CASTLE BIOSCIENCES

Transforming Disease Management

March 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: generating between $170-180 million in total revenue in 2023; 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 catalysts of continued growth in 2023, including (i) publication of a collaborative NCI study showing higher melanoma specific survival for patients tested with DecisionDx-Melanoma, (ii) our new GI and MyPath commercial team expansion reaching optimal productivity in Q2 2023, (iii) receiving a draft LCD for DecisionDx-SCC from Palmetto in the first half of 2023, (iv) the opening of our Pittsburgh lab in Q2 2023, and (v) further refinement of sales territories in our dermatologic, GI and mental health franchises; the potential of DecisionDx-Melanoma to aid in risk-aligned treatment plans for improved patient outcomes and survival rates; our expectations regarding timelines and milestones for our dermatologic, gastrointestinal and mental health franchises, and our expectation that we will receive early development data for our pipeline inflammatory skin disease test in the second half of 2023 and launch the test by 2025; and the potential of DecisionDx-Melanoma to aid in risk-aligned treatment plans for improved patient outcomes and survival rates. The words "anticipates," "can," "estimates," "expects," ""target" 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, the accuracy of our assumptions and expectations underlying our fiscal 2023 revenue target (including, without limitation, our assumptions or expectations regarding (i) continued reimbursement for our commercial tests at the current rates throughout 2023, (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 Annual Report on Form 10-K for the year ended December 31, 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.

Strong Performance in 2022

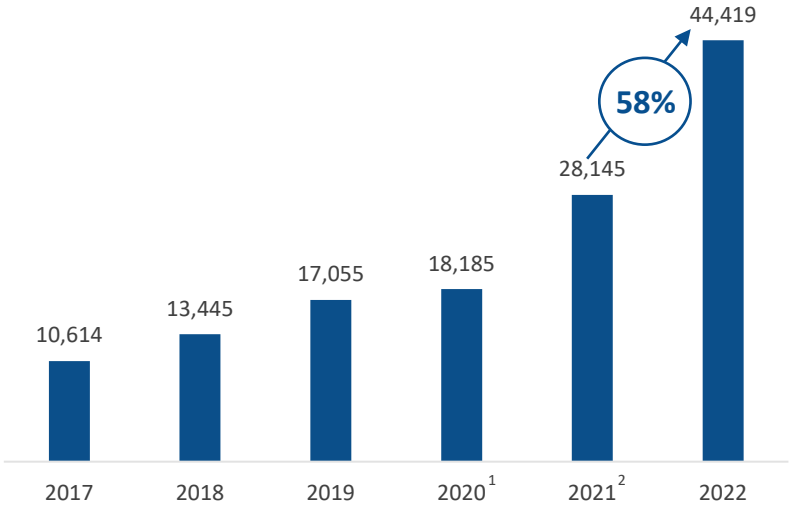
Expecting approximately $170 – 180 million in 2023 revenue

		2022	2021
Total test reports		**44,419**	28,145
Total Dermatology test reports		**37,331**	26,500
Revenues		**$137.0M**	$94.1M
Adj. Revenues[1]		**$139.0M**	$90.8M
Gross Margin		**70.6%**	81.1%
Adj. Gross Margin[1]		**77.0%**	82.6%
Net Loss		**$(67.1)M**	$(31.3)M
Adj. EBITDA[1]		**$(42.6)M**	$(14.9)M
Operating Cash Flow		**$(41.7)M**	$(19.0)M
Adj. Operating Cash Flow[1]		**$(41.7)M**	$(12.5)M
Cash, Cash Equivalents & Marketable Investment Securities	as of end of period	**$259M[2]**	$330M

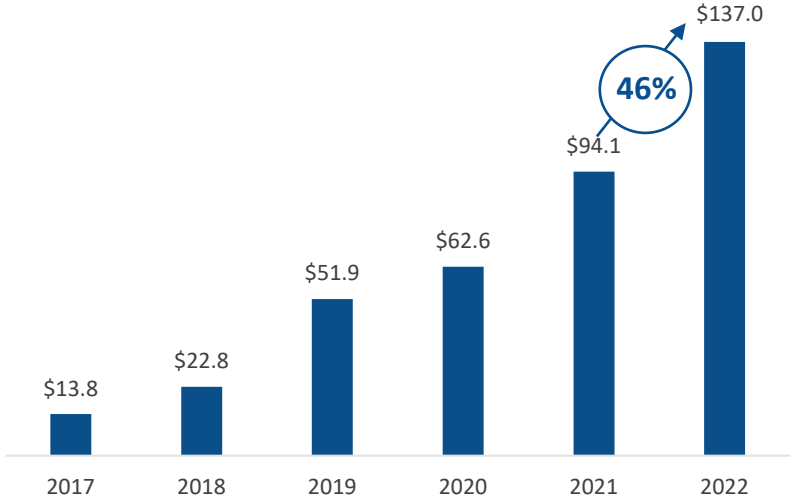
[1]See Non-GAAP reconciliations at the end of this presentation. [2]Cash use includes acquisition of AltheaDx.

Consistent Execution of Growth Initiatives Supports Long-Term Growth

2017-2022 Total Test Report Volume



2017-2022 Revenue



[1]Due to COVID-19, cutaneous melanoma diagnoses were down 20% for 2020; [2] Cutaneous melanoma diagnoses were down 11% for 2021.

Key 2022 Accomplishments

Delivered strong year-over-year growth in revenue (met top end of guided range) and test report volume (total test reports delivered in 2022 were **44,419** up 58% over 2021)

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

Developed expanded evidence supporting portfolio of innovative tests through the acceptance/publication of 14 peer-reviewed studies across all franchises

TissueCypher granted ADLT status by Medicare, recognizing the test for providing clinical diagnostic information that cannot be obtained from any other test or combination of tests

Transition of IDgenetix clinical services from San Diego lab and the folding of operations into our Phoenix location

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[1]ADLT=Advanced Diagnostic Laboratory Test

