CASTLE BIOSCIENCES

Transforming Disease Management

August 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 2023 revenue guidance of at least $180 million; our reiterated 2025 guidance relating to (i) total revenue of $255-$330 million and (ii) net operating cash flow positivity; our expected launch of our pipeline expansion by 2025, including receiving early development data for our IDENTITY study by the second half of 2023; the potential of DecisionDx-Melanoma test results to help inform more personalized patient management decisions; our belief that DecisionDx-SCC (i) could be used to guide ART the way PNI does in existing guidelines, (ii) may be a benefit to ART when appropriate high-risk patients are identified, (iii) can result in a 40% or greater reduction in risk, (iv) may inform appropriate clinical management decisions related to ART administration in high-risk SCC patients and (v) has the potential for significant cost savings to our healthcare system by helping ensure the appropriate patients receive costly therapies; our target of 15 committed sites for enrollment in our SIGNAL-MF study; our mission, vision, strategic guideposts and our strategies for driving long-term growth through strong execution and our operational guideposts; our estimated U.S. total addressable market for our commercially available tests; our positioning for continued growth and expected 2023 catalysts; our ongoing studies generating data and their impact on driving adoption of our tests; and study observations and interpretations of study data, including conclusions about the benefits and impact of our tests on treatment decisions and patient outcomes. The words "anticipates," "can," "could," "estimates," "expects," ""may," "potential," "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: our estimates and assumptions underlying our estimated U.S. total addressable market for our commercially available tests; the accuracy of our assumptions and expectations underlying our fiscal 2023 and three-year revenue and other financial targets and guidance (including, without limitation, our assumptions or expectations regarding continued reimbursement for our DecisionDx-SCC test at the current rate and reimbursement for our other products and subsequent coverage decisions, our estimated total addressable markets for our products and product candidates and the related expenses, capital requirements and potential needs for additional financing, the anticipated cost, timing and success of our product candidates, and our plans to research, develop and commercialize new tests and our ability to successfully integrate new businesses, assets, products or technologies acquired through acquisitions), the effects of macroeconomic events and conditions, including inflation and monetary supply shifts, labor shortages, liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets and recession risks, supply chain disruptions, outbreaks of contagious diseases (such as the COVID-19 pandemic) and geopolitical events (such as the ongoing Ukraine-Russia conflict), among others, 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 anticipated 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.

Castle Biosciences – Transforming Disease Management

Portfolio of Innovative Tests

Dermatology
Ophthalmology
Gastroenterology
Mental Health

Steadfast commitment to improving patient care through our innovative, actionable tests

Leader in the field of molecular diagnostics by challenging the status quo with deep scientific expertise, unique value insight and strong data

Core dermatology business and newer gastroenterology and mental health franchises driving solid test report volume growth

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Financial Performance Summary Q2 2023

		Q2 2023	Q2 2022
Total test reports		**16,820**	11,034
Total Dermatology test reports		**12,231**	9,424
Revenues		**$50.1M**	$34.8M
Adj. Revenues[1]		**$50.2M**	$34.3M
Gross Margin		**73.5%**	71.9%
Adj. Gross Margin[1]		**78.0%**	77.6%
Net Loss		**$(18.8)M**	$(1.6)M
Adj. EBITDA[1]		**$(5.3)M**	$(11.2)M
Operating Cash Flow		**$(3.8)M**	$(9.0)M
Cash, Cash Equivalents & Marketable Investment Securities	as of end of period	**$225.5M[2]**	$273.2M

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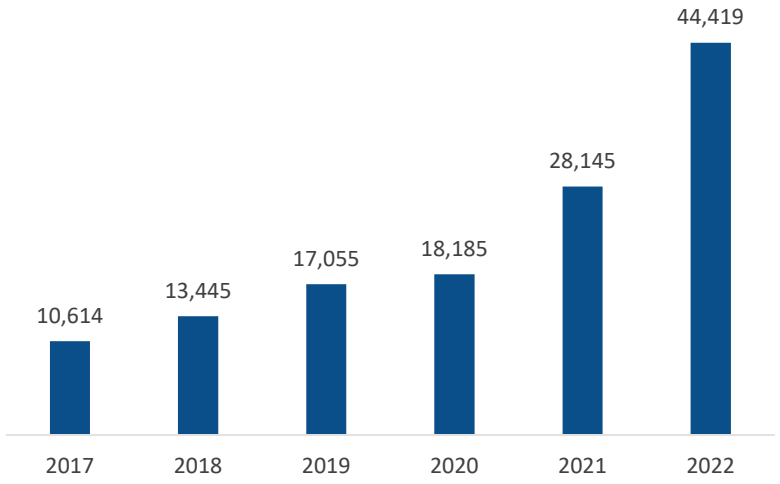
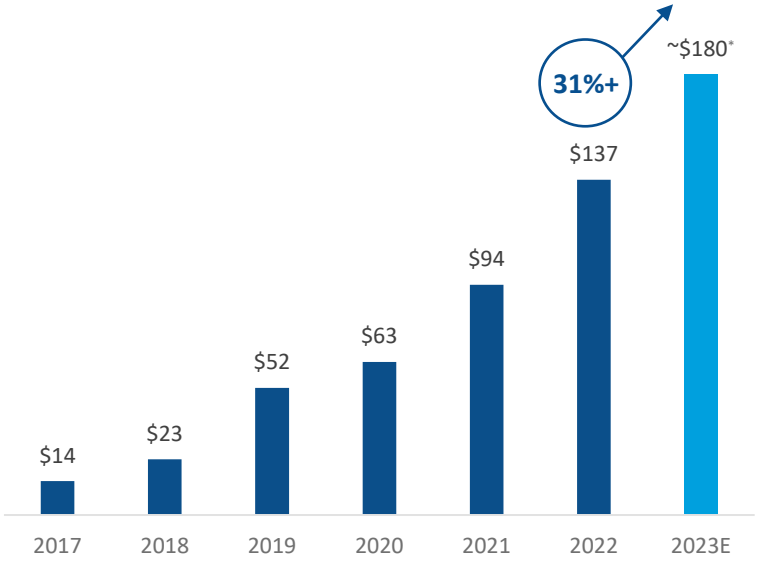
[1]See Non-GAAP reconciliations at the end of this presentation. [2]Year-over-year change in cash, cash equivalents and marketable securities includes the acquisition of AltheaDx in April 2022 and payout of annual bonuses in Q1 2023, among other uses.

