusted Revenue and Adjusted Gross Margin reflect adjustments to net revenues to exclude changes in variable consideration related to test reports delivered in previous periods. Adjusted Gross Margin further excludes acquisition-related intangible asset amortization. Adjusted Operating Cash Flow excludes the effects of repayments to Medicare of COVID-19 government relief advancements to healthcare providers.

We use Adjusted Revenue, Adjusted Gross Margin and Adjusted Operating Cash Flow internally because we believe these metrics provide useful supplemental information in assessing our revenue and cash flow performance reported in accordance with GAAP, respectively. We believe Adjusted Revenue and Adjusted Gross Margin are also useful to investors because they provide additional information on current-period performance by removing the effects of revenue adjustments related to tests delivered in previous periods and, with respect to Adjusted Gross Margin, acquisition-related intangible asset amortization, which we believe may facilitate revenue and gross margin comparisons to historical periods. We believe Adjusted Operating Cash Flow is also useful to investors as a supplement to GAAP measures in the assessment of our cash flow performance by removing the effects of COVID-19 government relief payments, which we believe are not indicative of our ongoing operations. However, these non-GAAP financial measures may be different from non-GAAP financial measures used by other companies, even when the same or similarly titled terms are used to identify such measures, limiting their usefulness for comparative purposes. These non-GAAP financial measures are not meant to be considered in isolation or used as substitutes for net revenues, gross margin or net cash (used in) provided by operating activities reported in accordance with GAAP and should be considered in conjunction with our financial information presented on a GAAP basis and language from our earnings press release. Accordingly, investors should not place undue reliance on non-GAAP financial measures. Reconciliations of these non-GAAP financial measures to the most directly comparable GAAP financial measures are presented in the slides that follow. We are not providing a target for or a reconciliation of Adjusted Gross Margin, the most directly comparable GAAP measure, for 2025 because we are unable to predict certain items contained in the GAAP measure without unreasonable efforts.

## Reconciliation of Non-GAAP Financial Measures (Unaudited)

The table below presents the reconciliation of adjusted revenue and adjusted gross margin, which are non-GAAP financial measures. See previous slide for further information regarding the Company's use of non-GAAP financial measures.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
<i>(in thousands)</i>				
<b>Adjusted revenue</b>				
Net revenues (GAAP)	\$ 37,011	\$ 23,475	\$ 98,701	\$ 69,046
Revenue associated with test reports delivered in prior periods	277	92	1,850	(4,130)
Adjusted revenue (Non-GAAP)	<u>\$ 37,288</u>	<u>\$ 23,567</u>	<u>\$100,551</u>	<u>\$ 64,916</u>
<b>Adjusted gross margin</b>				
Gross margin (GAAP) <sup>1</sup>	\$ 25,846	\$ 18,281	\$ 70,161	\$ 56,871
Amortization of acquired intangible assets	2,306	694	6,051	950
Revenue associated with test reports delivered in prior periods	277	92	1,850	(4,130)
Adjusted gross margin (Non-GAAP)	<u>\$ 28,429</u>	<u>\$ 19,067</u>	<u>\$ 78,062</u>	<u>\$ 53,691</u>
Gross margin percentage (GAAP) <sup>2</sup>	69.8 %	77.9 %	71.1 %	82.4 %
Adjusted gross margin percentage (Non-GAAP) <sup>3</sup>	76.2 %	80.9 %	77.6 %	82.7 %

<sup>1</sup> Calculated as net revenues (GAAP) less the sum of cost of sales (exclusive of amortization of acquired intangible assets) and amortization of acquired intangible assets.

<sup>2</sup> Calculated as gross margin (GAAP) divided by net revenues (GAAP).

<sup>3</sup> Calculated as adjusted gross margin (Non-GAAP) divided by adjusted revenue (Non-GAAP).

