



Transforming Patient  
Management

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January 10, 2022





# Disclaimers

## FORWARD-LOOKING STATEMENTS

The information in this presentation contains forward-looking statements and information 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 preliminary measures of our financial performance including our 2022 year end revenue guidance, statements concerning the estimated size of our total addressable market or our existing, potentially acquired and pipeline products, the impact, accuracy and effectiveness of our tests, including DecisionDx-Melanoma, DecisionDx-SCC, DecisionDx DiffDx-Melanoma, myPath Melanoma and Cernostics, Inc.’s (Cernostics) TissueCypher Barrett’s Esophagus Assay, on physicians, patients and their treatment plans, our prospects and plans and the objectives of management. The words “anticipates,” “believes,” “estimates,” “expects,” “intends,” “may,” “plans,” “projects,” “will,” “would” 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 effects of the COVID-19 pandemic on our business and our efforts to address its impact on our business, the timing and amount of revenue we are able to recognize in a given fiscal period, subsequent study results and findings that contradict earlier study results and findings, our tests', including DecisionDx-Melanoma, DecisionDx-SCC, DecisionDx DiffDx-Melanoma and myPath Melanoma, ability to provide the aforementioned benefits to patients and the risks set forth in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, 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 2021  
Information

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January 10, 2022



# Castle Biosciences is Transforming Patient Management

Providing actionable information addressing key questions in disease states with high unmet clinical needs

CUTANEOUS MELANOMA <sup>1,2</sup>	SQUAMOUS CELL CARCINOMA	UVEAL MELANOMA <sup>3</sup>	BARRETT'S ESOPHAGUS <sup>4</sup>	
 <b>PROGNOSTIC</b> Predicting Individual Risk of Recurrence or Metastasis in Stage I, II, and III Melanoma	 <b>DIAGNOSTIC</b> Highly Accurate and Objective Tests Characterizing Difficult-to-Diagnose Melanocytic Lesions	 <b>PROGNOSTIC</b> Better Identifies Risk of Metastasis in Patients with One or More Risk Factors	 <b>PROGNOSTIC</b> The Standard of Care for Evaluating Metastatic Risk in Uveal Melanoma	 BARRETT'S ESOPHAGUS ASSAY <b>PROGNOSTIC</b> Predicting Individual Risk of Progression to Esophageal Cancer in Barrett's Esophagus

<sup>1</sup>2022 CMS rate: DecisionDx-Melanoma, \$7193; <sup>2</sup>2022 CMS rate: myPath-Melanoma, \$1950

<sup>3</sup>2022 CMS rate: DecisionDx-UM, \$7776; <sup>4</sup>2022 CMS rate: TissueCypher BE, \$2513.25

<https://www.cms.gov/medicare/medicare-fee-service-payment/clinical-laboratory-fee-schedule-files/22clabq1>

## ■ Preliminary Fourth Quarter and Year-end 2021 Performance Results<sup>1</sup> (unaudited)




- Expect to meet or exceed top end of guided range of \$89-93M<sup>2</sup> for 2021 revenue

	4Q21	4Q20	2021	2020
Revenue	To be announced	\$17.3M	Meet or exceed top end of guided range <sup>2</sup>	\$62.6M
Total GEP test reports	8,242	5,157	28,118	18,185
DecisionDx-Melanoma	5,635	4,246	20,328	16,232
DecisionDx-SCC	1,265	428	3,510	485 <sup>3</sup>
CDO(myPath/Diff-Dx)	904	73 <sup>4</sup>	2,662	73 <sup>4</sup>
DecisionDx-UM	438	410	1,618	1,395



## 2021 Year-end Cash & Cash Equivalents expected to be ~\$330 Million<sup>1</sup>, and No Debt

Two acquisitions in 2021 support strategic growth

Cash and Cash Equivalents			
As of 3/31/21 \$407M	As of 6/30/21 \$368M	As of 9/30/21 \$363M	As of 12/31/21 <b>\$330M</b> (expected)
	Paid \$32.5M cash in Q22021 		Paid \$30M cash in Q42021  

# Pillars of Castle's Growth Story

Leveraging our dermatology foundation & replicating our experience in other disease areas

## Strong Core Derm Business



## Pipeline Initiatives



## Strategic Opportunities

myPath  
Melanoma

cernostics  
PROVIDING DEEPER TISSUE INSIGHTS  
tissuecypher  
BARRETT'S ESOPHAGUS ASSAY

## Targeted Complementary M&A Opportunities To Build Upon Our Foundational Business

Acquisition of Cernostics' TissueCypher aligns with strategy to drive additional growth

History of commercial success in dermatology expected to translate across markets

Focused on leveraging advanced technologies for innovative tests, including TissueCypher multi-analyte spatial biology

Focused on providing clinically actionable information to answer clinical questions (transforming disease management in areas with unmet clinical need)

Focused on accelerating the impact on patient care and health outcomes



Applying innovative  
diagnostics to inform disease  
management decisions

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Third Quarter 2021  
November 8, 2021



# Leading Dermatologic Diagnostics Company

Transforming the management of skin cancer and other dermatologic diseases with high unmet clinical need



Culture of Teamwork and Innovation

Suite of Dermatologic Prognostic And Diagnostic Tests



Expansive Body of Evidence

Strong Financial Position



Robust Pipeline

## Financial Summary 3Q 2021

	3Q21	3Q20
Revenue	\$23.5M	\$15.2M
Adj. Revenue <sup>1</sup>	\$23.6M	\$13.8M
Total GEP test reports <sup>2</sup>	7,727	4,779
Total Derm test reports <sup>2</sup>	7,352	4,461
Operating Cash Flow	\$(6.1)M	\$(3.0)M
Adj. Operating Cash Flow <sup>1</sup>	\$(3.0)M	\$(3.0)M
Gross Margin	78%	84%
Adj. Gross Margin <sup>1</sup>	81%	82%
Cash & Cash Equivalents	\$363M as of 9/30/2021	\$183M as of 9/30/2020

# Estimated ~\$5.5B U.S. Total Addressable Market<sup>1</sup>

- In market and pipeline tests, leveraging established dermatologic sales channels

Indication/ Test outcome	Trade Name	Reimbursement Status	Peer-Reviewed Publications	Primary Customers	Initial Launch Targets	Initial addressable market, patients <sup>2</sup>	Estimated U.S. TAM
Cutaneous melanoma/ Risk of metastasis	<b>DecisionDx</b> MELANOMA	MCR, MCRA Commercial – in process	30+	Derms (including Mohs), Surgeons	—	<b>~130k patients</b> classified as Stage I, II or III	~\$540M
Cutaneous squamous cell carcinoma/ Risk of metastasis	<b>DecisionDx</b> ·SCC	Expected draft LCD in 2021 Commercial – in process	5	Derms (including Mohs)	~4,968 current customers <sup>3</sup>	<b>~200k</b> w/ high-risk features	~\$820M
Suspicious pigmented lesions/ Melanoma status	<b>myPath</b> Melanoma  <b>DecisionDx</b> DiffDx·Melanoma	MCR, MCRA Commercial – in process	9	Dermaths, Derms	~1,801 current dermpath customers <sup>4</sup>	<b>~300k patients</b> w/indeterminant biopsy	~\$600M
		Expected draft LCD in 2021 Commercial – in process	2				
Pipeline Test- Inflammatory	Target launch anticipated by the end of 2025	N/A	N/A	Expected to utilize existing dermatologic sales channels	~4,968 current customers <sup>3</sup>	<b>~450k patients</b> eligible for systemic therapies	~\$1.9B
Other Pipeline Tests	Target launches anticipated by the end of 2025	N/A	N/A	Expected to utilize existing dermatologic sales channels	To be announced	To be announced	~\$1.7B

<sup>1</sup>U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors.

<sup>2</sup>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.

<sup>3</sup>Clinicians who ordered DecisionDx-Melanoma in last twelve months (as of 9/30/2021).

<sup>4</sup>Pathologists who provided clinical specimens for DecisionDx-Melanoma in last twelve months (as of 9/30/2021).

-MCR = Medicare. MCRA = Medicare Advantage; current customer estimates based on last twelve months.

# Clinical Portfolio And Pipeline Tests

- Potential to launch 3-5 new tests by the end of 2025

		Indication/ Test outcome	Discovery	Development	Commercial	Payer coverage
Skin Cancer	<b>DecisionDx</b> MELANOMA	Cutaneous melanoma/ Risk of metastasis	[Progress bar: 100%]			
	<b>DecisionDx</b> ·SCC	Cutaneous squamous cell carcinoma/ Risk of metastasis	[Progress bar: ~85%]			
	<b>myPath</b> DecisionDx <sup>Melanoma</sup> DiffDx·Melanoma	Suspicious pigmented lesions/ Melanoma status	[Progress bar: 100%]			
Eye Cancer	<b>DecisionDx</b> ·UM	Uveal Melanoma/ Risk of metastasis	[Progress bar: 100%]			
Pipeline	Target launch anticipated by the end of 2025	AD, PSO/ Prediction of systemic therapy response	[Progress bar: ~20%]			
Pipeline	Target launches anticipated by the end of 2025	Other clinical conditions	[Progress bar: ~20%]			

## Castle to Acquire Cernostics

Fuels mid- and long-term growth with TissueCypher® platform enabling GI franchise



- Acquisition of Cernostics brings a first-to-market risk stratification test for use in patients with Barrett's Esophagus:
  - Significant evidence: 6 validation and performance studies with TissueCypher
  - Medicare paid with a Clinical Laboratory Fee Schedule rate of \$2,513
  - Clinical use study demonstrates more than 50% change in patient management
  - Increases Castle's estimated U.S. TAM by ~\$1 billion<sup>1</sup>
- Cernostics adds spatial biology technology for use in additional GI and other diseases

## Cernostics Transaction and Transition Snapshot

\$30 million in cash  
or cash and stock  
due at closing<sup>1</sup>

Up to an additional  
\$50 million payable in cash  
and/or stock<sup>1</sup>, based on  
the achievement of certain  
milestones based on 2022  
performance<sup>2</sup>