Consistent Execution Of Growth Initiatives Supports Long-Term Growth

2017-2022 Total Test Report Volume



2017-2023 Revenue ($M)



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*2023 revenue guidance of at least $180 million, as of August 2, 2023

Key Q2 2023 Accomplishments

Delivered strong Q2 results, highlighted by year-over-year growth in our total test report volume (+52%) and revenue (+44%)

Opened new state-of-the-art lab in Pittsburgh, bringing Castle's total laboratory operations space to 52,000 square feet

Raised 2023 revenue guidance to at least $180 million, vs. $170-$180 million prior; reiterated 2025 guidance relating to (i) total revenue of $255-$330 million and (ii) net operating cash flow positivity

DecisionDx-SCC test received Advanced Diagnostic Laboratory Test (ADLT) status from the Centers for Medicare & Medicaid Services (CMS)

Publication of study data highlighting a clinician-derived, real-world algorithm that provides a framework to incorporate DecisionDx-SCC test results into clinical practice within NCCN guideline recommendations

Publication of study data from our collaboration with the National Cancer Institute's SEER Program Registries showing that testing with DecisionDx-Melanoma was associated with lower melanoma-specific and overall mortality relative to untested patients

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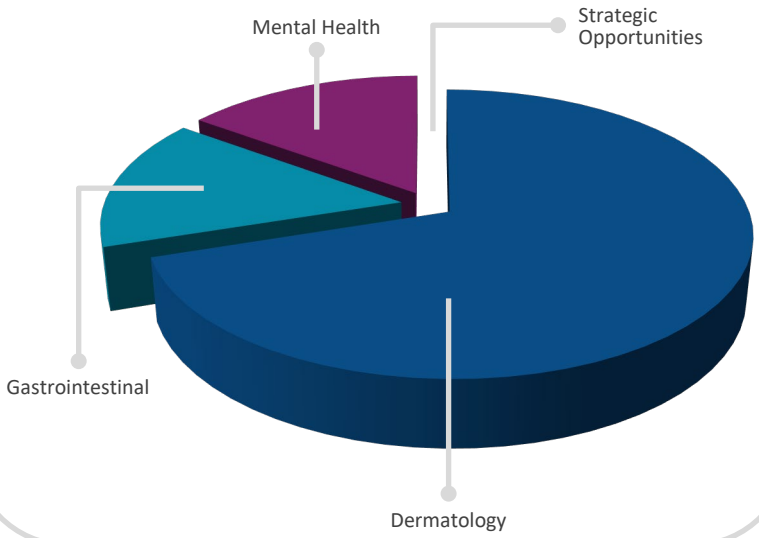
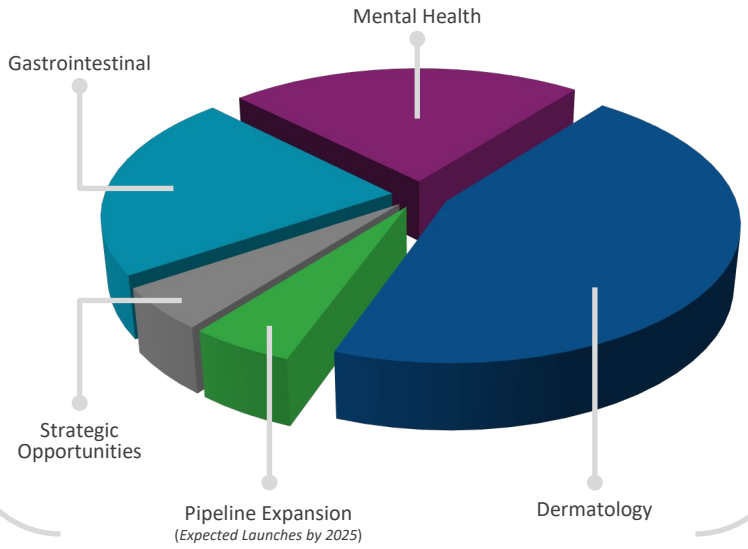
Driving Long-Term Growth Through Strong Execution And Our Operational Guideposts

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

PATIENT CARE JOURNEY	Screening	Diagnostic Support	Risk Stratification	Therapy Response	MRD/Recurrence Monitoring
Dermatology		MyPath Melanoma	Decision Dx Melanoma Decision Dx SCC	Inflammatory Skin Disease Pipeline Test	
Ophthalmology			Decision Dx UM		
Gastroenterology			TissueCypher Barrett's Esophagus		
Mental Health				IDgenetix PGx Testing	

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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 ~$5.7B to our U.S. TAM

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

18
Ongoing clinical research studies

317
Committed/contributing clinical research sites as of Q2 2023

~12,250+
Current patients enrolled in studies as of Q2 2023

~17,490
Patients enrolled in studies over lifetime of Castle[1]

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

Data as of June 30, 2023
[1]Number reflects studies that span Castle's dermatology, ophthalmology, gastroenterology and mental health portfolios, as well as tests that are currently in our development pipeline. Data for TissueCypher, IDgenetix and MyPath are reflective of studies that have occurred since Castle's acquisition of the tests. [2]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 [3]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.