Mission

Improving health through innovative tests that guide patient care

Vision

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

Values

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

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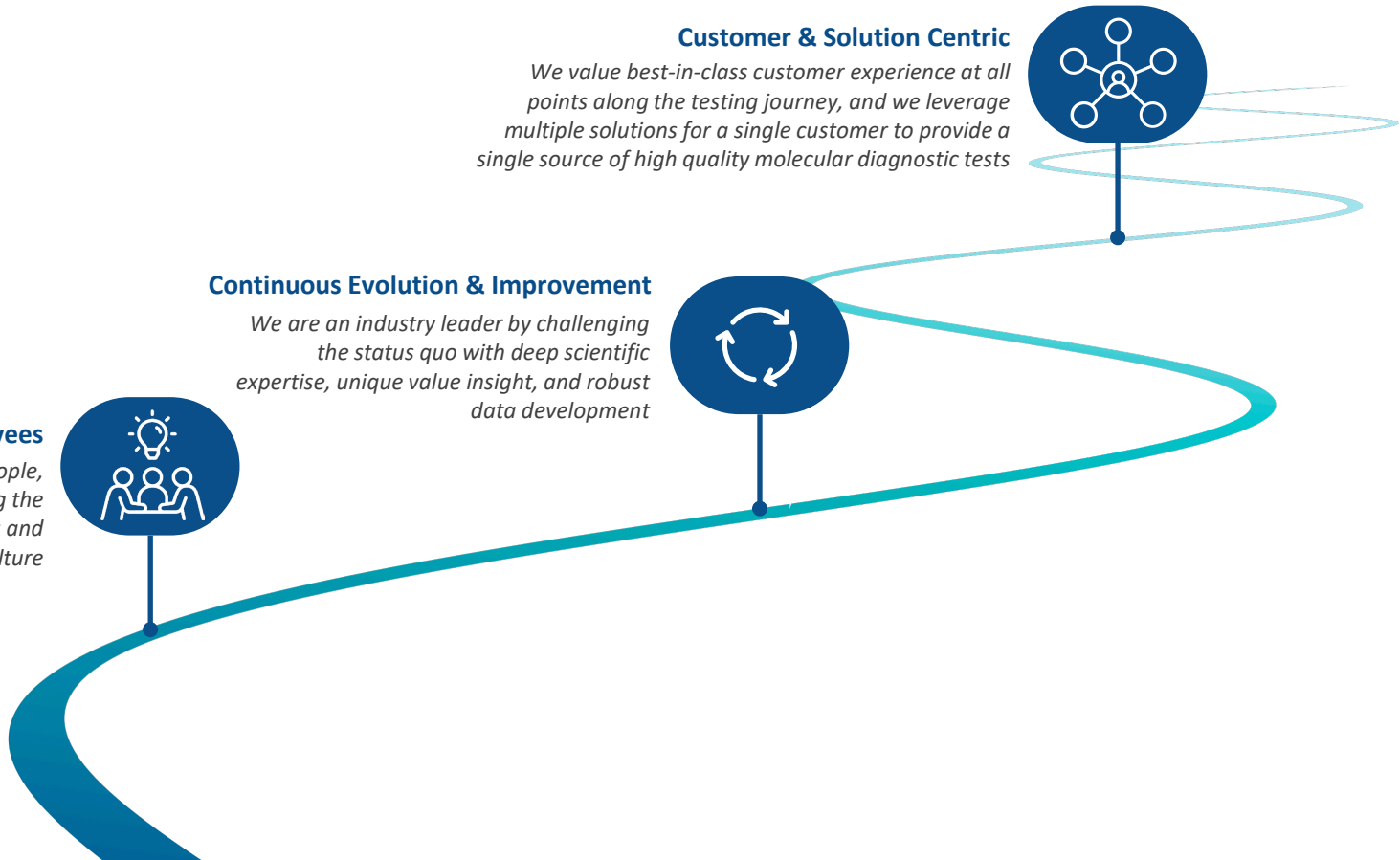
Three Strategic Guideposts That Create Value for Customers, Patients and Stockholders



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

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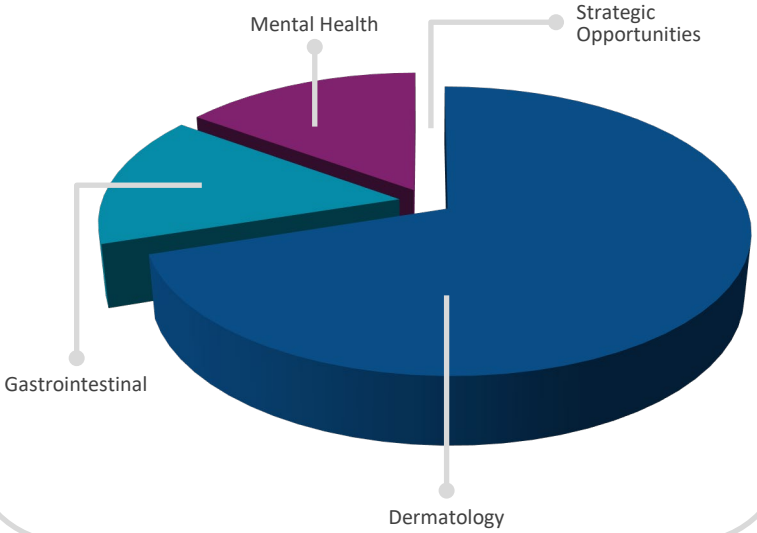
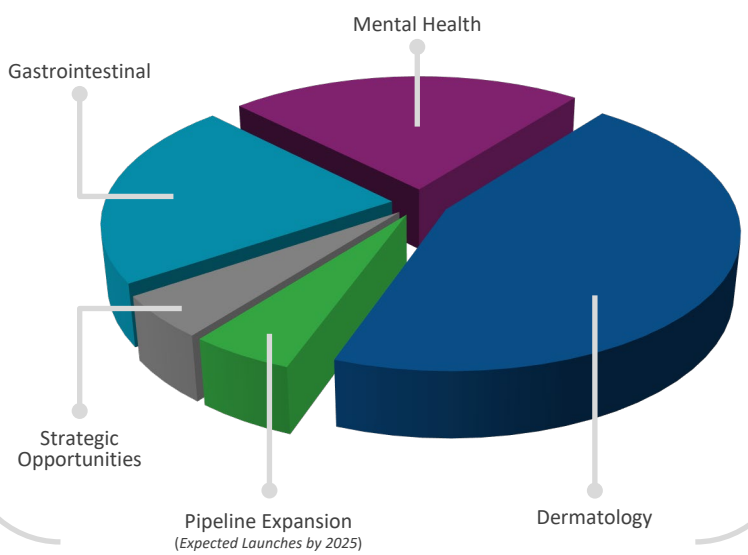
Driving Long-Term Growth through Strong Execution and our Operational Guideposts

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

Near- to Mid-term Growth



Mid- to Long-term Growth



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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

Dermatology		MyPath Melanoma	DecisionDx Melanoma DecisionDx SCC	Inflammatory Skin Disease Pipeline Test
Ophthalmology			DecisionDx UM	
Gastroenterology			TissueCypher Barrett's Esophagus	
Mental Health				IDgenetix

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Estimated ~$8B U.S. Total Addressable Market[1] 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[2]	~200K Patients w/high-risk features[2]	~300K Patients w/ diagnostically ambiguous lesions	~415K Patients receiving upper GI endoscopies/year who meet the intended use criteria for TissueCypher[3]	Based on indicated use of IDgenetix for patients diagnosed with depression, anxiety and other mental health conditions
~$540M	**~$820M**	**~$600M**	**~$1B**	**~$5B**

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)

[1]U.S. TAM = Total addressable market 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

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Well Positioned for Continued Growth with Expected 2023 Catalysts

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

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

Expect draft LCD for DecisionDx-SCC from Palmetto in 1H 2023

Pittsburgh lab opening in Q2 2023, bringing Castle's total laboratory operations space combined to 52,000 square feet

Further refinement of sales territories in our Derm, GI and Mental Health franchises

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

13
Ongoing clinical research studies

231
Committed/contributing clinical research sites at year-end 2022

~11,200+
Patients[1] enrolled in studies at year-end 2022

~14,200+
Patients enrolled in studies over lifetime of Castle[2]

Ongoing collaboration with NCI/SEER has allowed for analyses of 9,200+ patients clinically tested with DecisionDx-Melanoma[3] and 2,900+ patients clinically tested with DecisionDx-UM[4] to date

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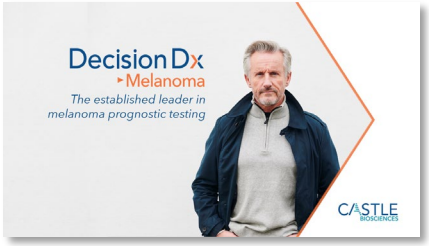
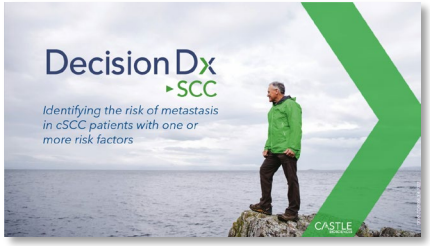
Data for first three boxes as of Dec. 31, 2022; Data for fourth box as of March 6, 2022.
[1]One TissueCypher study involves patients and ~250 physicians; [2]Number reflects studies that span Castle's dermatology, ophthalmology and gastroenterology portfolios; [3]SEER cancer registries linked CM cases 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.

