



Transforming Disease  
Management

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August 8, 2022





# 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: estimated sizes of the total addressable markets of our current and future commercial and pipeline products within our dermatologic, GI and mental health franchises; our expectations with respect to future financial or operations performance, including revenue opportunities for our tests; the impact, accuracy and effectiveness of our commercial and pipeline tests on physicians, patients and their treatment plans, including the potential impact of DecisionDx-Melanoma on survival rates, and their individual or collective impact on our prospects and plans, including any objectives of management related thereto; the ability of our tests to provide valuable, clinically actionable risk stratification information to clinicians and patients, improve health and guide patient care; expected expansion of outside sales territories and laboratory facilities; our progress roadmaps for our tests; expected launch dates for tests in our pipeline expansion and estimates regarding their total addressable markets or future success; expectations regarding LCD effective timeframes and reimbursement capabilities; our ability to utilize existing relationships and build a suite of complementary tests in a single call point; increases in headcount in furtherance of our pipeline tests, clinical research and development and other expected drivers of growth, as well as efficiencies and synergies from capital expenditures related to expansion of laboratory facilities contributing to our growth; our ability to develop clinical evidence and publish peer-reviewed reports and studies that increase adoption among providers and commercial payors; estimated healthcare cost savings provided by our tests; the ability of our risk stratification tests to classify risk of metastasis in ways that better support risk-appropriate treatment than reliance on traditional clinicopathologic risk factors alone; program milestones for our pipeline test designed to predict systemic therapy response and the potential of systemic therapy guidance tools to streamline therapeutic interventions for patients and avoid ineffective, expensive medication courses; integration timelines, expected future revenue contributions, potential cost savings, growth expectations and strategic opportunities for our TissueCypher test and GI franchise, and our IDgenetix test and our mental health franchise; and our ability to integrate our recent acquisitions into our existing business and the ability of such acquisitions to complement our existing business. The words “anticipates,” “believes,” “can,” “could,” “estimates,” “expects,” “may,” “plans,” “potential,” “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, subsequent study or trial results and findings may contradict earlier study or trial results and findings, including with respect to the diagnostic and prognostic tests discussed in this presentation, actual application of our tests may not provide the aforementioned benefits to patients, and the risks set forth under the heading “Risk Factors” in our Quarterly Report on Form 10-Q for the three months ended June 30, 2022, and in our other filings with the SEC. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements, except as may be required by law.