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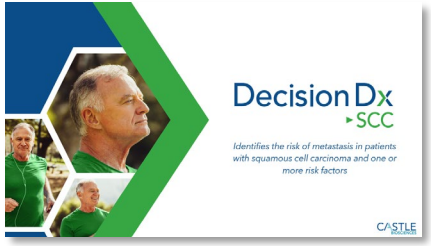
First-To-Market Dermatologic Franchise, Additional Growth Opportunities

Diagnostic Support

Risk Stratification



Therapy Response

Strong provider growth and continued adoption with approximately 570 new[1] ordering clinicians and approximately 2,060 total ordering clinicians for dermatologic tests for the quarter ended June 30, 2023

[1] New=clinician who ordered a Castle dermatologic test for the first time.

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Decision Dx ▸ Melanoma

Clinical Validity and Utility

Demonstrated clinical validity, utility and impact, backed by more than 40 peer-reviewed publications, including two recent publications (Bailey et al. and Dhillon et al.) demonstrating an association with testing and improved patient outcomes

ADLT Status

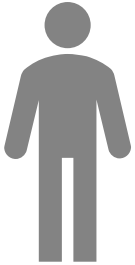
Classified as an Advanced Diagnostic Laboratory Test (ADLT) by the Centers for Medicare & Medicaid Services (CMS), meaning it provides new clinical diagnostic information that cannot be obtained from any other test or combination of tests[1]

Reimbursement

Reimbursement coverage through Medicare Administrative Contractor (MAC), Noridian, the MAC that oversees our Phoenix laboratory and is part of the MolDX® program that assesses molecular diagnostic technologies

[1]Centers for Medicare & Medicaid Services: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Downloads/Guidance-for-Laboratories-on-ADLTs.pdf

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



Individual Risk of Sentinel Lymph Node Positivity

=

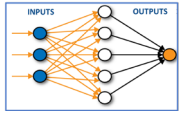
Individual Risk of Recurrence

=

DecisionDx-Melanoma Class Result

+

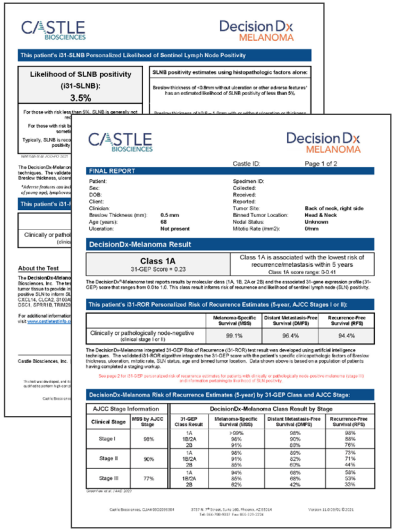
Breslow Thickness
Ulceration
Mitotic Rate
Age



Neural network with AI algorithm

+

Breslow Thickness
Ulceration
Mitotic Rate
SLN Status
Age
Tumor Location



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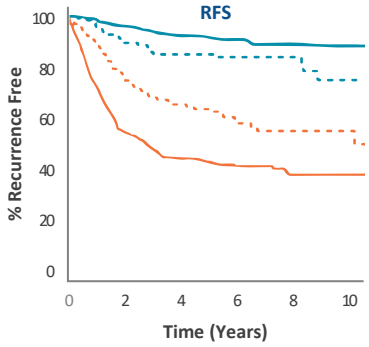
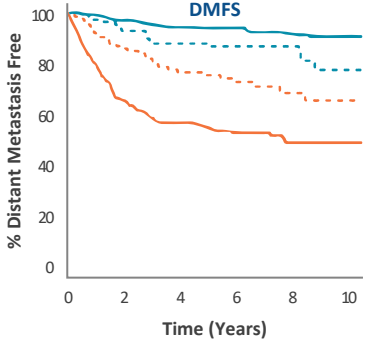
Whitman et al. *JCO PO* 2021; Jarell et al. *JAAD* 2022

DecisionDx-Melanoma 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 (DecisionDx-Melanoma)	**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

DecisionDx-Melanoma Results Guided Treatment Decisions And Led To Improved Patient Outcomes

Independent, multi-center study of SLN negative patients (n=634)

Tested Group (n=307): DecisionDx ▸Melanoma CLASS 2A/2B	Untested Control Group (n=327): Patients without testing
Adhered to routine imaging every 6-12 months	Imaging driven by clinical symptoms or physical exam findings

Key Findings:

- Routine surveillance imaging in SLN-, high-risk patients detected melanoma recurrence **~10 months earlier** than those without routine imaging.
- Tumor burden at detection was significantly lower in patients tested compared to those not tested (27.6mm vs 73.1mm)
- At study end, patients tested had **better overall survival** than those not tested (76% vs 50%, p-value= 0.027)

"Patients who received routine imaging after high-risk GEP test scores had an earlier recurrence diagnosis with lower tumor burden, leading to better clinical outcomes."