First-to-Market Dermatologic Franchise, Additional Growth Opportunities

Diagnostic Support

Risk Stratification





Therapy Response[1]

Strong provider growth and continued adoption with ~2,312 new ordering clinicians and ~7,670 total ordering clinicians for our dermatologic tests for the year ended Dec. 31, 2022[2]

[1]Target launch anticipated by the end of 2025
[2]New=clinician who ordered a Castle dermatologic test for the first time.

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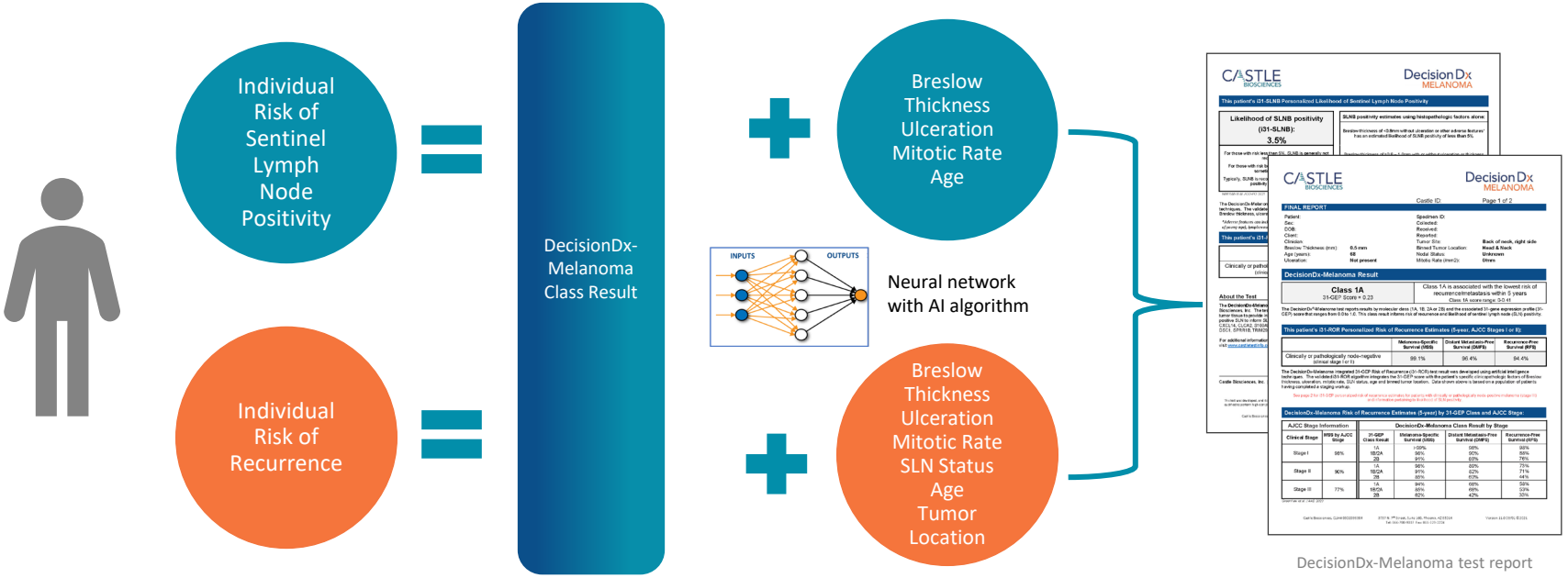
DecisionDx ▸Melanoma

DecisionDx-Melanoma Provides Answers for *Two* Critical Clinical Questions



DecisionDx-Melanoma test report

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

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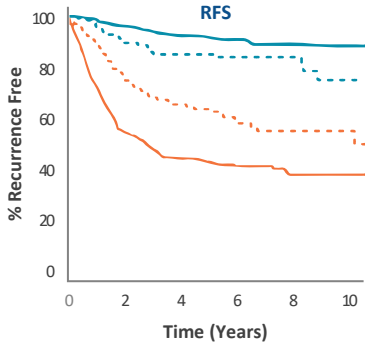
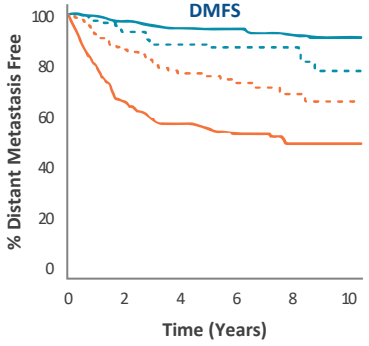
Whitman et al. *JCO PO* 2021; Jarell et al. *JAAD* 2022

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
31-GEP test	**2.90 (2.01-4.19), p<0.001**	**2.75 (1.76-4.32), p<0.001)**

DecisionDx-Melanoma

- Quantifies expression of 31 genes from primary tumor using RT-PCR
- Applies validated algorithm

Class 1A Lowest Risk

Class 1B/2A Increased Risk

Class 2B Highest Risk

31-GEP class result remains a consistent component of all DecisionDx-Melanoma reports

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Greenhaw et al. *JAAD* 2020

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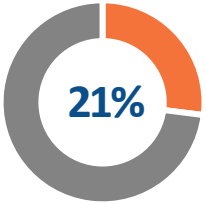
DecisionDx ▸Melanoma

Collaboration with the National Cancer Institute

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

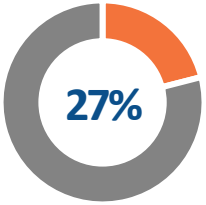
NCI/SEER Data Linked with DecisionDx-Melanoma Test Results

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)
Hazard Ratio‡	**0.79 (0.67-0.93)**	**P=0.006**



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)
Hazard Ratio‡	**0.73 (0.54-0.97)**	**P=0.03**

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

Kurley et al. Presented at European Association of Dermoto Oncology (EADO) conference in Seville, Spain; April 21-23, 2022

‡Hazard ratio (HR) was computed using the untested patients as referenced for 31-GEP tested cohort. A HR less than 1.0 demonstrates improved survival in 31-GEP tested patients. Diagnosis date 2016 and onward.