Expected close prior  
to year end 2021<sup>3</sup>

Expect Cernostics  
CEO and other staff  
to join Castle

Expect to hire a GI  
commercial team with  
13-15 outside sales  
territories; reporting  
to Castle's Chief  
Commercial Officer

<sup>1</sup> up to Castle's sole discretion <sup>2</sup> milestones related to revenue and reimbursement

<sup>3</sup> subject to the delivery of certain financial statements to the Company, continued employment of certain Cernostics personnel and satisfaction of other customary conditions to closing

# Castle's Revenue Growth Story

2021

2022/2023

2025

## Dermatologic Franchise

Cutaneous Melanoma  
Suspicious Pigmented Lesions

**Decision Dx**  
**MELANOMA**  
*(Expanded LCD effective Dec 2020)*

**myPath**  
Melanoma  
*(Acquired in May 2021; LCD in effect)*

Cutaneous Melanoma  
Squamous Cell Carcinoma  
Suspicious Pigmented Lesions

**Decision Dx**  
**MELANOMA**

**Decision Dx-SCC**  
*(Potential LCD effective in 2023)*

**myPath**  
Melanoma  
**Decision Dx<sup>®</sup> DiffDx-Melanoma**  
*(Potential LCD effective in 2023)*

Cutaneous Melanoma  
Squamous Cell Carcinoma  
Suspicious Pigmented Lesions  
Additional Tests for Dermatologic Conditions

**Decision Dx**  
**MELANOMA**

**Decision Dx-SCC**

**myPath**  
Melanoma  
**Decision Dx<sup>®</sup> DiffDx-Melanoma**

**Pipeline Expansion**  
*(Expected launches ~2025)*

## Gastrointestinal Franchise\*

Barrett's Esophagus

**tissuecypher**  
BARRETT'S ESOPHAGUS ASSAY

Barrett's Esophagus

**tissuecypher**  
BARRETT'S ESOPHAGUS ASSAY

**Pipeline Growth Opportunities**

# Decision Dx

## MELANOMA

*Informing clinical decision making  
for patients with invasive melanoma*



# DecisionDx-Melanoma: After Diagnosis Of Cancer



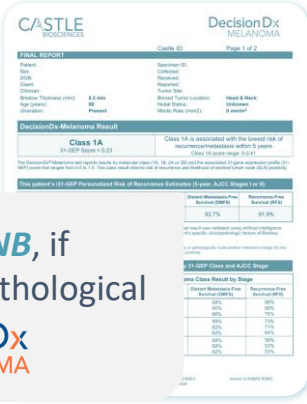
Patient *presents* with mole/melanocytic lesion



**Potential Diagnosis:**

- Positive for melanoma
- Negative
- Uncertain malignant potential

Physician may *order SLNB*, if warranted per clinicopathological features and **DecisionDx MELANOMA**



Biopsy performed

If melanoma, clinician orders **DecisionDx MELANOMA** to answer *SLNB* and/or *management* questions:

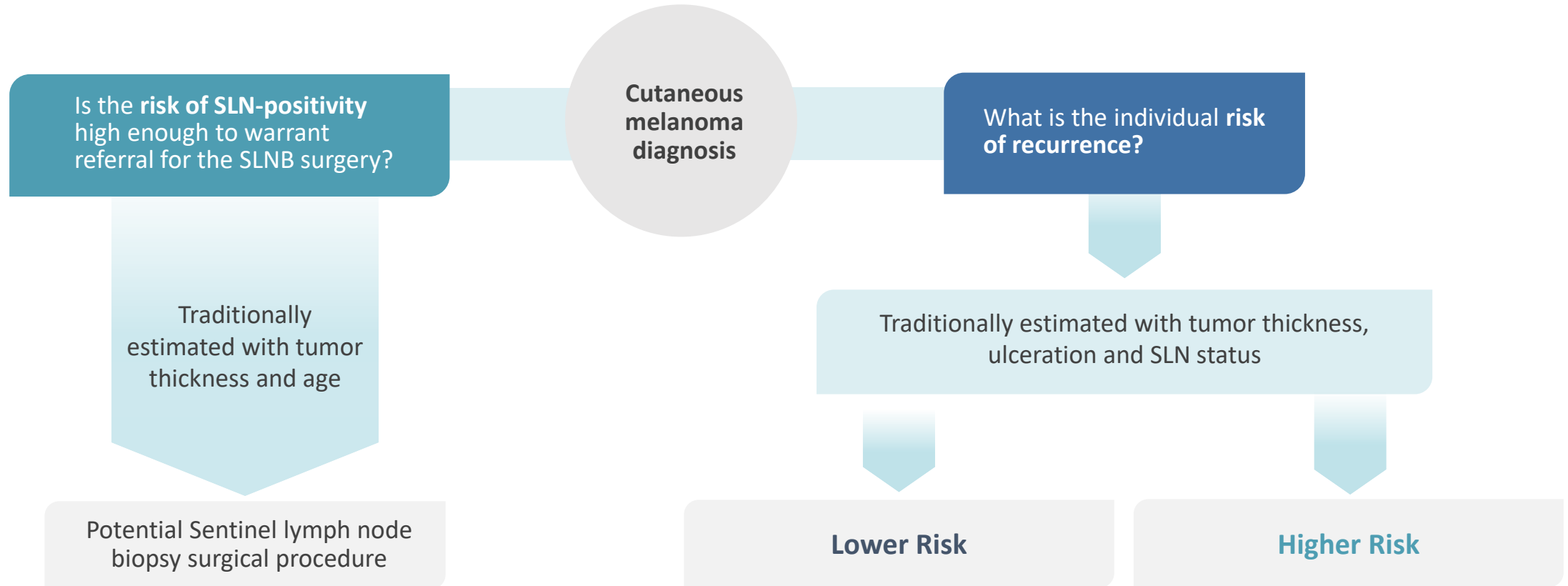
- Is the risk of SLN-positivity high enough to warrant referral for the SLNB surgery?
- What is the individual risk of recurrence?



Management *plan determined*, based on *personalized risk*

# Following Diagnosis, Two Primary Clinical Questions Help Guide Melanoma Management

Choosing risk-appropriate level of management is key



# DecisionDx-Melanoma: After Diagnosis For More Accurate Risk Assessments

Stage I – III  
melanoma  
diagnosis

## DecisionDx MELANOMA

CM  
tumor  
tissue

RNA isolation

RT-PCR: cDNA generation and amplification, RT-PCR

qPCR: open array card, 31-gene  
expression profile

GEP analysis with a proprietary  
algorithm to predict class

### Class 1A

*Lowest risk* of recurrence and/or  
metastasis within 5 years

### Class 1B/2A

*Increased risk* of recurrence and/or  
metastasis within 5 years

### Class 2B

*Highest risk* of recurrence and/or  
metastasis within 5 years

## Problem 1: There Is A Need For Better Stratification Of Risk Of Positive SLN To Inform Surgery Discussions

There are limitations of current staging

**Majority of patients (~88%) subjected to a SLNB are negative and derive little to no benefit<sup>1-2</sup>**

**MSLT-I demonstrated *no survival benefit* and *low sensitivity* (2/3 of melanoma deaths in SLN negative group)<sup>3</sup>**

**18% median false negative rate for nodal recurrence<sup>4</sup>**

**Reduce exposure to anesthesia risks and surgical complications (rate = 11%)<sup>5</sup>**

Average reimbursed cost of SLNB is \$20-24k

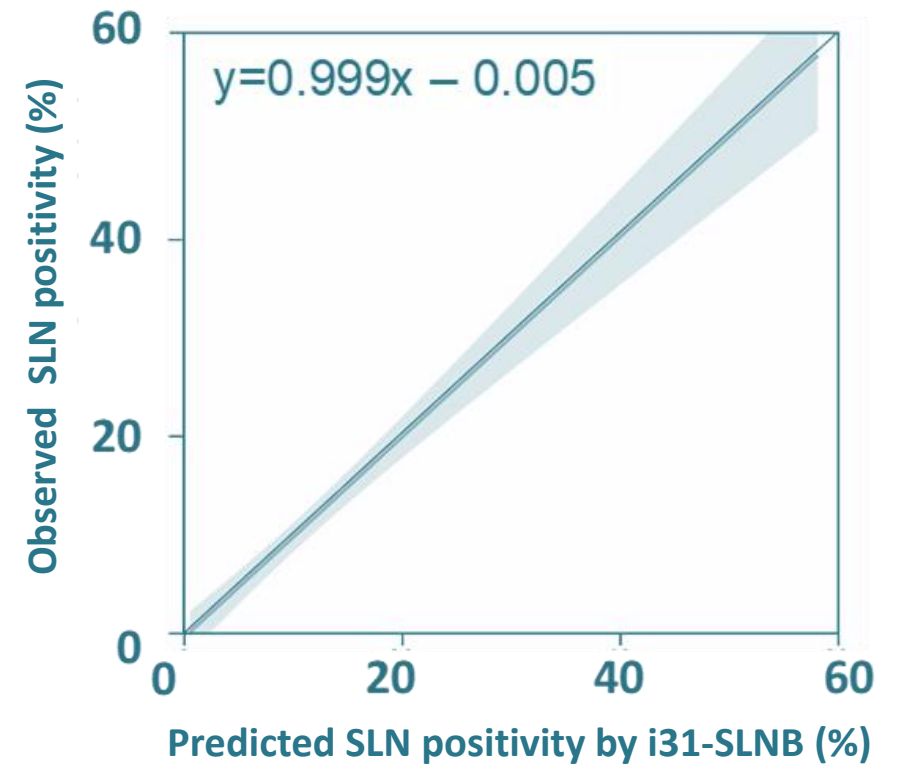
## DecisionDx-Melanoma Identifies Those At Low Risk For A Positive SLN

Integrates clinicopathologic features to offer precise and personalized likelihood of sentinel lymph node positivity in T1-T4 patients