Dhillon et al. *Archives of Derm Research* 2023.

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DecisionDx ▸Melanoma

Collaboration with the National Cancer Institute

Linking DecisionDx-Melanoma clinical testing with patients captured in the National Cancer Institute's SEER Program Registries

NCI/SEER Data Linked With DecisionDx-Melanoma Test Results

Data analysis of real-world, unselected, clinically tested patients showed that DecisionDx-Melanoma testing was associated with lower melanoma-specific and overall mortality relative to untested patients

29%

Lower 3-year melanoma-specific mortality rate in patients clinically tested vs untested

Group	3-year MSS (95% CI)	Deaths, % (n/N)
31-GEP Tested	97.4% (96.6-98.2%)	1.7% (57/3258)
Matched Untested	96.1% (95.5-96.6%)	2.5% (242/9774)
Hazard Ratio‡		**0.71 (0.53-0.94) p=0.018**

17%

Lower 3-year overall mortality rate in patients clinically tested vs untested

Group	3-year OS (95% CI)	Deaths, % (n/N)
31-GEP Tested	92.4% (91.1-93.6%)	5.2% (170/3258)
Matched Untested	90.9% (90.1-91.7%)	6.2% (610/9774)
Hazard Ratio‡		**0.83 (0.70-0.99) p=0.034**

Tested: n=3,258
Not Tested: n=9,774

› **Data show DecisionDx-Melanoma provided significant, independent risk stratification of patients with cutaneous melanoma, beyond AJCC8 stage, which may help inform more personalized patient management decisions**

Bailey et al. *JCO PO*, 2023. ‡Hazard ratio (HR) was computed using the untested patients as reference for 31-GEP tested cohort. An HR less than 1.0 demonstrates improved survival in 31-GEP tested patients. Diagnosis and 31-GEP test date 2016-2018. AJCC8=American Joint Committee on Cancer Eighth Edition

DecisionDx ▸Melanoma

Clinical Use Of DecisionDx-Melanoma Shows Favorable Outcomes When Compared To Other Standard Of Care Prognostic Tests

Sentinel Lymph Node Biopsy (SLNB)

- MSLT-I found that SLN biopsy had no impact on 10-year melanoma specific survival[1]
- SLN positivity is no longer the gateway to immunotherapy[2]

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 (>3.5mm)	Not significant (p=.56)	Not impacted

Oncotype DX - Breast[3]	3-yr BCSS
Oncotype DX - Breast	99.6%
Match Untested	99.1%
Absolute Mortality Difference	0.50% (p<0.05)

Oncotype DX showed absolute BCSS mortality difference of 0.5% at 3 years over those not tested

DecisionDx-Melanoma	3-yr MSS[4]
DecisionDx-Melanoma	97.4%
Match Untested	96.1%
Absolute Mortality Difference	1.3% (p<0.05)

DecisionDx-Melanoma showed absolute MSS mortality difference of 1.3% at 3 years over those not tested[4]

DecisionDx-Melanoma shows more than 2x the survival benefit

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1. Morton et al. *N Engl J Med.* 2014. 2. Luke et al. *Lancet*. 2022. 3. Zhang et al. *Breast Cancer Res Treat*. 2020 4. Bailey et al. *JCO PO*. 2023.
*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***

137,200+

Patients with a clinical ***DecisionDx-Melanoma*** order from ***12,190+ 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
Data as of June 30, 2023

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DecisionDx-SCC

Clinical Validity and Utility

Demonstrated validity, utility and impact, backed by 13 peer-reviewed publications, including data showing that DecisionDx-SCC can significantly impact patient management plans in a risk-appropriate manner within established guidelines[1]

ADLT Status

Classified as an Advanced Diagnostic Laboratory Test (ADLT) by the Centers for Medicare & Medicaid Services (CMS), meaning it provides new clinical diagnostic information that cannot be obtained from any other test or combination of tests[2]

Real-World Use Framework

Study in *Clinical, Cosmetic and Investigational Dermato*logy highlights a clinician-derived, real-world algorithm that provides a framework to incorporate DecisionDx-SCC test results into clinical practice within NCCN guidelines recommendations

[1]Adapted from Litchman et al. CMRO 2020; Goldberg et al. Presented at Winter Clinical Dermatology, January 14-19, 2022; [2]Centers for Medicare & Medicaid Services: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Downloads/Guidance-for-Laboratories-on-ADLTs.pdf

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

SCC patients with one or more risk factors

DecisionDx ▸SCC

- Quantifies expression of 40 genes from primary tumor using RT-PCR
- Applies a validated neural network algorithm
- Accurately classifies patients as low, moderate or high biological risk