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[1]

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[2]	3-yr BCSS*
Breast Cancer Test	99.6%
Matched Untested	99.1%
Absolute Mortality Difference	**0.50% (p<0.05)**

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

DecisionDx Melanoma

DecisionDx Melanoma	3-yr MSS[3]
DecisionDx-Melanoma	97.7%
Matched Untested	96.6%
Absolute Mortality Difference	**1.1% (p<0.05)**

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

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[1]Morton et al. *N Engl J Med* 2014; [2]Zhang et al. *Breast Cancer Res Treat.* 2020; [3]Kurley et al. EADO 2022. *https://apps.automeris.io/wpd/

DecisionDx-Melanoma Is Supported by Significant Scientific Evidence

10,000+

Total patients included in studies including ***independent validation***

40+

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

120,200+

Patients with a clinical ***DecisionDx-Melanoma*** order from ***11,200+ 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

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*According to SORT system, used by American Academy of Dermatology
Following a diagnosis of cutaneous melanoma, providers make two important treatment decisions – whether to recommend SLNB and what type/frequency of follow up should be used.
Data as of Dec. 31, 2022

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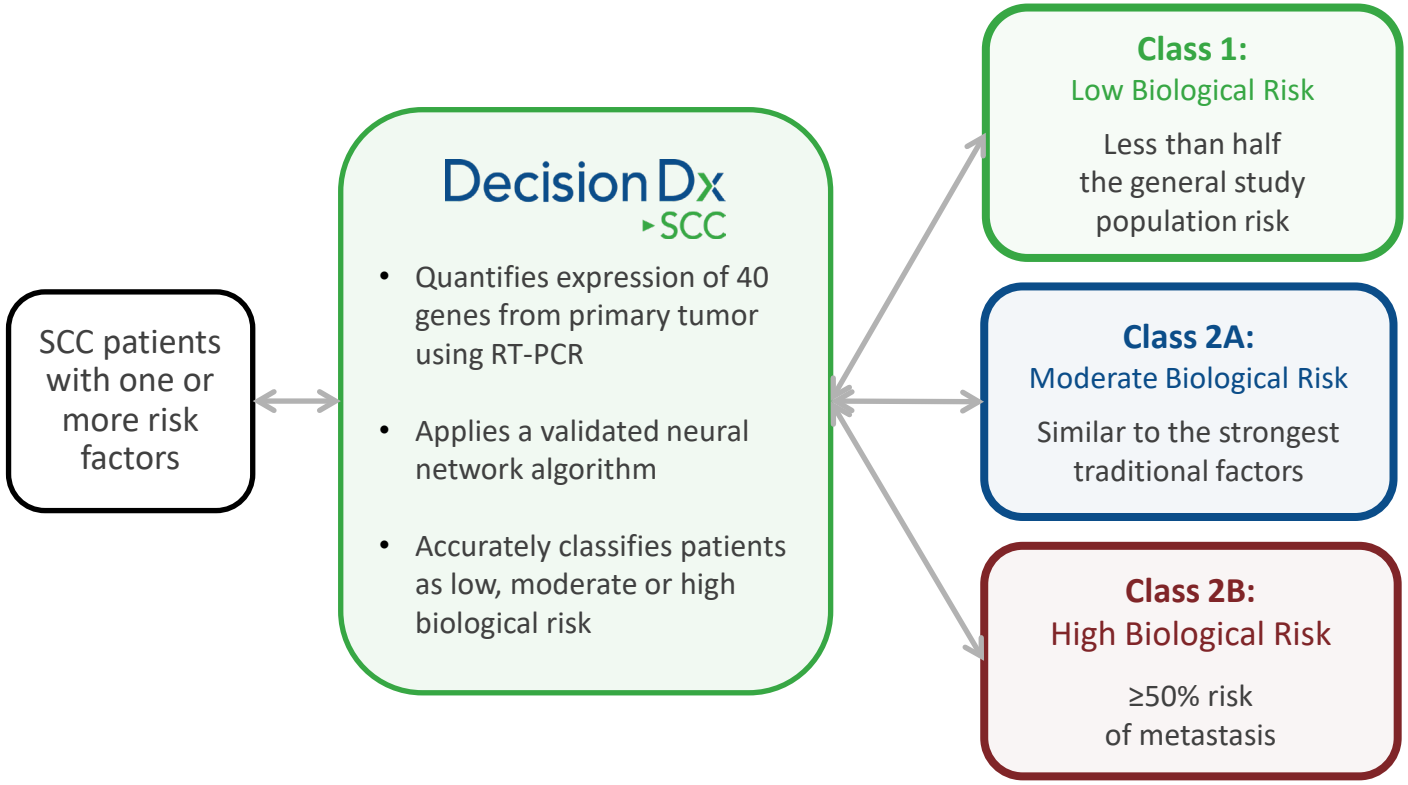
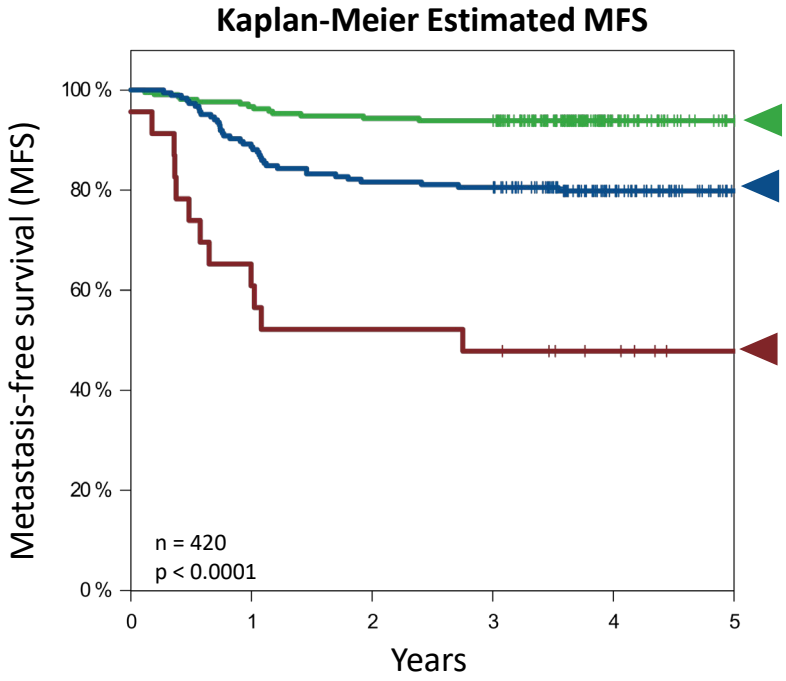
DecisionDx-SCC

DecisionDx-SCC Provides Independent Risk Stratification to Inform SCC Management Decisions