- › DecisionDx-Melanoma i31-SLNB accurately identifies low risk (<5%) of SLN positivity in patients with T1-T4 staged disease<sup>1</sup>
- › i31-SLNB accurately identifies patients within the 5-10% and >10% ranges of SLN positivity risk<sup>1</sup>
- › In T1aHR cases, patients with a Class 2B (highest risk) could be more reliably and appropriately considered for SLNB<sup>1</sup>

**DecisionDx-Melanoma could result in 74% fewer SLNB surgeries, potentially saving the U.S. healthcare system \$250M<sup>2,3</sup>**

*Highly concordant prediction of SLN positivity rate compared to observed rates*



## Problem 2: There Is A Need For Improved Prognostic Accuracy To Determine The Most Appropriate Melanoma Management Strategy

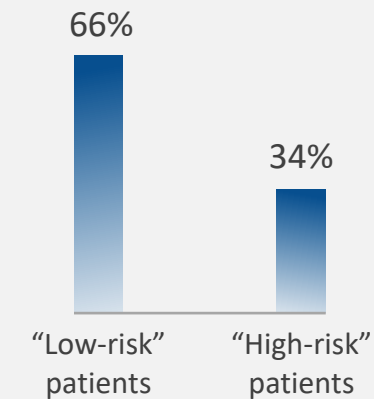
Current population-based risk assessments miss patients with aggressive tumor biology

Early detection, lower tumor burden associated with better therapy responses, survival outcomes<sup>1-5</sup>

Appropriate surveillance, including imaging of high-risk patients, is critical<sup>1-5</sup>

AJCC clinicopathologic factors are helpful clinically, but the majority of deaths occur in patients diagnosed with early-stage disease<sup>6-8</sup>

### DEATHS FROM MELANOMA





## Introducing i31-Risk Of Recurrence (ROR)

Integrating the DecisionDx-Melanoma score with clinicopathologic factors in a validated algorithm



*DecisionDx-Melanoma class result is an **independent** and **significant** variable in risk of recurrence outcomes*



## AJCC Only Provides Population-Based Melanoma- Specific Survival (MSS)

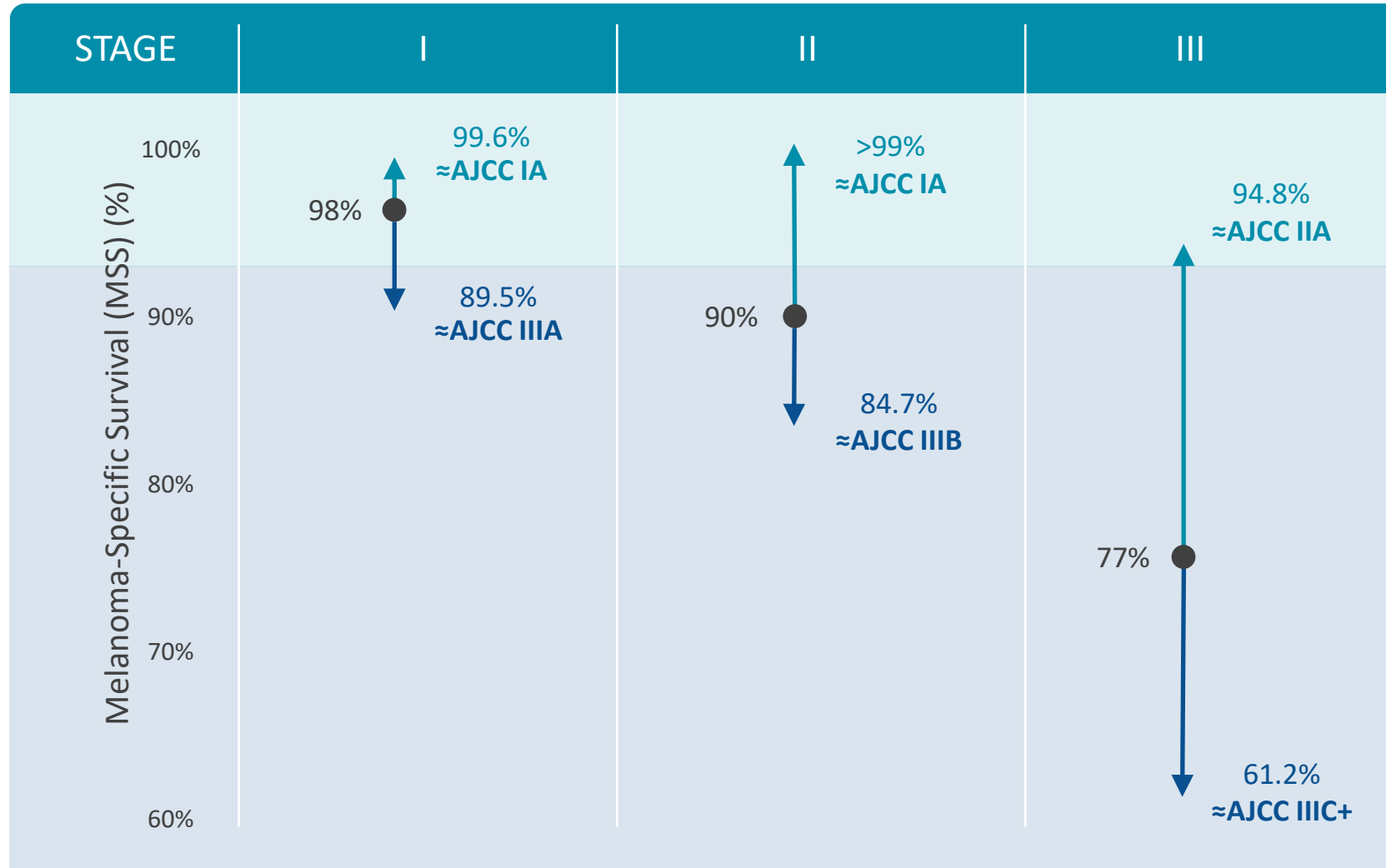
Our new model provides personalized MSS, distant metastasis-free survival (DMFS) and recurrence-free survival (RFS)

Observed outcomes in the patient population.

	AJCC Stage	5-year RFS	5-year DMFS	5-year MSS	AJCC 5-year MSS (%)
<b>Observed</b> % (95% CI)	I	93.4%	95.3%	98.6%	98%
<b>Observed</b> % (95% CI)	II	68.2%	76.9%	91.3%	90%
<b>Observed</b> % (95% CI)	III	52.0%	57.6%	77.3%	77%
<b>Midpoint</b>	IIA/IIB	>69.8%: Low-risk ≤69.8%: High-risk	>82.6%: Low-risk ≤82.6%: High-risk	>91.1%: Low-risk ≤91.1%: High-risk	

- › Observed MSS for this cohort aligns with that of AJCCv8
- › High risk vs. low-risk is established using Stage IIA/IIB cut point where clinical management intensity diverges (e.g., IIB patients are eligible for advanced imaging)