Class 1:
Low Biological Risk

Less than half the general study population risk

Class 2A:
Moderate Biological Risk

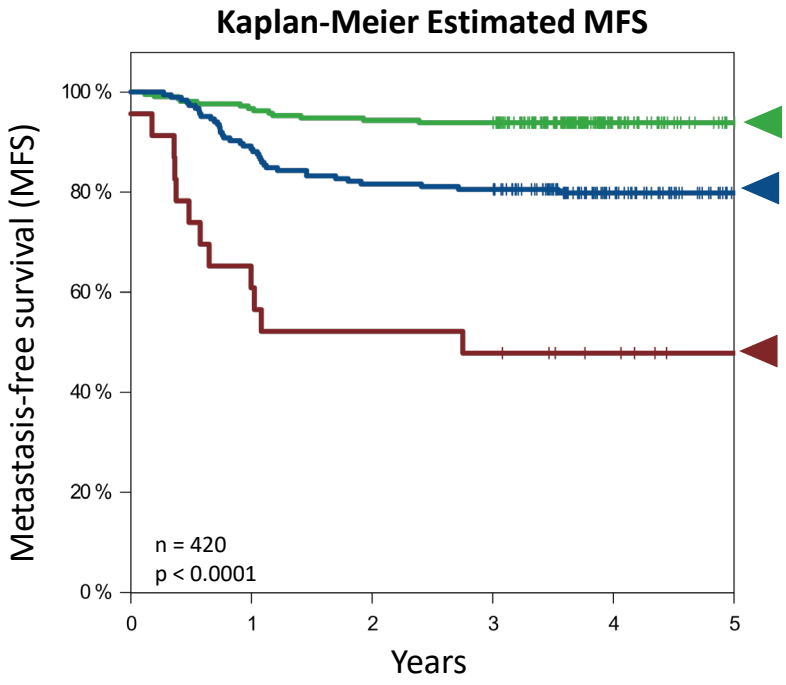
Similar to the strongest traditional factors

Class 2B:
High Biological Risk

≥50% risk of metastasis

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

Class 2A And Class 2B are Strong, Independent Predictors of Metastasis

Univariate Analysis

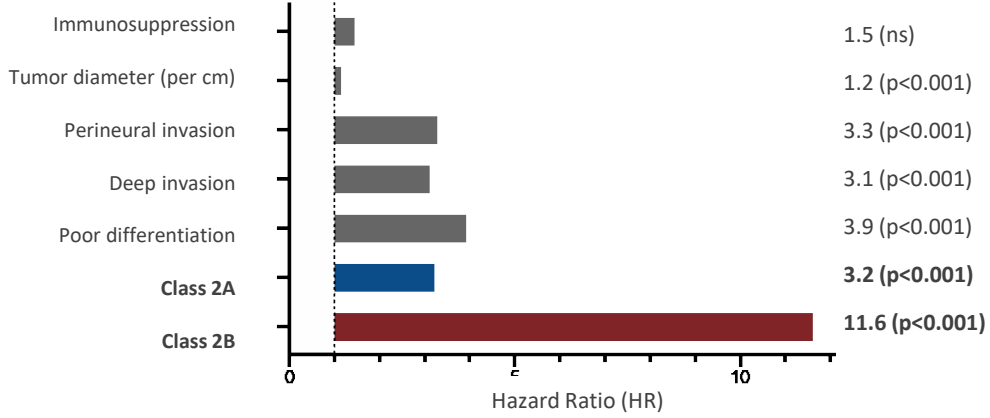
Class 2A univariate HR of 3.2 is similar to deep invasion, poor differentiation or PNI

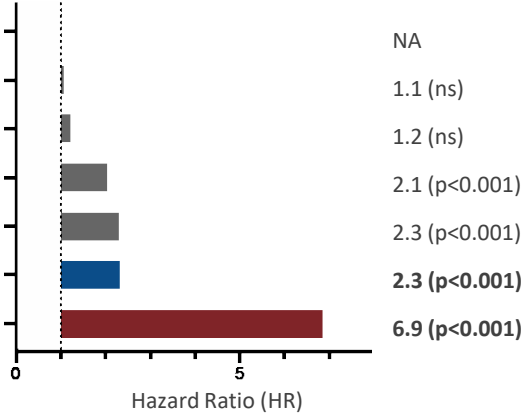
Class 2B univariate HR of 11.6 is ~3x that of the strongest prognostic risk factors

Multivariate Analysis

Class 2A multivariate HR of 2.3 is independent and similar to deep invasion and poor differentiation

Class 2B multivariate HR of 6.9 is 3x that of the strongest prognostic risk factors





Class 2A and 2B result are independent of and have stronger Hazard Ratios compared to PNI in this multivariate analysis

Deep invasion: beyond subcutaneous fat, depth >6mm, or Clark level V.; Wysong et al. *JAAD* 2021; Ibrahim et al. *Future Oncology* 2021

Who is eligible for Adjuvant Radiation Therapy (ART)?

ART is a recommended treatment plan option for high-risk SCC patients by all relevant guideline groups

American Academy of Dermatology Association

ART recommended for cSCC with:

- Concern for perineural invasion (PNI)
- High risk for regional or distant metastasis

ACR American College of Radiology

ART recommended for primary cSCC if:

- Extensive PNI
- Large caliber nerve invasion (LCNI)
- Positive margins following surgery

NCCN National Comprehensive Cancer Network®

ART recommended/considered for primary cSCC if:

- Extensive PNI
- Large caliber nerve invasion (LCNI)
- Positive margins following surgery
- Presence of other poor prognostic features
- High risk for regional or distant metastasis