Wysong et al. *JAAD* 2021; Ibrahim et al. *Future Oncology* 2021

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

Wysong et al. *JAAD* 2021; Ibrahim et al. *Future Oncology* 2021

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MyPath
▸Melanoma

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

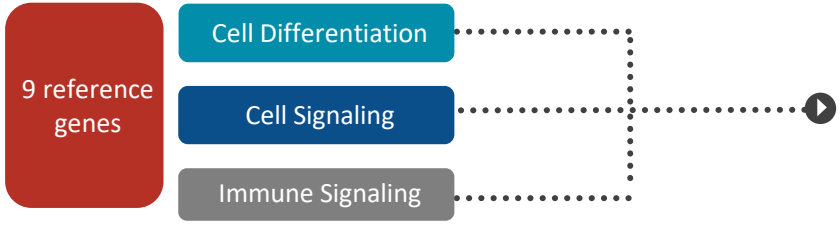
These difficult-to-diagnose lesions are commonly sent for second opinions to expert dermatopathologists who have more experience with challenging cases; however, the nature of many lesions remains ambiguous with discordant rates of lesions in this category of 25-43% (Elmore et al. 2017)

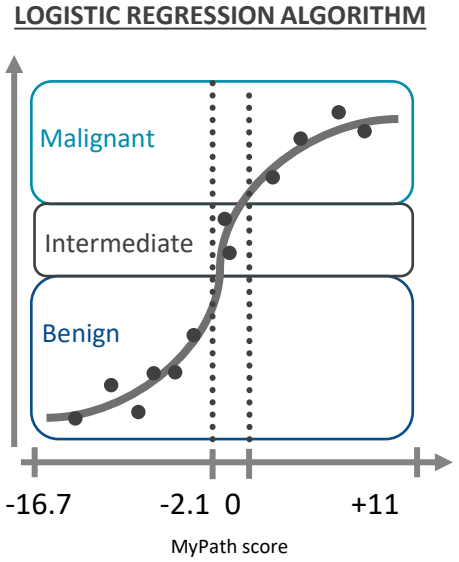
Diagnostic ambiguity can lead to clinical management uncertainty and overtreatment, leading to unnecessary excisions and increased patient morbidity, and undertreatment, with the potential for missing diagnoses of malignant melanoma

MyPath for Use in Ambiguous Melanocytic Lesions

MyPath Melanoma

Expression of each gene group is calculated and normalized to the control genes. The aggregated score for each gene group is input into a trained logistic regression algorithm which weights each input and calculates a single score and classification of benign, intermediate or malignant.





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Clarke et al. *J Cutan Pathol* 2015

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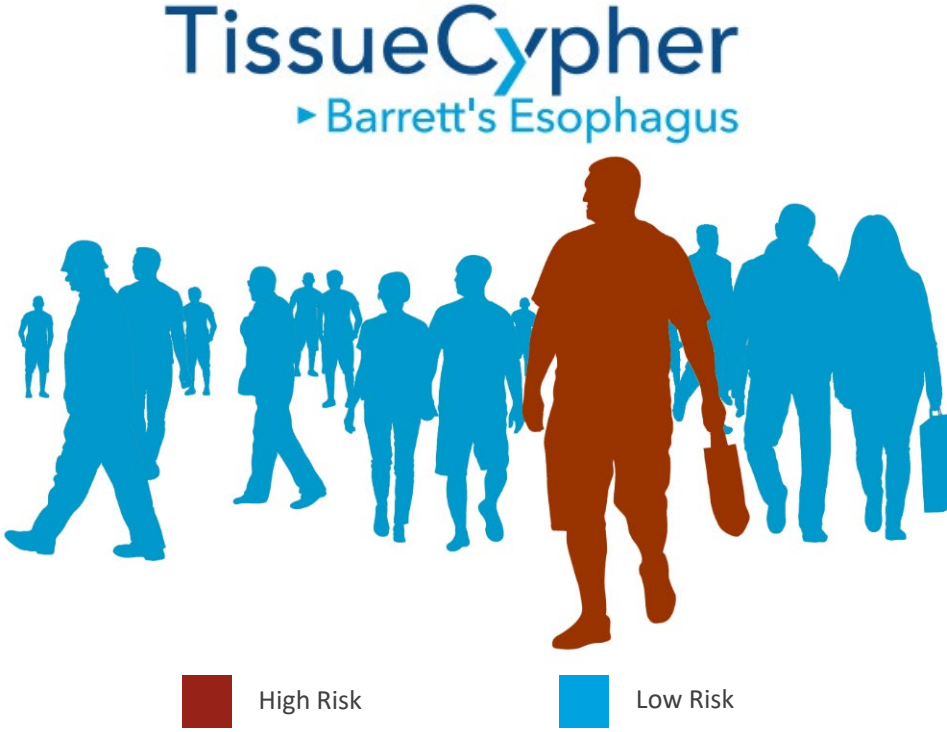
TissueCypher

Barrett's Esophagus

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

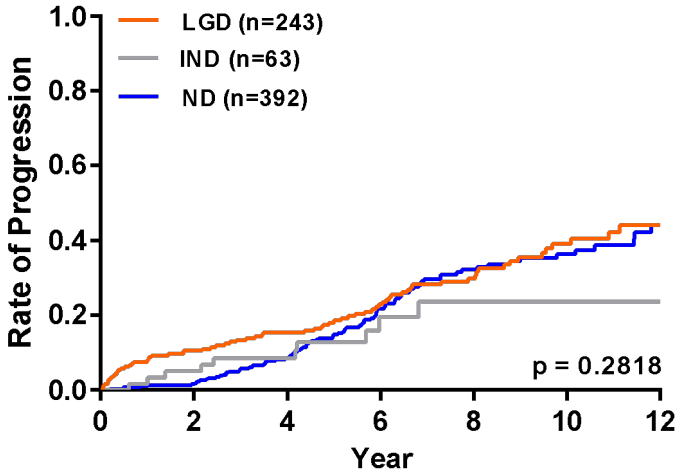
Individualize 5-year risk of progression to HGD or EAC

- 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

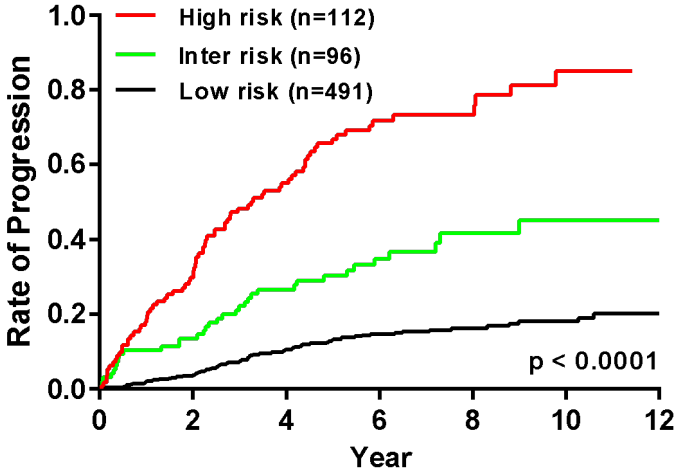


TissueCypher Is the Strongest Independent Predictor of Progression

Original Pathologic Diagnosis



TissueCypher



HR = 7.7 (high- vs. low-risk) p<0.0001

HR = 2.8 (inter- vs. low-risk) p<0.0001

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

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HR = Hazard ratio. Pooled analysis completed by Castle Biosciences. [1]Critchley-Thorne et al. *Cancer Epidemiol Biomarkers Prev* 2016; [2]Critchley-Thorne et al. *Cancer Epidemiol Biomarkers Prev* 2017; [3]Davison et al. *Am J Gastroenterol* 2020; [4]Frei et. al. *Clin Transl Gastroenterol* 2020; 5 Frei et. al. *Am J Gastroenterol* 2021