# DecisionDx-Melanoma Further Stratifies Risk Of Recurrence Beyond AJCC (8TH Ed.) Staging



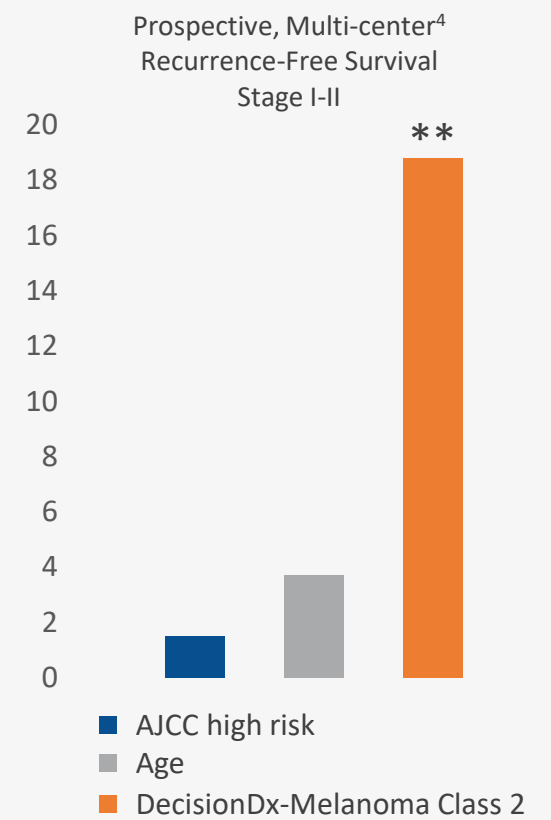
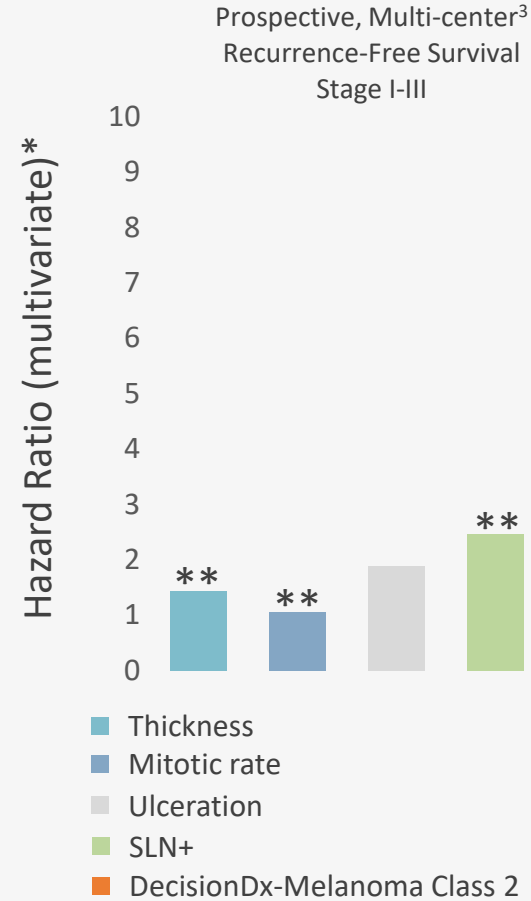
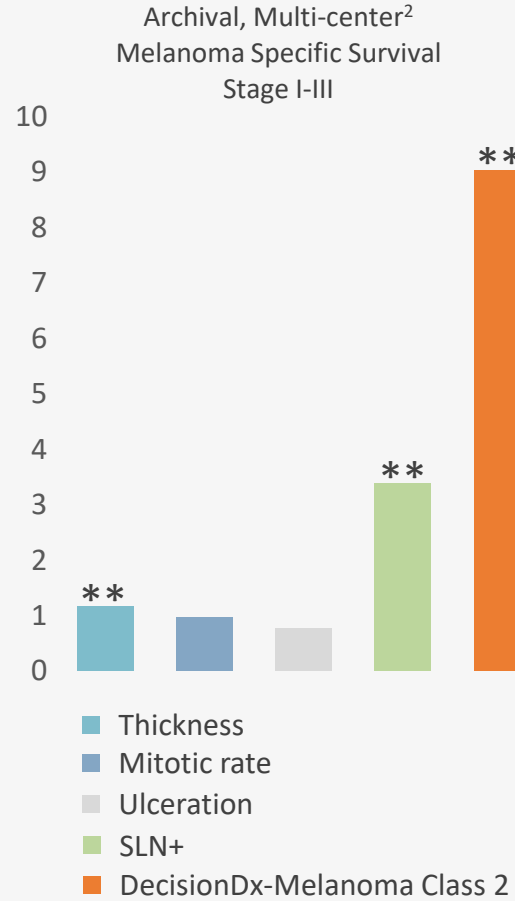
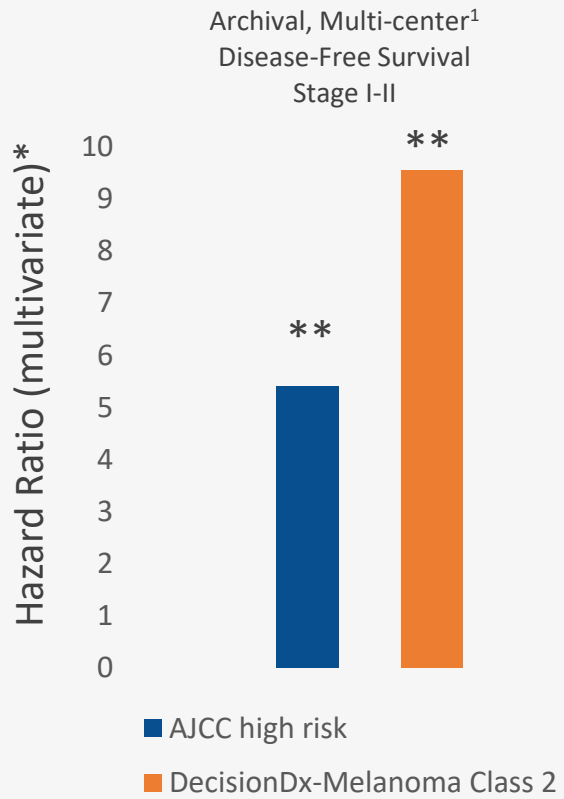
**NCCN Risk Category**

- Low Risk Stage I-IIA
- High Risk Stage IIB-III

● AJCC MSS  
 ▲ Castle Class 1A MSS  
 ▲ Castle Class 2B MSS



# DecisionDx-Melanoma Is A Significant, Independent Predictor Of Outcomes



\*Hazard ratio is continuous for thickness, categorical for other endpoints; \*\*Statistically significant Data shown are from the first and most recent publications for archival and prospective studies  
<sup>1</sup>Gerami et al. *Clin Cancer Res* 2015. <sup>2</sup>Gastman et al. *Jrnl Amer Acad Dermatol* 2019. <sup>3</sup>Hsueh et al. *Jrnl Hematol Oncol* 2017. <sup>4</sup>Podlipnik et al. *Jrnl Eur Asso Veneral and Derm* 2019.

# DecisionDx-Melanoma Changed Management For 50% Of Patients

4 consecutive clinical impact studies:  
**47-53% change** in *risk-of-recurrence-based management*

## Changes in patient management include:



Imaging and labs



Sentinel lymph node biopsy guidance



Clinical visit frequency



Referrals

Study	Design	# of Patients	% Change in Management
Berger <sup>1</sup>	Prospectively tested cohort, multi-center. Retrospective pre-test / post-test management.	156	<b>53%</b>
Dillon <sup>2</sup>	Prospective, multi-center: pre-test / post-test management	247	<b>49%</b>
Farberg <sup>3</sup>	169 physician impact study: patient vignettes with pre-test / post-test management	n/a	<b>47-50%</b>
Schuitevoerder <sup>4</sup>	Prospectively tested cohort, single center. Retrospective pre-test / post-test management; modeling of prospective cohort	91	<b>52%</b>

## DecisionDx-Melanoma: Well-studied, Informs Cancer Management Decisions

>6,000

Patients included in studies including *independent validation*

33+

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

84,000+

Patients with a *DecisionDx-Melanoma* order from more than *8,500 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

*Identifying the risk of metastasis in patients with cutaneous squamous cell carcinoma with one or more risk factors*



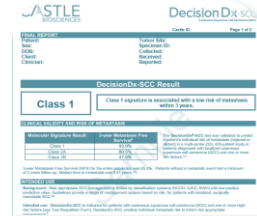
# Patient Journey: Where DecisionDx-SCC Fits



Lesion suspicious for skin cancer **discovered** by patient or PCP



**Diagnosis** of SCC with  $\geq 1$  risk factor



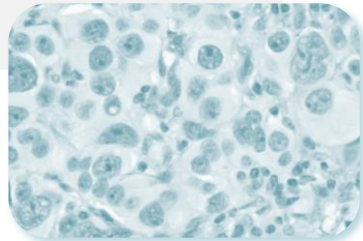
Test results **received** for **DecisionDx-SCC**

Patient **referred** to a dermatologist who performs a skin exam

### History and physical

- Complete skin exam
- Regional lymph node exam

### Skin biopsy



Order **placed** for **DecisionDx-SCC**



### Treatment plan defined

- Curettage and electrodesiccation
- Standard excision
- Excision with wide margins
- Mohs



## Problem: The Unmet Need In High-Risk SCC Patients

Who is really at low risk or high risk for metastasis?

*Deaths* from SCC are now estimated to **exceed those from melanoma**

**~20% of SCC patients** (200,000 annually) have **one or more clinical** or **pathological risk factors**, and a subset will **develop metastasis**

They suffer the majority of SCC mortality

These factors alone are often not specific enough to determine risk-appropriate treatment and further management

SCC treatment plans are guided by risk of metastasis

Risk-appropriate SCC management is **currently limited by classification systems** (NCCN, BWH, AJCC) with **low positive predictive value** (PPV)

## Designed To Predict Individual Metastatic Risk To Inform Risk-Appropriate Management

### Decision Dx-SCC

For **high-risk** SCC patients with one or more risk factors

**200,000** high-risk patients annually;

**\$820M** U.S TAM<sup>1</sup>

Validated in **420-patient cohort** of high-risk SCC from 33 U.S. centers

5 **peer-reviewed publications** to date;

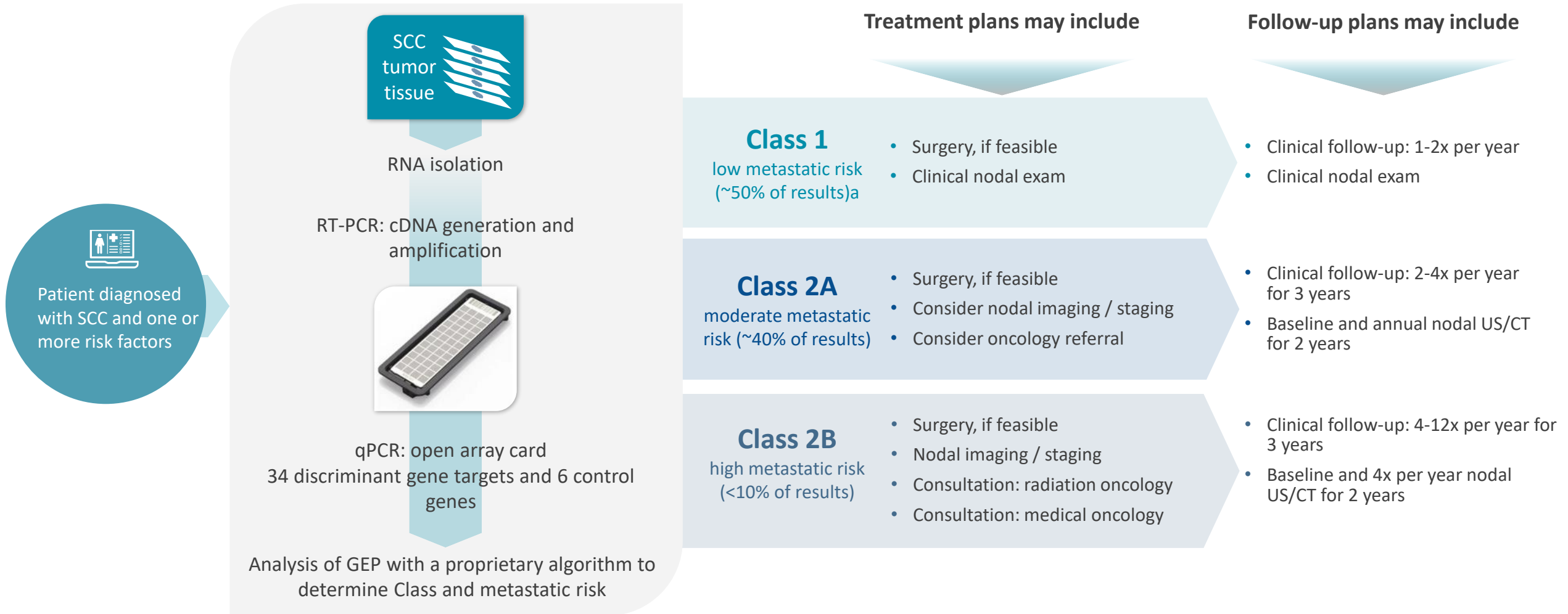
Over **2,320 patients** have been enrolled in studies to date from **110 centers**