ASTRO Targeting Cancer Care

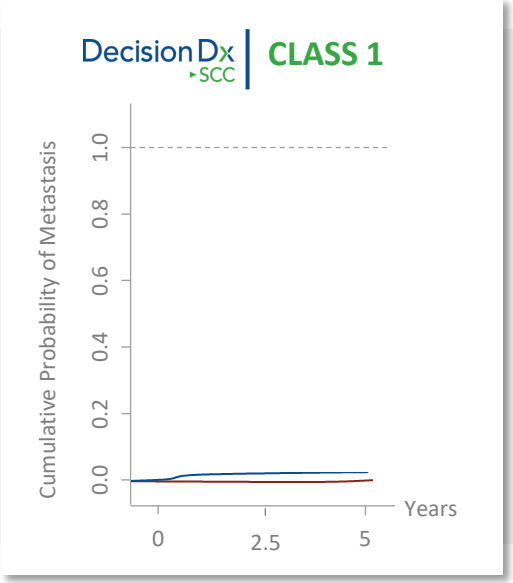
ART recommended for SCC if:

- Gross clinical or radiologic PNI
- Close surgical margins where further surgery cannot be performed
- Recurrent tumors
- AJCC8 T3 and T4 tumors
- Desmoplastic or infiltrative tumors in chronically immunosuppressed patients

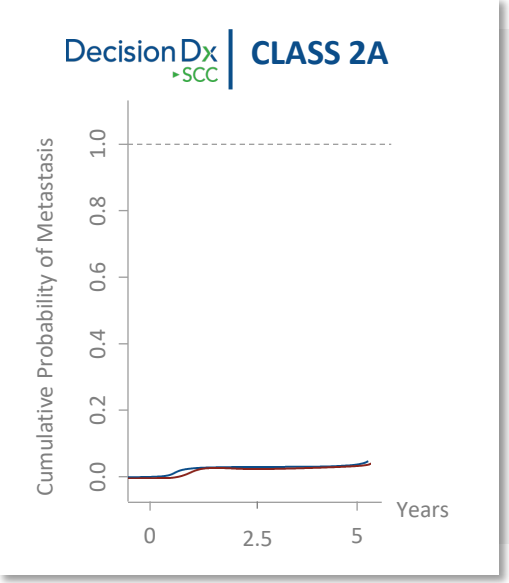
Of 7,317 patients tested, 99% could be considered for ART under NCCN criteria

Newman et al. *Head & Neck* 2021; Ruiz et al. *JAAD* 2022

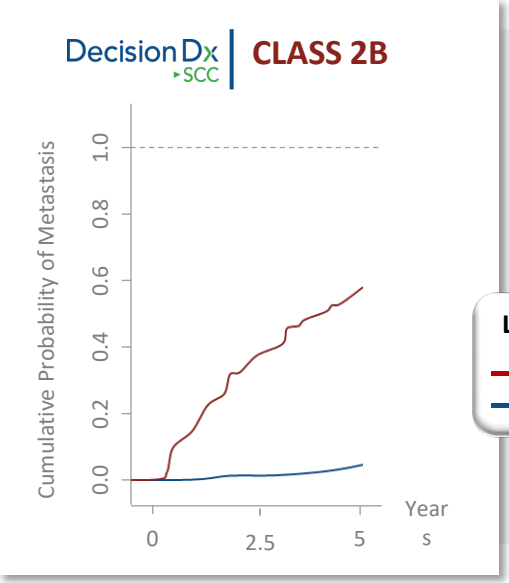
Matched Control Analysis Supports Use Of DecisionDx-SCC To Inform Adjuvant Radiation Therapy (ART) Treatment Decisions (n=920)



No significant impact of ART in cohort as a whole or within Class 1



No significant impact of ART in cohort as a whole or within Class 2A



LEGEND:
- No ART
- ART

ART treated Class 2B patients see significant reduction in metastasis*

Castle Biosciences data on file; manuscript in preparation; *Class 2B p<0.001

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MyPath Melanoma

Clinical Validity and Utility

Demonstrated validity, utility and impact, backed by 11 peer-reviewed publications demonstrating the performance and utility of the test in providing objective information to aid in diagnosis in ambiguous melanocytic lesions

ADLT Status

Classified as an Advanced Diagnostic Laboratory Test (ADLT) by the Centers for Medicare & Medicaid Services (CMS), meaning it provides new clinical diagnostic information that cannot be obtained from any other test or combination of tests[1]

Guideline Support

1. National Comprehensive Cancer Network guidelines for cutaneous melanoma in the principles for molecular testing 2. American Society of Dermatopathology in the Appropriate Use Criteria for ancillary diagnostic testing 3. American Academy of Dermatology guidelines of care for the management of primary cutaneous melanoma

[1]Centers for Medicare & Medicaid Services: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Downloads/Guidance-for-Laboratories-on-ADLTs.pdf

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

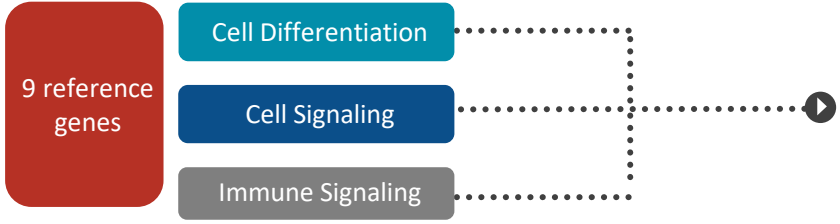
These difficult-to-diagnose lesions are commonly sent for second opinions to expert dermatopathologists who have more experience with challenging cases; however, the nature of many lesions remains ambiguous with discordant rates of lesions in this category of 25-43% (Elmore et al. 2017)