## Reconciliation of Non-GAAP Financial Measures (Unaudited)

The table below presents the reconciliation of adjusted operating cash flow, which is a non-GAAP financial measure. See slide 47 for further information regarding the Company's use of non-GAAP financial measures.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
<i>(in thousands)</i>				
<b>Adjusted operating cash flow</b>				
Net cash used in operating activities (GAAP)	\$ (5,224)	\$ (6,133)	\$ (35,655)	\$ (16,202)
Medicare advance payment <sup>1</sup>	—	3,178	—	5,351
HHS provider relief funds <sup>2</sup>	—	—	—	(1,882)
<b>Adjusted operating cash flow (Non-GAAP)</b>	<b>\$ (5,224)</b>	<b>\$ (2,955)</b>	<b>\$ (35,655)</b>	<b>\$ (12,733)</b>

1. We received an advance payment of \$8.3 million from the Centers for Medicare & Medicaid Service (CMS), for which recoupment has commenced in April 2021. We recorded the receipt of the payment as a liability on our balance sheet and, in accordance with GAAP, it was included in net cash provided by operating activities in the period received. We have excluded receipt of the advance payment from adjusted operating cash flow, but as claims were submitted for reimbursement and applied against this balance, we included the advance payment in adjusted operating cash flow to the extent that Medicare claims submitted for reimbursement were applied to the balance.
2. We received a one-time payment of \$1.9 million in relief funds automatically allocated to Medicare providers under the Coronavirus Aid, Relief and Economic Security Act (CARES Act) from the U.S. Department of Health and Human Services (HHS).

# Appendix



# ESG Focus Areas for 2022 and Beyond



Environmental policy



Environmental metrics



DEI statement



DEI metrics



DEI action plan/roadmap

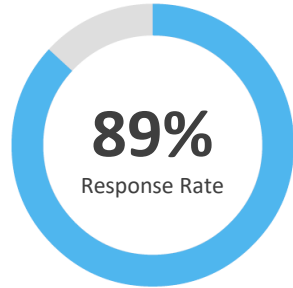


Vendor code of conduct/supplier standard

# Employee Engagement is Part of our Core Strategy for Success

Based on the results of Castle's annual employee survey<sup>1</sup>

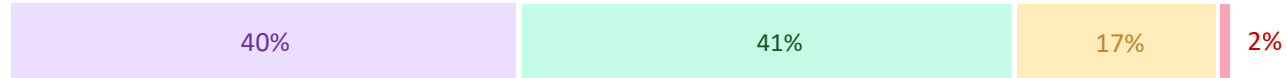
2022



Healthcare benchmark  
response rate: 59%

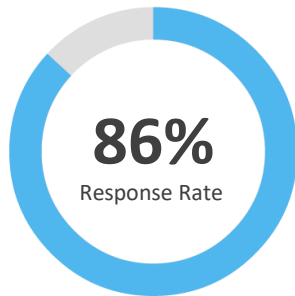
Castle employee  
engagement score: **81%**