Utilizing **existing sales channels:** dermatologists (including Mohs surgeons)

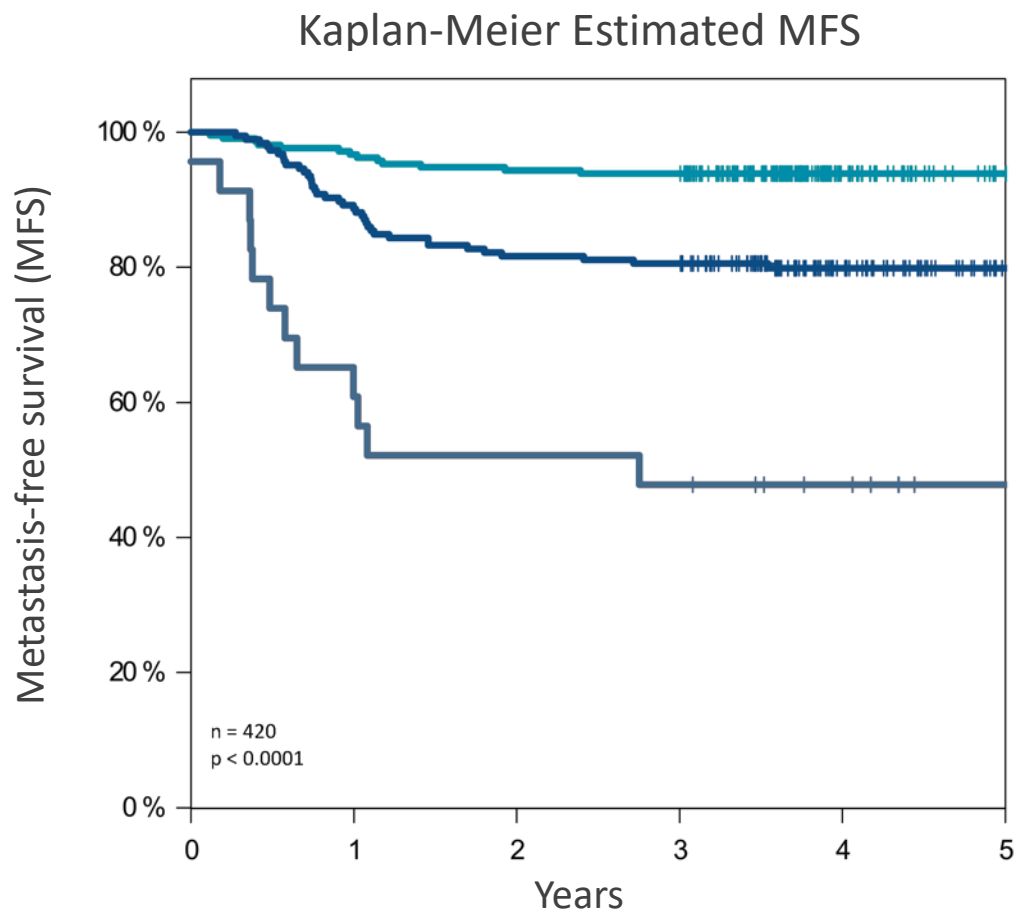
Incorporation of DecisionDx-SCC with traditional risk factors can **improve patient classification** compared to traditional risk factors alone

# Workflow For DecisionDx-SCC: Process Identical To DecisionDx-Melanoma

DecisionDx-SCC results can inform management decisions within established guidelines



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



## Class 1 – Low Biological Risk

Less than half the general study population risk

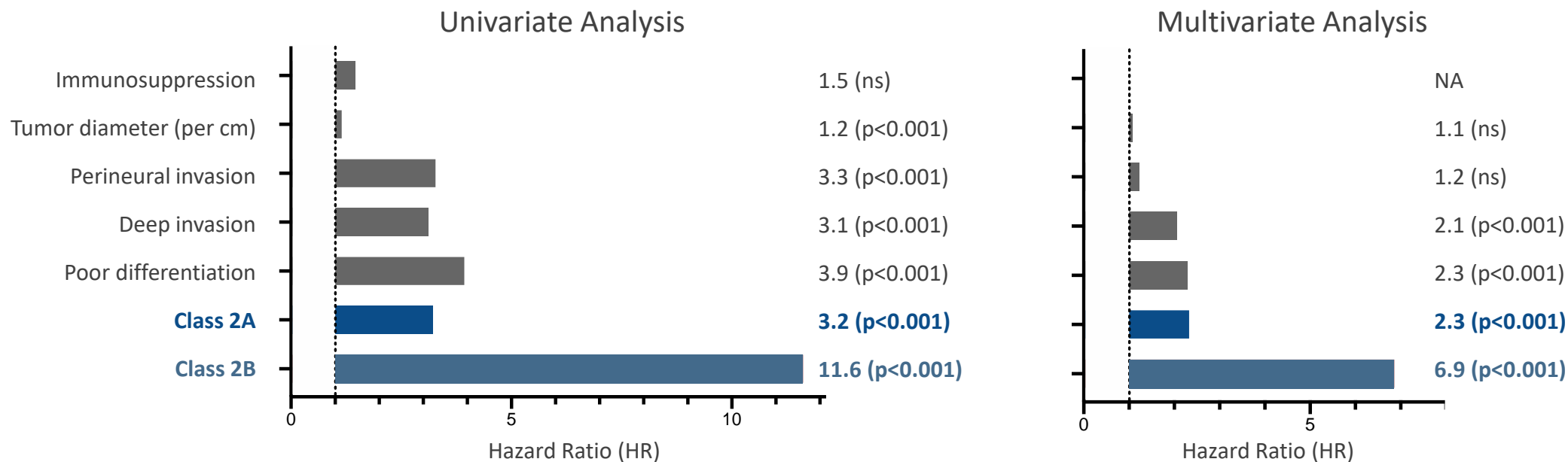
## Class 2A – Moderate Biological Risk

Similar to the strongest traditional factors

## Class 2B – High Biological Risk

≥50% risk of metastasis

# Class 2A And Class 2B Are Independent Predictors Of Metastasis



## What is the impact of DecisionDx-SCC?

An SCC with deep invasion is **2.1x more likely** to metastasize than without

Adding a Class 2A results shifts that to **4.8x more likely** to metastasize

Adding a Class 2B result shifts that to **14.5x more likely** to metastasize

# Comprehensive Diagnostic Offering

*Highly accurate and objective tests for melanocytic lesions of unknown malignant potential*

myPath  
Melanoma

DecisionDx  
DiffDx Melanoma

Comprehensive  
**Diagnostic** Offering

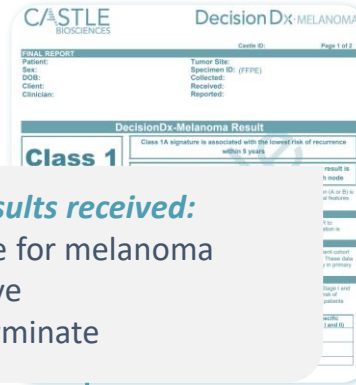
# Dermatopathologists And Dermatologists Work Together To Diagnose Melanoma



Patient *presents with mole* to PCP or dermatologist

Biopsy *results received*:

- Positive for melanoma
- Negative
- Indeterminate



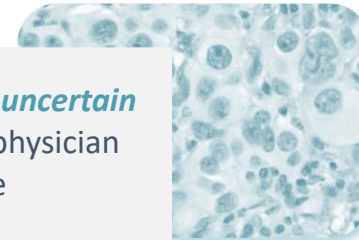
*Melanoma diagnosis confirmed*; physician can initiate management plan with **DecisionDx MELANOMA**



Physician may order *biopsy*

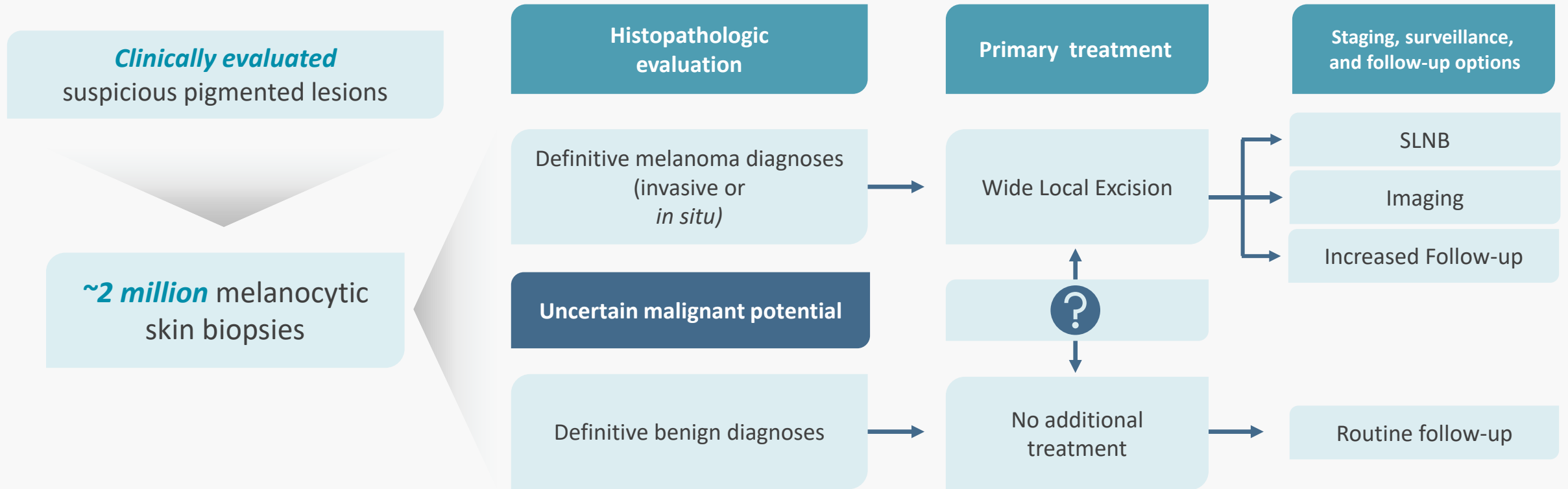


If biopsy results show *uncertain malignant* potential, physician orders Comprehensive Diagnostic Offering