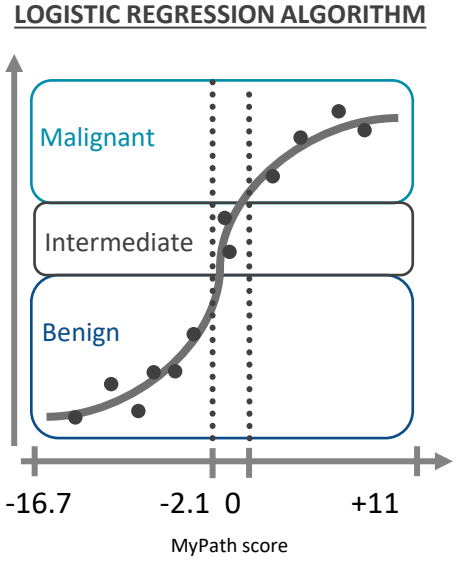
Diagnostic ambiguity can lead to clinical management uncertainty and overtreatment, leading to unnecessary excisions and increased patient morbidity, and undertreatment, with the potential for missing diagnoses of malignant melanoma

MyPath Melanoma 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

Clinical Validity and Utility

Demonstrated validity, utility and impact, backed by 10 peer-reviewed publications demonstrating the ability and performance of the test in risk-stratifying patients with Barrett's esophagus to guide risk-appropriate treatment decisions

ADLT Status

Classified as an Advanced Diagnostic Laboratory Test (ADLT) by the Centers for Medicare & Medicaid Services (CMS), meaning it provides new clinical diagnostic information that cannot be obtained from any other test or combination of tests[1]

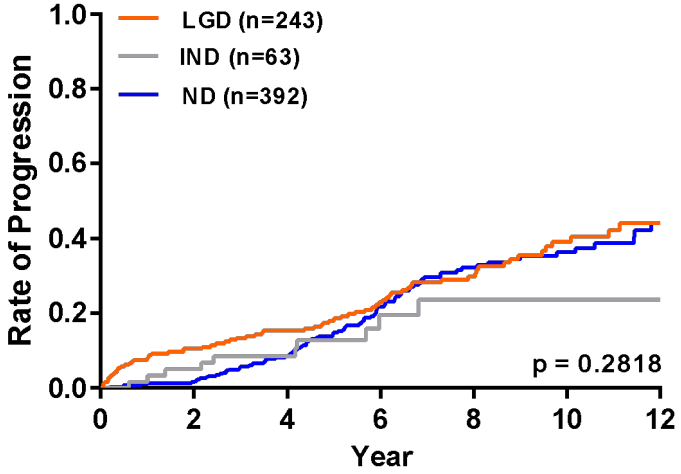
AGA Clinical Practice Update

Recognized by the American Gastroenterological Association in the 2022 Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus as a tool that may be used by physicians to risk stratify non-dysplastic patients

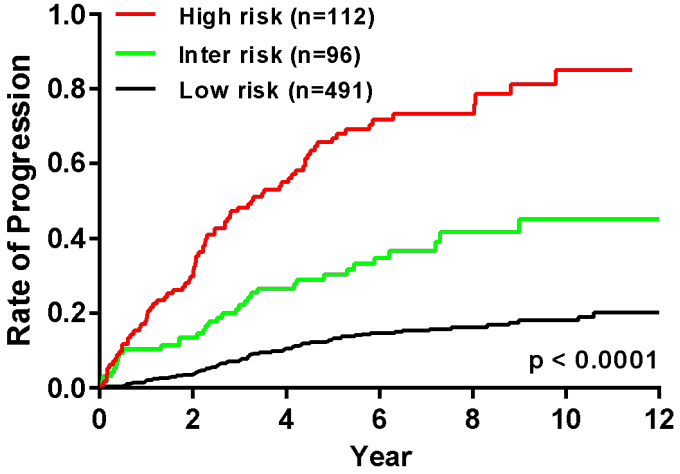
[1]Centers for Medicare & Medicaid Services: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Downloads/Guidance-for-Laboratories-on-ADLTs.pdf

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

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IDgenetix ▸ PGx Testing

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

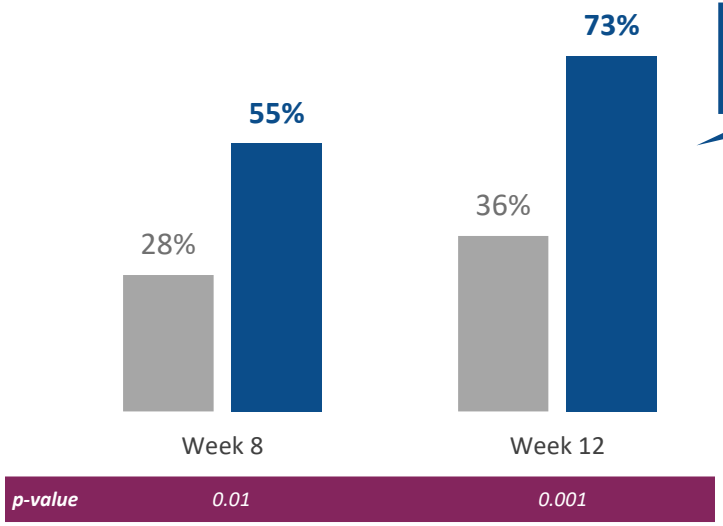
Easy to Use

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

2.5x Increase In Remission Rates For Severe Depression Demonstrated Enhanced Clinical Outcomes vs. Standard Of Care