## **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**



## Castle Remains Focused on Transforming Disease Management

Strategic principles that create value for customers, patients and stockholders



Address areas  
with unmet  
clinical need



Leverage advanced  
technologies to  
develop innovative  
tests



Provide robust data to  
support the clinical  
value of our tests

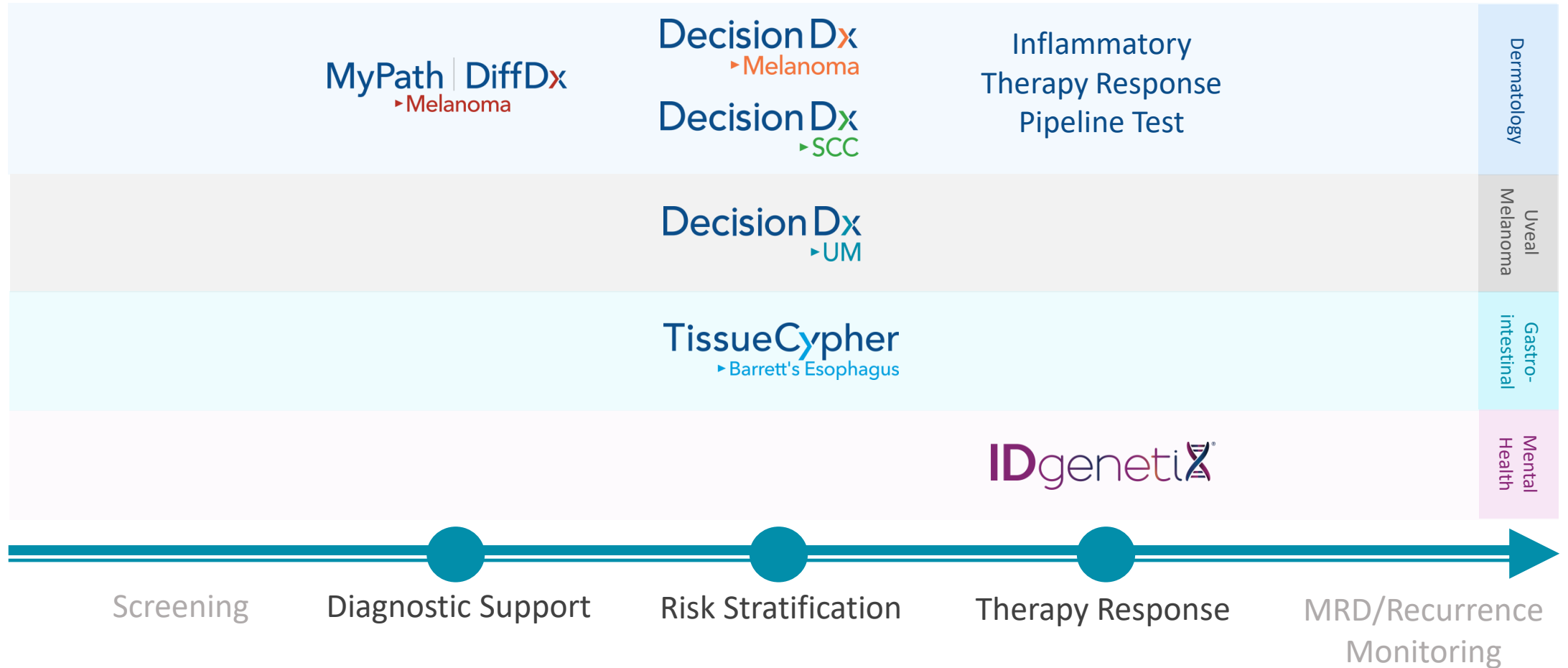


Accelerate test  
adoption through  
proven commercial  
excellence



# Answering Clinical Questions to Guide Care Along the Patient Journey

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



Patient Care Continuum



## Financial Performance Summary Q2 2022

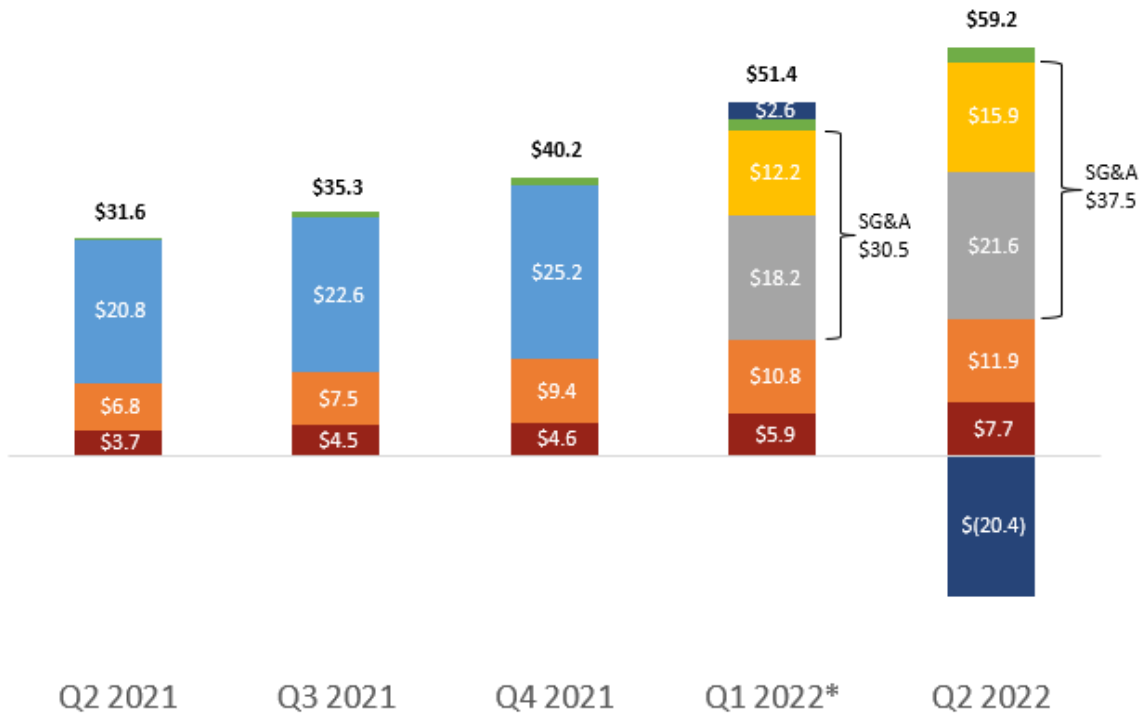
	2021	→	2022
Total test reports	7,007		<b>11,034</b>
Total Derm test reports	6,539		<b>9,424</b>
Revenue	\$22.8M		<b>\$34.8M</b>
Adj. Revenue <sup>1</sup>	\$22.9M		<b>\$34.3M</b>
Gross Margin	82.6%		<b>71.9%</b>
Adj. Gross Margin <sup>1</sup>	83.9%		<b>77.6%</b>
Operating Cash Flow	\$(6.4)M		<b>\$(9.0)M</b>
Adj. Operating Cash Flow <sup>1</sup>	\$(4.3)M		<b>\$(9.0)M</b>
Cash & Cash Equivalents	\$368M		<b>\$273M</b>
	as of 06/30/2021		as of 06/30/2022



# Q2 2022 Operating Expenses

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

## Operating Expense by Quarter<sup>1</sup>



- Change in fair value of contingent consideration
- Intangible Asset Amortization
- SG&A
- R&D
- Cost of sales

\*Detailed SG&A breakdown initiated in Q1 2022

- General and Administrative
- Sales and Marketing

## Key Drivers for Q2 2022 OpEx

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

<sup>1</sup>Amounts in millions. Operating expenses rounded and summarized as presented