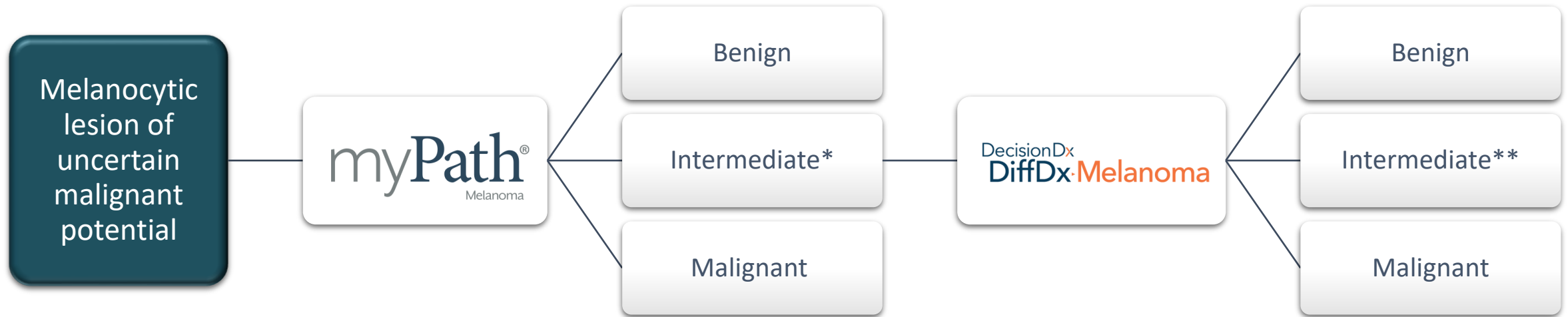


myPath<sup>®</sup> Melanoma DecisionDx DiffDx:Melanoma

# The Clinical Issue: Uncertainty Creates An Over- Or Under-Treatment Dilemma



## Comprehensive Diagnostic Offering Improves Clinically Actionable Reporting For ~99% of Concerning Lesions



With an order of Castle's comprehensive diagnostic offering, upon receipt at our lab, Castle will perform myPath Melanoma on submitted cases. If the case results in an intermediate result or fails to produce a result, we now have the ability to perform DecisionDx DiffDx to provide additional diagnostic clarity.

40 \*For purposes of reporting and consistency in the Comprehensive Diagnostic Offering, the term "indeterminate" will now be referred to as "intermediate" for myPath Melanoma. \*\*If both GEP tests result as intermediate, myPath Melanoma will be reported with a note stating that DiffDx-Melanoma was also intermediate.

## Leveraging The Strengths Of myPath Melanoma And DecisionDx DiffDx-Melanoma For The Benefit Of Patient Care



Designed to be used as an **adjunct to histopathology** when the distinction between a benign nevus and a malignant melanoma cannot be made confidently by histopathology alone

**Both tests included in NCCN guidelines;** myPath Melanoma is currently covered under a **MoIDX LCD through Noridian**

**5-7 day turnaround** time/similar to other ancillary tests

A definitive result is received in **~99% of lesions** submitted for testing

After melanoma diagnosis, clinicians can order DecisionDx-Melanoma; **uses same tissue sample**

Interpreted in the context of other clinical, laboratory and histopathologic information, the Comprehensive Diagnostic Offering is designed to **add diagnostic clarity** and **confidence** for dermatopathologists, while **helping dermatologists** better **understand the clinical implications** for more informed patient care

## Pipeline

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# Expanding Castle's Genomic Tests To Non-Skin Cancer Medical Dermatology

Innovative pipeline test for predicting systemic therapy response

Psoriasis

Atopic Dermatitis

Related Conditions

## Factors Defining Success

Committed to dermatology and informing clinical management decisions

Robust development pipeline and proven track record of AI-informed GEP algorithms

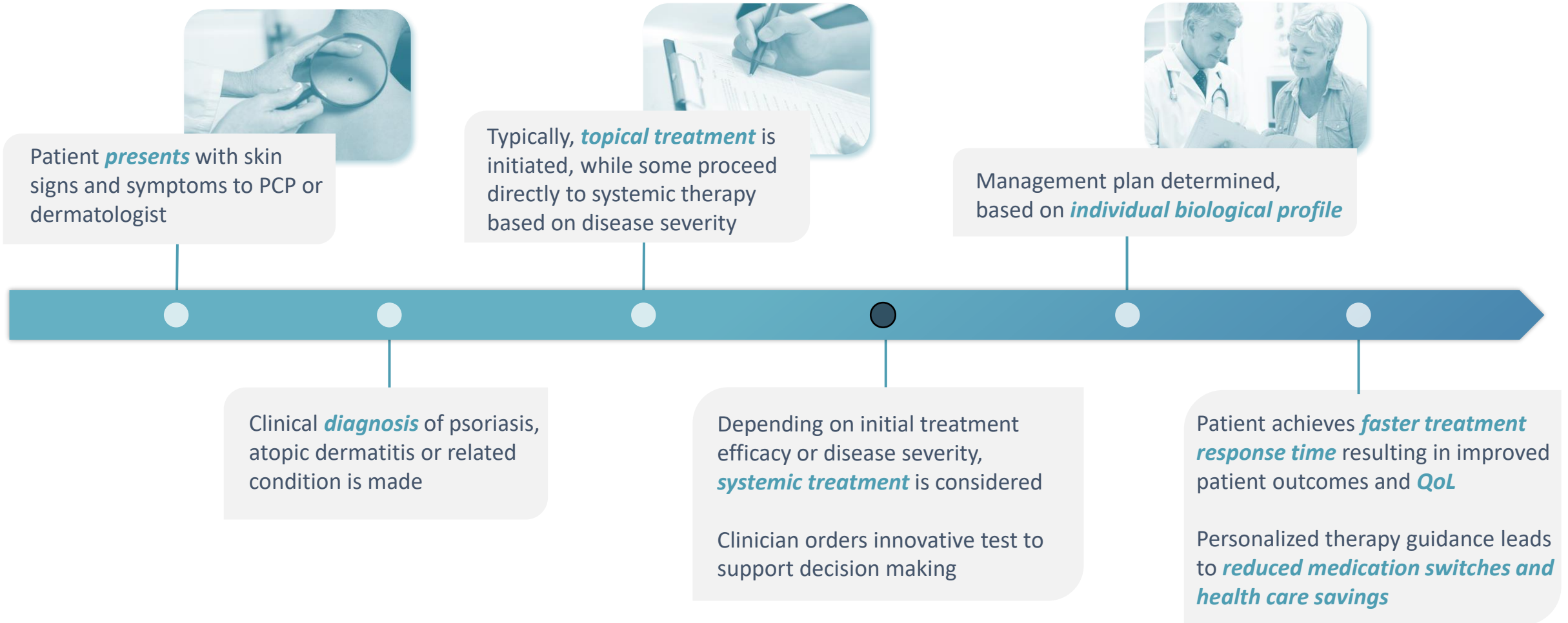
Steering committee with world-class KOLs

Large study investment for development and validation

	Psoriasis	Atopic Dermatitis
Gender	49% Female	53% Female
Age at Diagnosis (average)	Early fifties	Mid thirties
Severity	~30% moderate to severe	>50% moderate to severe

# ■ Patient Journey For Psoriasis, Atopic Dermatitis And Related Conditions

- Expands our reach into non-skin cancer, medical dermatologic diseases



## Problem: The Unmet Need In Moderate To Severe Psoriasis And Atopic Dermatitis

Common skin diseases with significant patient impacts and costs to health care system

Psoriasis (PSO) and Atopic Dermatitis (AD) are among the most frequently seen skin rashes, and their diagnosis is most often made clinically by the treating clinician

Treatments are significantly different for PSO and AD. Previously, treatments for AD were inexpensive (e.g., topical steroids), but are now costly (e.g., Dupixent for ~\$38k/year). Costly therapies for moderate/severe psoriasis are common (e.g., Humira for ~\$68k/year)

Cutaneous T Cell Lymphoma (CTCL) can mimic clinical presentation of AD and PSO. A subset of patients with PSO (approximately 20-30% of affected individuals) will go on to develop psoriatic arthritis, which can produce irreversible joint damage and significant patient morbidity

**Systemic therapy guidance tools have the potential to streamline therapeutic interventions for patients and avoid ineffective, expensive medication courses**

# Decision Dx·UM

*The Standard of Care for  
Evaluating Metastatic Risk in  
Uveal Melanoma*



## DecisionDx-UM: Standard Of Care

### Strong Evidence Base

- 21 peer-reviewed publications, **2,700+ patients**

### Widespread adoption

- **85-90%+** of U.S. ocular oncology institutions order
- **1,395 reports** issued in 2020

### Broad Coverage

- **156+ million** total lives covered
- Medicare LCD **covers patients** with a confirmed diagnosis and no evidence of metastatic disease
- “Existing ADLT” **status effective** May 2019
- 2021 Medicare rate of ~\$7800

### AJCC and NCCN Guideline Inclusion

## Uveal Melanoma – A Rare Eye Cancer

~**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 3 years

## Decision Dx-UM

(Uveal Melanoma)

15-Gene Expression Profile (GEP) Test

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

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



## Market And Financial Overview

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# Estimated ~\$5.5B U.S. Total Addressable Market<sup>1</sup>

- In market and pipeline tests, leveraging established dermatologic sales channels