Response Rate

≥ 50% Reduction from Baseline

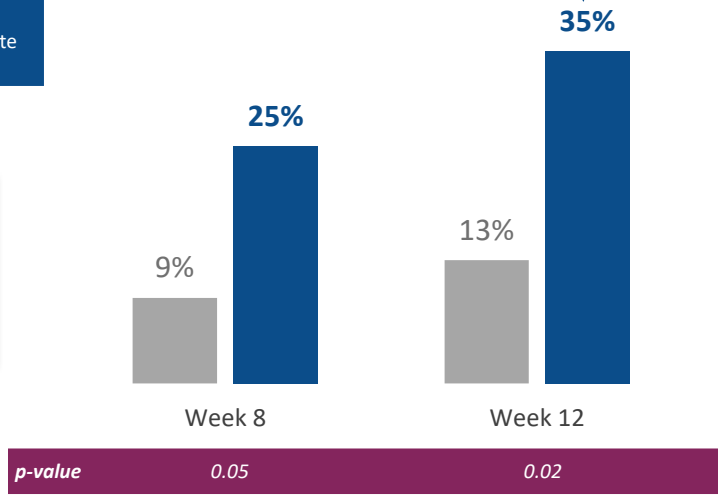


2x
increase in response rate vs. control

Remission Rate

Patients Achieving Remission

>2.5x
increase in remission rate vs. control



Standard of Care
IDgenetix

Bradley et al. *J Psychiatr Res* 2018.

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DecisionDx ▸UM

Clinical Validity and Utility

Demonstrated validity, utility and impact, backed by 24 peer-reviewed publications demonstrating the performance and utility of the test in predicting individual risk of metastasis in patients with uveal melanoma

ADLT Status

Classified as an Advanced Diagnostic Laboratory Test (ADLT) by the Centers for Medicare & Medicaid Services (CMS), meaning it provides new clinical diagnostic information that cannot be obtained from any other test or combination of tests[1]

Guideline Inclusion

Included in the National Comprehensive Cancer Network guidelines as a prognostic method for determining risk of metastasis and in the American Joint Committee on Cancer Eighth Edition (AJCC8) staging manual as part of the clinical care of uveal melanoma because the results are “clinically significant.”

[1]Centers for Medicare & Medicaid Services: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Downloads/Guidance-for-Laboratories-on-ADLTs.pdf

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
- 2023 Medicare rate of $7,776

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

57
Committed Sites

759
Patients Enrolled[1]

2021

Q2-Q3
Steering committee formed with top KOLs

Q3
First patient enrolled

2022

Q2
Proof of RNA extraction method concept

2023

2H 2023
Early development data expected

2025

2025
Target launch

Program Milestones

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Data as of June 29, 2023; [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 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. Adjusted Gross Margin further excludes acquisition-related intangible asset amortization. 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 and Adjusted EBITDA internally because we believe these metrics provide useful supplemental information in assessing our revenue and operating 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 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 June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
(in thousands)				
Adjusted revenues				
Net revenues (GAAP)	$ 50,138	$ 34,838	$ 92,175	$ 61,690
Revenue associated with test reports delivered in prior periods	88	(578)	1,705	300
Adjusted revenues (Non-GAAP)	$ 50,226	$ 34,260	$ 93,880	$ 61,990
Adjusted gross margin				
Gross margin (GAAP)[1]	$ 36,832	$ 25,055	$ 66,465	$ 44,315
Amortization of acquired intangible assets	2,248	2,097	4,470	3,745
Revenue associated with test reports delivered in prior periods	88	(578)	1,705	300
Adjusted gross margin (Non-GAAP)	$ 39,168	$ 26,574	$ 72,640	$ 48,360
Gross margin percentage (GAAP)[2]	73.5 %	71.9 %	72.1 %	71.8 %
Adjusted gross margin percentage (Non-GAAP)[3]	78.0 %	77.6 %	77.4 %	78.0 %

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 EBITDA, which is a non-GAAP financial measure. See slide 39 for further information regarding the Company's use of non-GAAP financial measures.

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
(in thousands)				
Adjusted EBITDA				
Net loss	$ (18,777)	$ (1,648)	$ (47,981)	$ (26,271)
Interest income[1]	(2,399)	(370)	(4,735)	(400)
Interest expense	3	4	7	7
Income tax expense (benefit)	16	(1,957)	30	(1,823)
Depreciation and amortization expense	3,040	2,628	5,932	4,779
Stock-based compensation expense	12,849	8,783	26,374	17,202
Change in fair value of contingent consideration	—	(20,398)	—	(17,836)
Acquisition related transaction costs	—	1,711	—	1,711
Adjusted EBITDA (Non-GAAP)	$ (5,268)	$ (11,247)	$ (20,373)	$ (22,631)

1. Beginning in the fourth quarter of 2022, we began excluding interest income from the calculation of Adjusted EBITDA. The prior-year period presented herein has been recast to conform to the current period presentation.

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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	equillium
Derek Maetzold	CASTLE BIOSCIENCES
Mara Aspinall	BLUESTONE VENTURE PARTNERS, LLC
Brad Cole	EXACT SCIENCES
Tiffany Olson	CardinalHealth™
Miles D. Harrison	GALDERMA
Kimberlee Caple	ThermoFisher SCIENTIFIC
Ellen Goldberg	CHORD Consulting