IDgenetix: Precision Medicine Designed to Streamline Medication Selection for Mental Health

Next Generation PGx

- Eliminate trial and error prescribing
- 3 in 1 test:
  - Drug-gene interactions
  - Drug-drug interactions
  - Lifestyle factors

Unrivaled Efficacy

- 2x improved chance of medication response vs. control
- >2.5x improved chance of remission of depression symptoms vs. control

Easy to Use

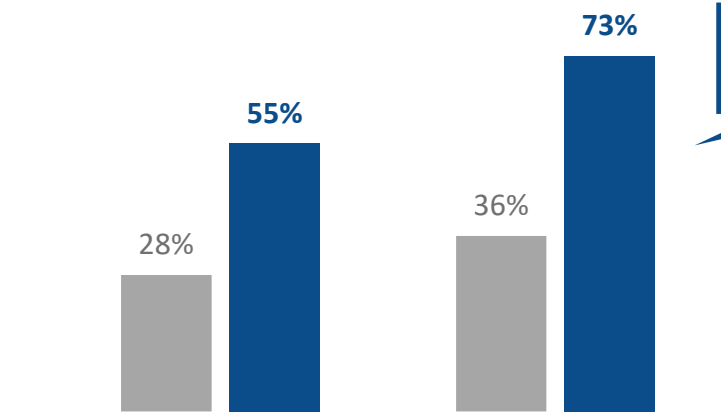
- 10 mental health and pain conditions in one report
- <1 minute to collect DNA sample
- 3-5 days to receive test report
- Specialized sales and medical science liaison support

Bradley et al. *J Psychiatr Res* 2018.

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

Response Rate

≥ 50% Reduction from Baseline

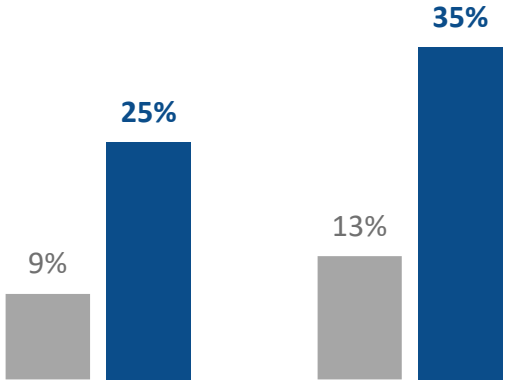


2x
increase in response rate vs. control

Remission Rate

Patients Achieving Remission

>2.5x
increase in remission rate vs. control



	Week 8	Week 12
p-value	*0.01*	*0.001*

	Week 8	Week 12
p-value	*0.05*	*0.02*

Control
IDgenetix

Bradley et al. *J Psychiatr Res* 2018.

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DecisionDx-UM

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

Strong Evidence Base

- 24 peer-reviewed publications with ***3,600+ 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
- ***1,711 reports*** issued in 2022

Broad Reimbursement

- In 2022, more than 100 commercial insurers covered DecisionDx-UM
- 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

DecisionDx ▸UM

15-Gene Expression Profile (GEP) Test

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

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

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Inflammatory Skin Disease

Pipeline test to predict response to systemic therapies with target launch by the end of 2025

Castle Has Started Two Studies to Aid in Treatment of Inflammatory Skin Diseases

IDENTITY

- Help guide therapy selection for atopic dermatitis and psoriasis
- Prospectively enrolling, multi-center study
- Sample obtained through non-invasive skin scraping sample collection method

SIGNAL-MF

- Identify mycosis fungoides (MF)[1] – a type of cutaneous T-cell lymphoma that can mimic atopic dermatitis or psoriasis
- Sample obtained through non-invasive skin scraping sample collection method
- Prospectively enrolling, multi-center study
- Targeting 15 sites for enrollment; 16 committed[2]

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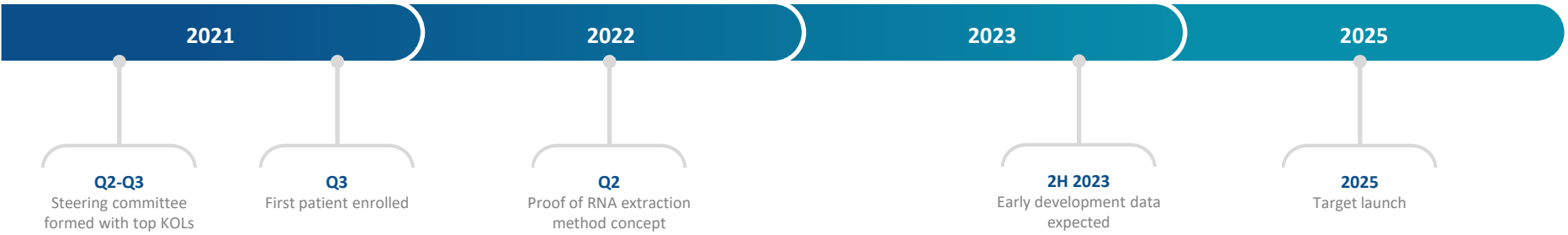
[1]For MF, the most common type of CTCL, the incidence is ~1,600 new cases per year (as of 2016) according to Teras et al, CA, 2016; [2]Data as of 02/03/23

IDENTITY Study

Castle's inflammatory skin disease pipeline test is being developed to predict systemic therapy response

54
Committed Sites

507
Patients Enrolled[1]



Program Milestones

Data as of 02/03/23; [1]patients with moderate-to-severe disease

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Thank you

Use Of Non-GAAP Financial Measures (Unaudited)

In this presentation, we use the metrics of Adjusted Revenues, Adjusted Gross Margin, Adjusted Operating Cash Flow and Adjusted EBITDA, which are non-GAAP financial measures and are not calculated in accordance with generally accepted accounting principles in the United States (GAAP). Adjusted Revenues and Adjusted Gross Margin reflect adjustments to net revenues to exclude changes in variable consideration related to test reports delivered in previous periods but not recorded as revenues until a subsequent period. 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. Adjusted EBITDA excludes from net loss interest income, interest expense, income tax expense (benefit), depreciation and amortization expense, stock-based compensation expense, change in fair value of contingent consideration, and acquisition-related transaction costs.

We use Adjusted Revenues, Adjusted Gross Margin, Adjusted Operating Cash Flow and Adjusted EBITDA 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 that Adjusted Revenues, when used in conjunction with our test report volume information, facilitates investors' analysis of our current-period revenue performance and average selling price performance by excluding the effects of revenue adjustments related to test reports delivered in prior periods, since these adjustments may not be indicative of the current or future performance of our business. We believe that providing Adjusted Revenues may also help facilitate comparisons to our historical periods. Adjusted Gross Margin is calculated using Adjusted Revenues and therefore excludes the impact of revenue adjustments related to test reports delivered in prior periods, which we believe is useful to investors as described above. We further exclude acquisition-related intangible asset amortization in the calculation of Adjusted Gross Margin. We believe that excluding acquisition-related intangible asset amortization may facilitate gross margin comparisons to historical periods and may be useful in assessing current-period performance without regard to the historical accounting valuations of intangible assets, which are applicable only to tests we acquired rather than internally developed. 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 payment activity, which we believe are not indicative of our ongoing operations. We believe Adjusted EBITDA may enhance an evaluation of our operating performance because it excludes the impact of prior decisions made about capital investment, financing, investing and certain expenses we believe are not indicative of our ongoing performance, such as acquisition-related transaction costs. 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.