Indication/ Test outcome	Trade Name	Reimbursement Status	Peer-Reviewed Publications	Primary Customers	Initial Launch Targets	Initial addressable market, patients <sup>2</sup>	Estimated U.S. TAM
Cutaneous melanoma/ Risk of metastasis	<b>DecisionDx</b> MELANOMA	MCR, MCRA Commercial – in process	30+	Derms (including Mohs), Surgeons	—	<i>~130k patients</i> classified as Stage I, II or III	~\$540M
Cutaneous squamous cell carcinoma/ Risk of metastasis	<b>DecisionDx</b> ·SCC	Expected draft LCD in 2021 Commercial – in process	5	Derms (including Mohs)	~4,968 current customers <sup>3</sup>	<i>~200k</i> w/ high-risk features	~\$820M
Suspicious pigmented lesions/ Melanoma status	<b>myPath</b> Melanoma  <b>DecisionDx</b> DiffDx·Melanoma	MCR, MCRA Commercial – in process	9	Dermaths, Derms	~1,801 current dermpath customers <sup>4</sup>	<i>~300k patients</i> w/indeterminant biopsy	~\$600M
		Expected draft LCD in 2021 Commercial – in process	2				
Pipeline Test- Inflammatory	Target launch anticipated by the end of 2025	N/A	N/A	Expected to utilize existing dermatologic sales channels	~4,968 current customers <sup>3</sup>	<i>~450k patients</i> eligible for systemic therapies	~\$1.9B
Other Pipeline Tests	Target launches anticipated by the end of 2025	N/A	N/A	Expected to utilize existing dermatologic sales channels	To be announced	To be announced	~\$1.7B

<sup>1</sup>U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors.

<sup>2</sup>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.

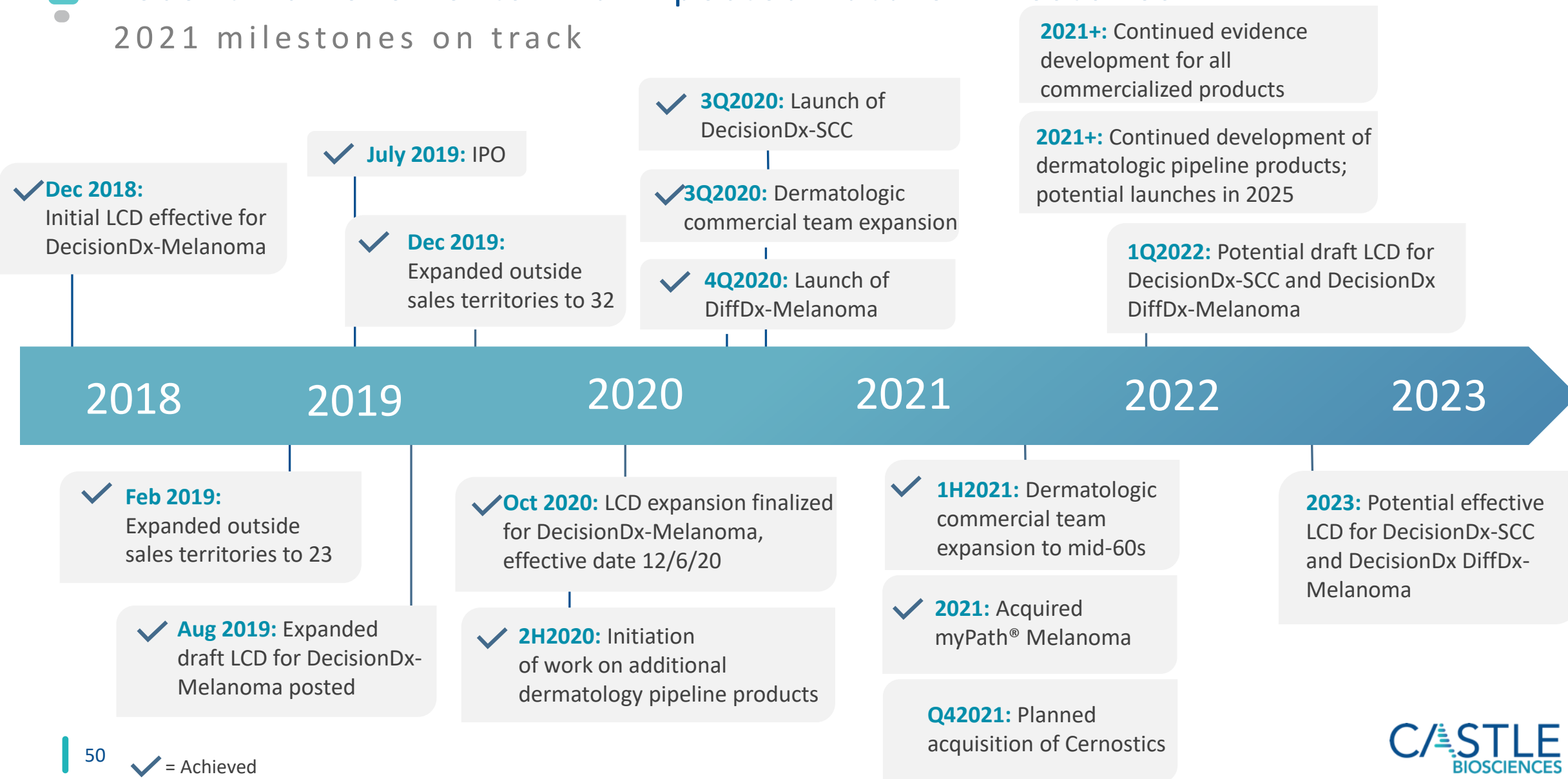
<sup>3</sup>Clinicians who ordered DecisionDx-Melanoma in last twelve months (as of 9/30/2021).

<sup>4</sup>Pathologists who provided clinical specimens for DecisionDx-Melanoma in last twelve months (as of 9/30/2021).

-MCR = Medicare. MCRA = Medicare Advantage; current customer estimates based on last twelve months.

# Recent Achievements And Expected Future Milestones

2021 milestones on track



# Factors Driving Near-And Long-Term Growth

## REVENUE



### Test Report Volume

- Expanded dermatologic commercial team trained as of July 1, 2021

### Reimbursement

- Strong ASP growth
- DecisionDx-Melanoma \$7,193 PAMA rate through 2021
- DecisionDx-UM \$7,776 PAMA rate through 2021

## PROFITABILITY



### Gross Margins

- 78% in Q32021; 81% adjusted gross margin
- Continued margin expansion of existing products (increasing ASPs and efficiencies of scale) could be offset by uptake of pipeline products ahead of reimbursement

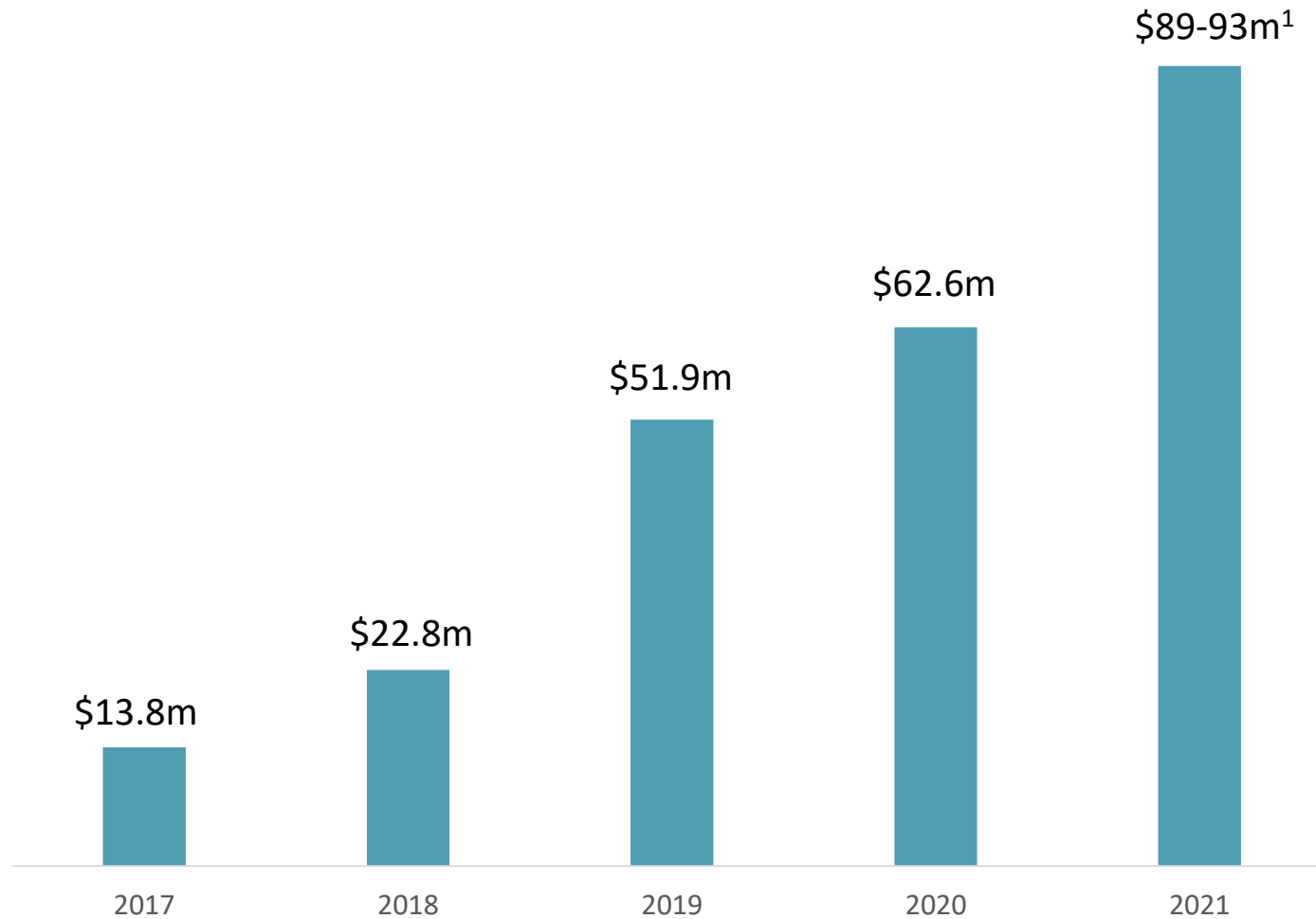
## PIPELINE



### New Product Development

- Launched two skin cancer tests in 2020 with estimated \$1.4B+ U.S. TAM
- Leverage of our existing skin cancer sales channels to support new products
- Initiated new pipeline products in dermatologic diseases with high unmet need; potential to launch 3-5 new tests by the end of 2025