Healthcare benchmark  
average engagement score: **53%**



● Enthusiastically engaged ● Engaged ● Disengaged ● Deeply disengaged

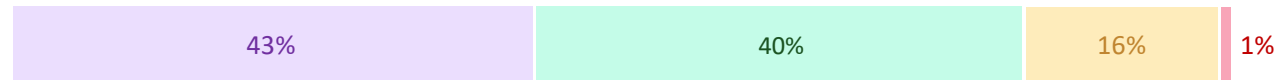
2021



Healthcare benchmark  
response rate: 63%

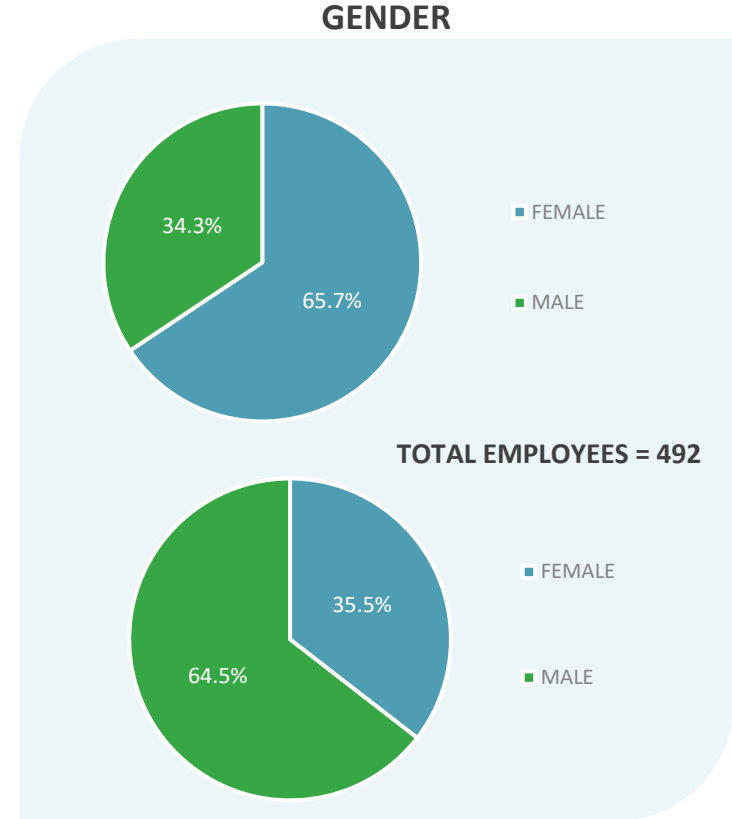
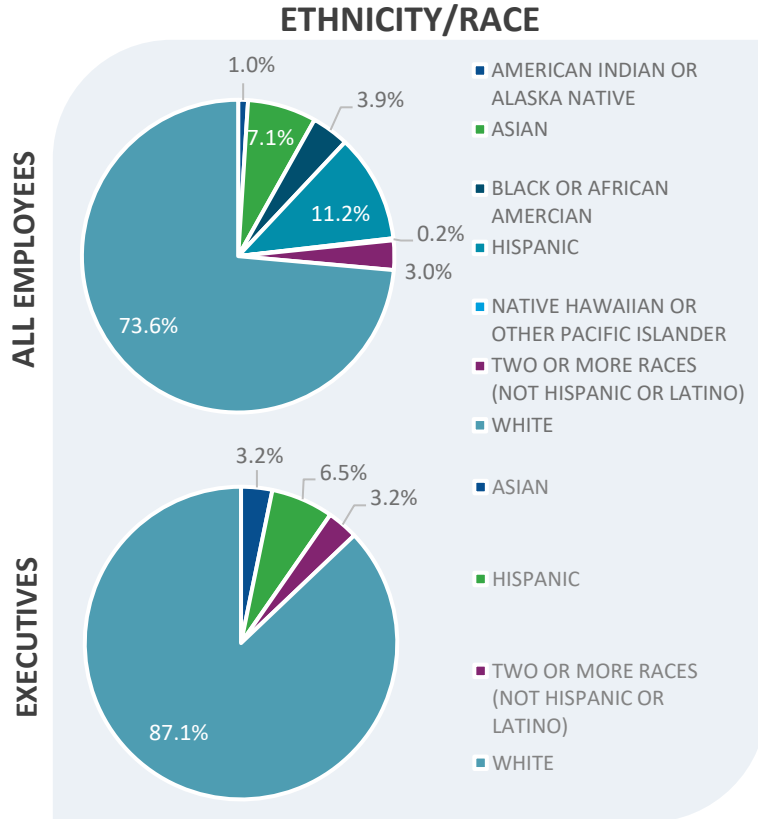
Castle employee  
engagement score: **83%**

Healthcare benchmark  
average engagement score: **66%**



● Enthusiastically engaged ● Engaged ● Disengaged ● Deeply disengaged

# Commitment to Diversity



# Award-Winning Company

Committed to cultivating a culture of innovation, continuous growth and advancement



2019 Technology Innovation in Melanoma Award Winner

# Leadership Team Overview

## MANAGEMENT TEAM

Derek Maetzold

Founder, Director, President and CEO



Frank Stokes

Chief Financial Officer



Toby Juvenal

Chief Commercial Officer



Stuart  
Pharmaceuticals

Kristen Oelschlager, RN, CHC

Chief Operating Officer



Robert Cook, PhD

Senior Vice President, Research & Development



Northwestern



Matthew Goldberg, MD

Medical Director



Alice Izzo

Senior Vice President, Marketing



## BOARD OF DIRECTORS

Dan Bradbury



Derek Maetzold



Mara Aspinall



Brad Cole



Tiffany Olson



Miles D. Harrison



Kimberlee Caple



Ellen Goldberg

CHORD Consulting