Reconciliation of Non-GAAP Financial Measures (Unaudited)

The table below presents the reconciliation of adjusted revenues 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 December 31,		Twelve Months Ended December 31,	
	2022	2021	2022	2021
(in thousands)				
Adjusted revenues				
Net revenues (GAAP)	$ 38,338	$ 25,039	$137,039	$ 94,085
Revenue associated with test reports delivered in prior periods	(806)	780	1,987	(3,324)
Adjusted revenues (Non-GAAP)	$ 37,532	$ 25,819	$139,026	$ 90,761
Adjusted gross margin				
Gross margin (GAAP)[1]	$ 26,603	$ 19,434	$ 96,764	$ 76,305
Amortization of acquired intangible assets	2,215	1,008	8,266	1,958
Revenue associated with test reports delivered in prior periods	(806)	780	1,987	(3,324)
Adjusted gross margin (Non-GAAP)	$ 28,012	$ 21,222	$107,017	$ 74,939
Gross margin percentage (GAAP)[2]	69.4 %	77.6 %	70.6 %	81.1 %
Adjusted gross margin percentage (Non-GAAP)[3]	74.6 %	82.2 %	77.0 %	82.6 %

1. 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.
2. Calculated as gross margin (GAAP) divided by net revenues (GAAP).
3. Calculated as adjusted gross margin (Non-GAAP) divided by adjusted revenues (Non-GAAP).

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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 38 for further information regarding the Company's use of non-GAAP financial measures.

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2022	2021	2022	2021
(in thousands)				
Adjusted operating cash flow				
Net cash used in operating activities (GAAP)	$ (6,000)	$ (2,781)	$ (41,655)	$ (18,983)
Medicare advance payment[1]	—	2,999	—	8,350
HHS provider relief funds[2]	—	—	—	(1,882)
Adjusted operating cash flow (Non-GAAP)	$ (6,000)	$ 218	$ (41,655)	$ (12,515)

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 (used in) 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).

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Reconciliation of Non-GAAP Financial Measures (Unaudited)

The table below presents the reconciliation of adjusted EBITDA, which is a non-GAAP financial measure. See slide 38 for further information regarding the Company's use of non-GAAP financial measures.

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2022	2021	2022	2021
(in thousands)				
Adjusted EBITDA				
Net loss	$ (20,618)	$ (6,430)	$ (67,138)	$ (31,292)
Interest income [1]	(2,275)	(17)	(3,968)	(68)
Interest expense	4	1	17	1
Income tax expense (benefit)	57	(8,725)	(1,766)	(8,720)
Depreciation and amortization expense	2,841	1,451	10,543	3,407
Stock-based compensation expense	9,923	6,851	36,321	21,740
Change in fair value of contingent consideration	(300)	—	(18,287)	—
Acquisition related transaction costs	—	—	1,711	—
Adjusted EBITDA (Non-GAAP)	$ (10,368)	$ (6,869)	$ (42,567)	$ (14,932)

1. Beginning in the fourth quarter of 2022, we began excluding interest income from the calculation of Adjusted EBITDA. Prior periods presented herein have been recast to conform to the current period presentation.

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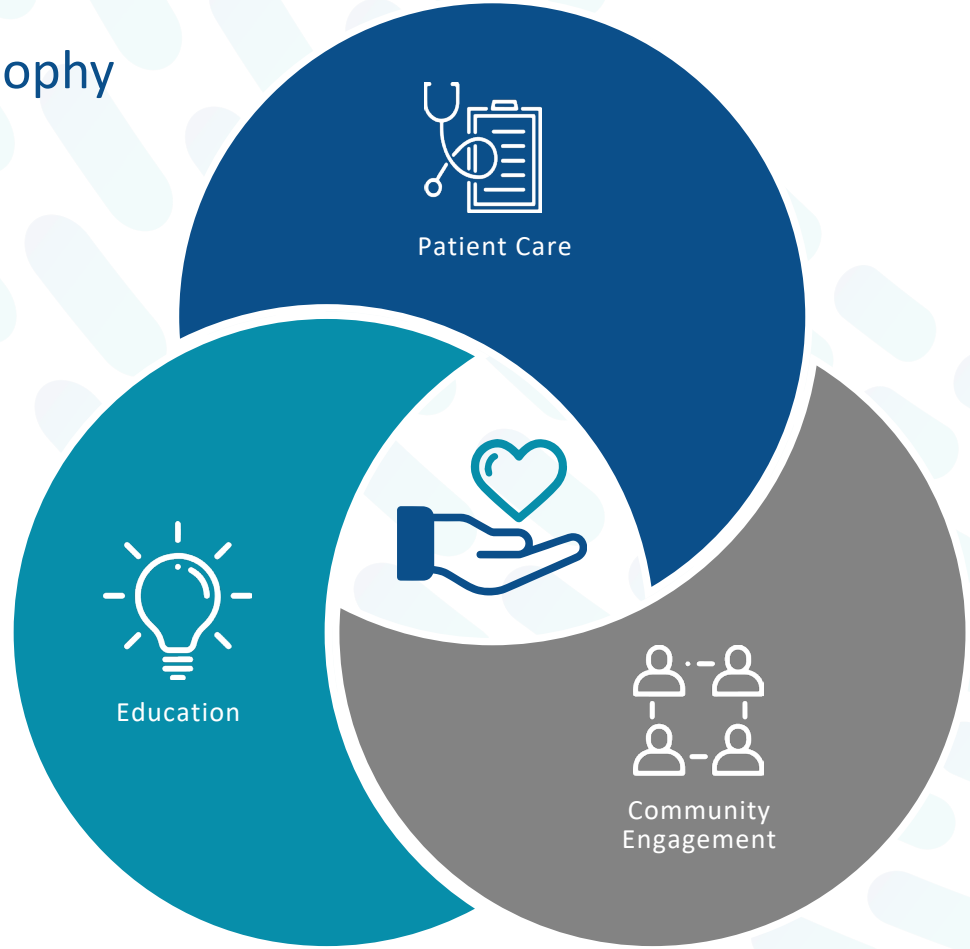
Appendix

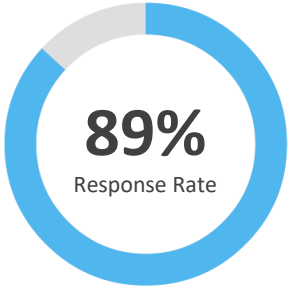
Our Giving Philosophy



Employee Engagement is Part of our Core Strategy for Success

Based on the results of Castle's annual employee survey[1]