Consistent Execution on Growth Initiatives Helps Enable Long-term Revenue Growth  
Expected revenue growth 2017 to 2021 CAGR ~60%



<sup>1</sup> Castle guidance for 2021 revenue as of Nov. 8, 2021

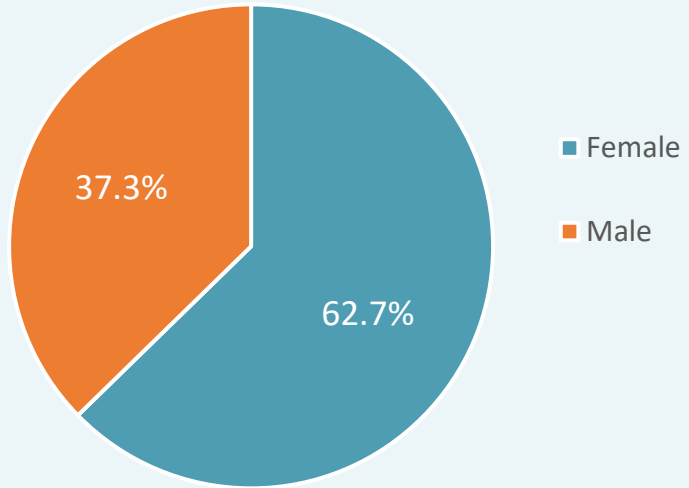
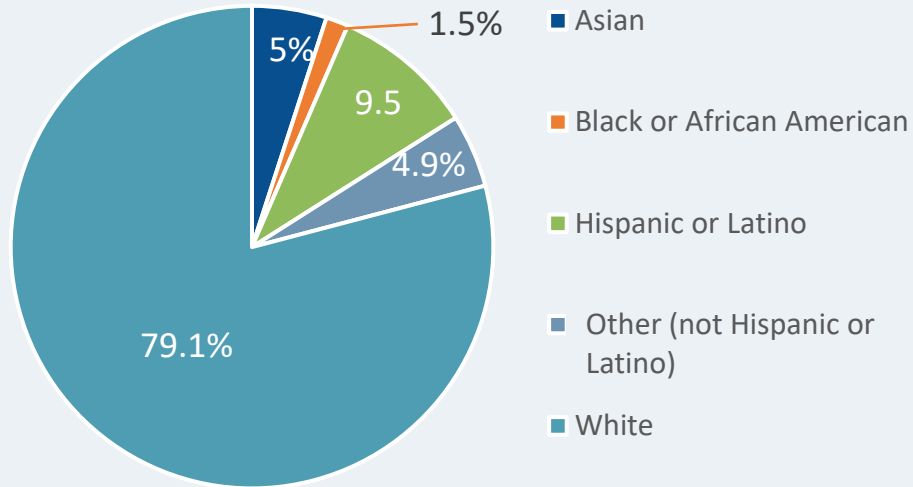


# Commitment To Diversity

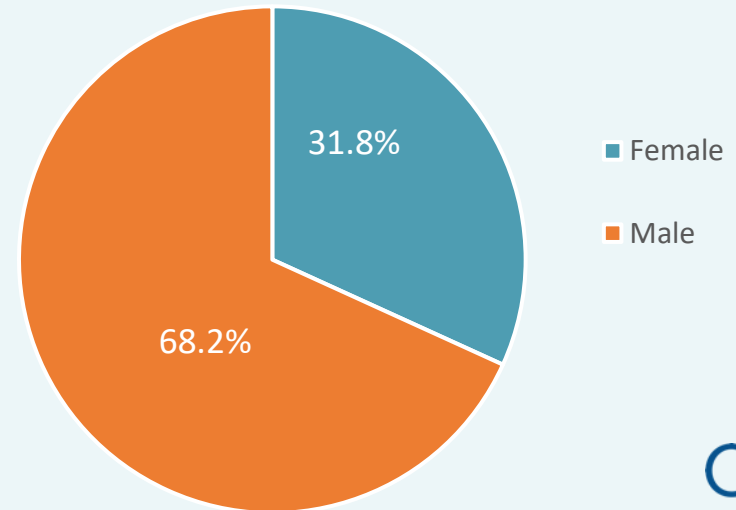
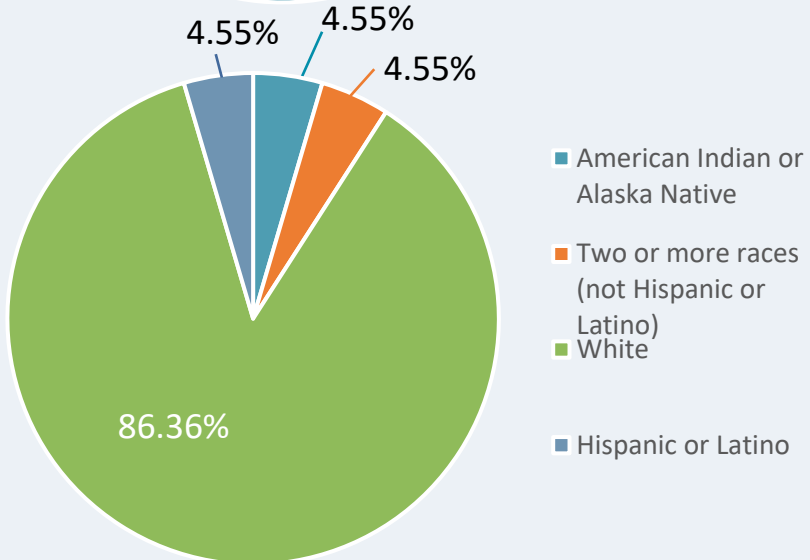
## ETHNICITY/RACE

## GENDER

All Employees



Executives



## Award-Winning Company

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



“New on Wall Street”



“Market Value, Market Return & Revenue Growth”



#7 on Top 100 List



#126 out of top 250 companies with revenue between \$50 million and \$2 billion



Awarded for the DecisionDx®-SCC and DecisionDx® DiffDx™-Melanoma genomic tests



2019 Technology Innovation in Melanoma Award Winner

# Leading Dermatologic Diagnostics Company

Transforming the management of skin cancer and other dermatologic diseases with high unmet clinical need



Culture of Teamwork and Innovation

Suite of Dermatologic Prognostic And Diagnostic Tests



Expansive Body of Evidence

Strong Financial Position



Robust Pipeline

**C/STLE**  
BIOSCIENCES

THANK YOU

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## 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 cash activity associated with COVID-19 government relief payments 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, 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 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 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 GAAP basis. 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 next slide.

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

The table below presents the reconciliation of adjusted revenue and adjusted gross margin, which are non-GAAP measures. See "Use of Non-GAAP Financial Measures (UNAUDITED)" on the 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,	
	2021	2020	2021	2020
<i>(in thousands)</i>				
<b>Adjusted revenue</b>				
Net revenues (GAAP)	\$ 23,475	\$ 15,217	\$ 69,046	\$ 45,350
Revenue associated with test reports delivered prior periods	92	(1,450)	(4,130)	(223)
Adjusted revenue (Non-GAAP)	<u>\$ 23,567</u>	<u>\$ 13,767</u>	<u>\$ 64,916</u>	<u>\$ 45,127</u>
<b>Adjusted gross margin</b>				
Gross margin (GAAP) <sup>1</sup>	\$ 18,281	\$ 12,742	\$ 56,871	\$ 38,338
Amortization of acquired intangible asset	694	—	950	—
Revenue associated with test reports delivered prior periods	92	(1,450)	(4,130)	(223)
Adjusted gross margin (Non-GAAP)	<u>\$ 19,067</u>	<u>\$ 11,292</u>	<u>\$ 53,691</u>	<u>\$ 38,115</u>
Gross margin percentage (GAAP) <sup>2</sup>	77.9 %	83.7 %	82.4 %	84.5 %
Adjusted gross margin percentage (Non-GAAP) <sup>3</sup>	80.9 %	82.0 %	82.7 %	84.5 %

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

<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 measure. See "Use of Non-GAAP Financial Measures (UNAUDITED)" on the 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,	
	2021	2020	2021	2020
<i>(in thousands)</i>				
<b>Adjusted operating cash flow</b>				
Net cash (used in) provided by operating activities (GAAP)	\$ (6,133)	\$ (2,955)	\$ (16,202)	\$ 10,295
Medicare advance payment <sup>1</sup>	3,178	—	5,351	(8,350)
HHS provider relief funds <sup>2</sup>	—	—	(1,882)	(1,882)
<b>Adjusted operating cash flow (Non-GAAP)</b>	<b>\$ (2,955)</b>	<b>\$ (2,955)</b>	<b>\$ (12,733)</b>	<b>\$ 63</b>

- \* In April 2020, 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 is 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 are submitted for reimbursement and applied against this balance, we include the advance payment in adjusted operating cash flow to the extent that Medicare claims submitted for reimbursement have been applied to the balance.
- \* In April 2020, 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

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# LEADERSHIP TEAM OVERVIEW

## MANAGEMENT TEAM

**Derek Maetzold**

*Founder, Director, President and CEO*



**Frank Stokes**

*Chief Financial Officer*



**Bernhard Spiess**

*Chief Business 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*



## BOARD OF DIRECTORS

Dan Bradbury



Derek Maetzold



Mara Aspinnall



Brad Cole



Tiffany Olson



Miles D. Harrison



Kimberlee Caple



Ellen Goldberg

CHORD Consulting