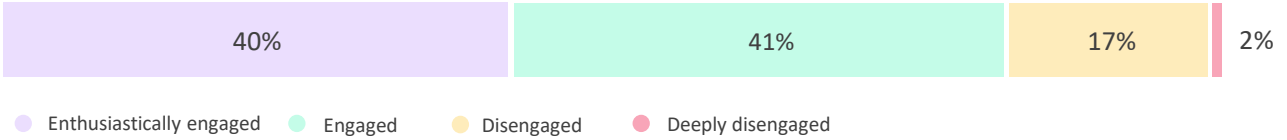
2022



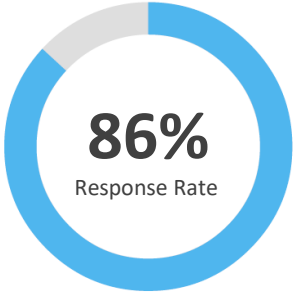
Healthcare benchmark response rate: 59%

Castle employee engagement score: **81%**

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



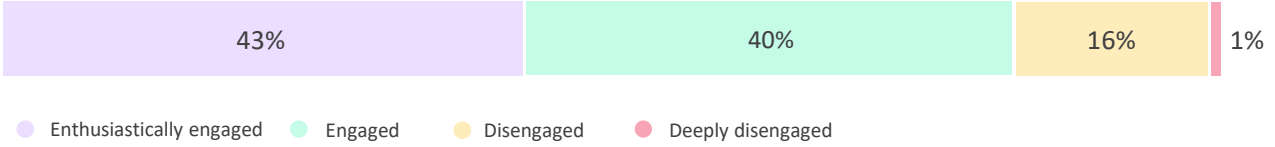
2021



Healthcare benchmark response rate: 63%

Castle employee engagement score: **83%**

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



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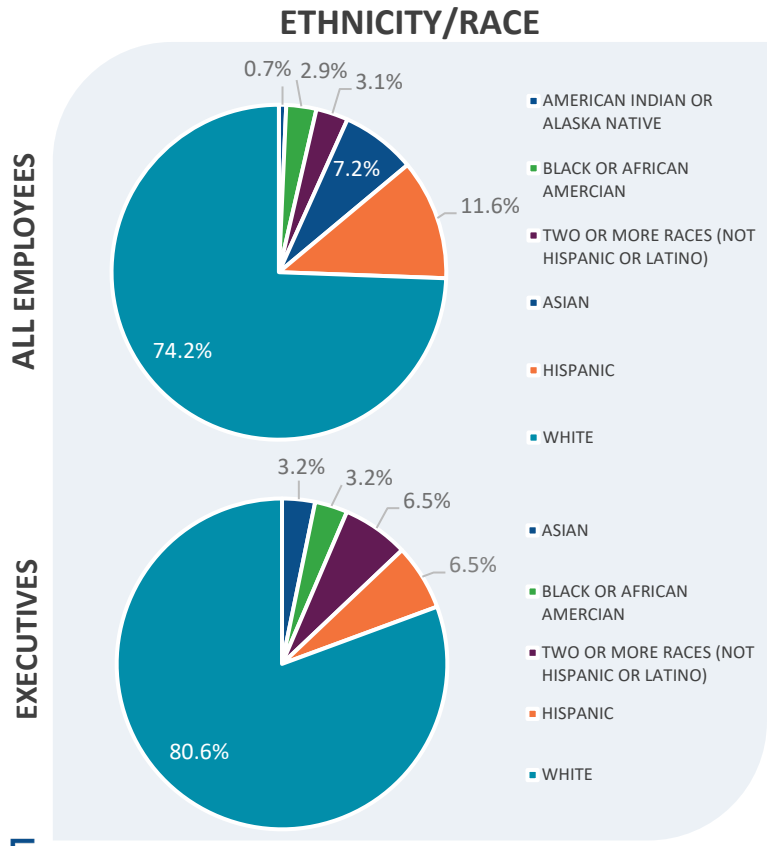
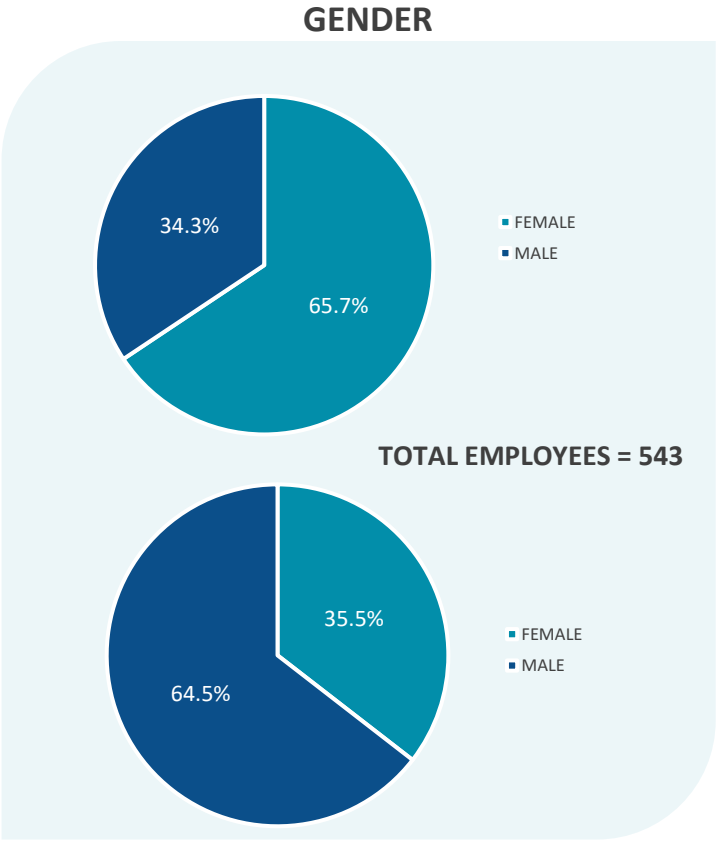
[1]Data from June 2022 employee engagement survey administered by Energage

Commitment to Diversity





Data as of Dec. 31, 2022; Executive= Executive Director or Regional Business Director level and above

Award-Winning Company

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

TOP WORK PLACES 2021 HOUSTON CHRONICLE

TOP WORK PLACES 2022 HOUSTON CHRONICLE

TOP WORK PLACES 2022 USA

TOP WORK PLACES 2023 USA

TOP WORK PLACES 2022 azcentral.

Inc. Best-Led Companies 2021

MEDTECH BREAKTHROUGH AWARD 2021
BEST NEW TECHNOLOGY SOLUTION - ONCOLOGY -

MEDTECH BREAKTHROUGH AWARD 2022
BEST NEW TECHNOLOGY SOLUTION - DERMATOLOGY -

HOUSTON CHRONICLE CHRON 100 HOUSTON'S LEADING COMPANIES PRESENTED BY TEXASINC 2020

HOUSTON CHRONICLE CHRON 100 HOUSTON'S LEADING COMPANIES PRESENTED BY TEXASINC 2021

The Healthcare Technology Report
The Top 100 Healthcare Technology Companies of 2021

AMERICAN SKIN ASSOCIATION

2019 Technology Innovation in Melanoma Award Winner

CASTLE BIOSCIENCES

Leadership Team Overview

MANAGEMENT TEAM

Derek Maetzold
Founder, Director, President and CEO

Frank Stokes
Chief Financial Officer

Toby Juvenal
Chief Commercial Officer

Kristen Oelschlager, RN, CHC
Chief Operating Officer

Robert Cook, PhD
Senior Vice President, Research & Development

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