## Key Q2 and Recent 2022 Accomplishments



Achieved strong growth over Q2 2021, in our total test report volume (+57%) and revenue (+53%)



Expanded NCI / SEER Registries data shared at EADO Congress showed patients diagnosed with melanoma and tested with DecisionDx-Melanoma had 27% improvement in MSS<sup>2</sup> compared to untested patients



Finalization of Medicare LCDs for DecisionDx-Melanoma; coverage remains unchanged



Medical review and pricing for DecisionDx-SCC completed by Novitas



Acquisition of AltheaDx and IDgenetix test completed



Draft foundational LCD for melanoma diagnostic tests published providing coverage criteria for DiffDx-Melanoma; expect finalization by end of Q2 2023; current coverage for MyPath remains unchanged



Expanded Medicare coverage for IDgenetix includes seven additional mental health conditions beyond major depressive disorder



Commercial team organizational structure modifications to lay groundwork for upcoming sales team optimization



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



Three new peer-reviewed studies published in GI and Derm<sup>3</sup>

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

Dermatology			Gastroenterology	Mental Health
Cutaneous melanoma/ risk of metastasis	Cutaneous squamous cell carcinoma/ risk of metastasis	Suspicious pigmented lesions/melanoma status	Barrett's esophagus/ risk of progression to esophageal cancer	Mental health therapy response
~130K Patients classified as Stage I, II or III <sup>2</sup>	~200K Patients w/ high-risk features <sup>2</sup>	~300K Patients w/ indeterminant biopsy <sup>2</sup>	~384K Patients receiving upper GI endoscopies/year who meet the intended use criteria for TissueCypher <sup>3</sup>	Based on indicated use of IDgenetix for patients diagnosed with depression, anxiety and other mental health conditions
~\$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)

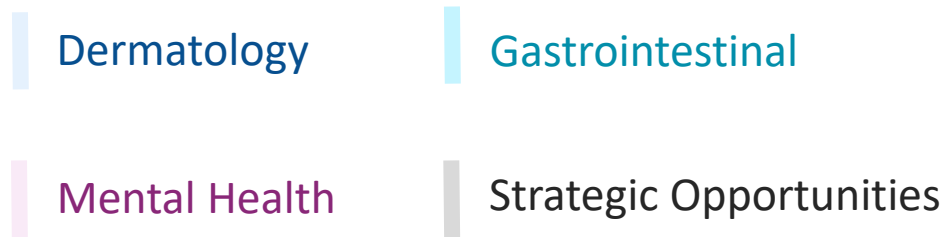
<sup>1</sup>U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors.

<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.

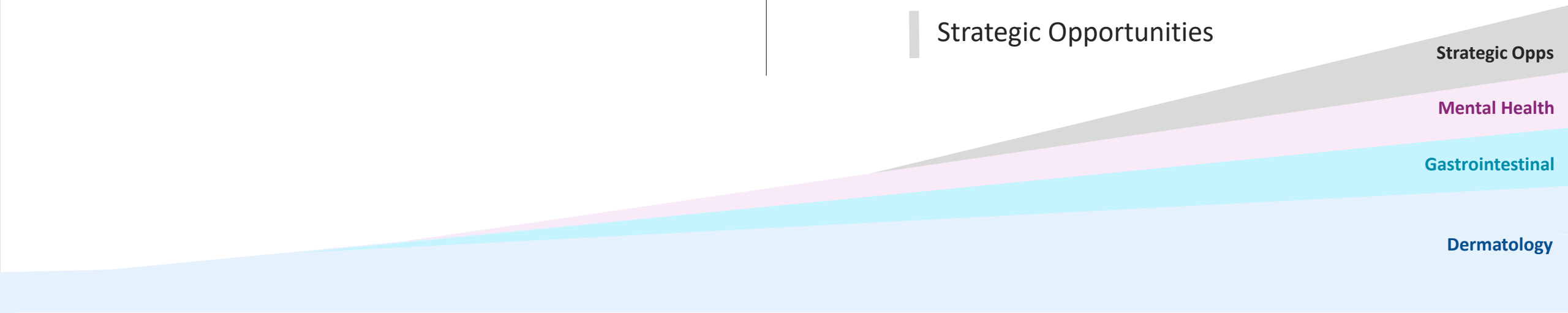
<sup>3</sup>384,000 upper GI endoscopies/year with confirmed dx of BE (ND, IND, LGD) x \$2,513 = U.S. only TAM of ~\$1 billion

# Driving Long-Term Growth through our Foundational Strategy: Strong Core Derm Business, Pipeline Initiatives and Strategic Opportunities

Near-to Mid-term Growth  
2022-2024



Mid-to Long-term Growth  
2024 and beyond





# Operational Growth Pillars

Consistent execution furthers our leading position in dermatology and in the Dx space

## Strong Core Derm Business



- Continuing provider education
- Optimizing commercial team
- Evolving our go-to-market strategy
- Data that drives value: NCI/SEER collaboration

## Pipeline Initiatives



- Ability to answer clinical questions/impact patient care
- Utilizing our areas of expertise (genomics, spatialomics, AI) to develop innovative tests
- Focusing on complementary/adjacent disease states

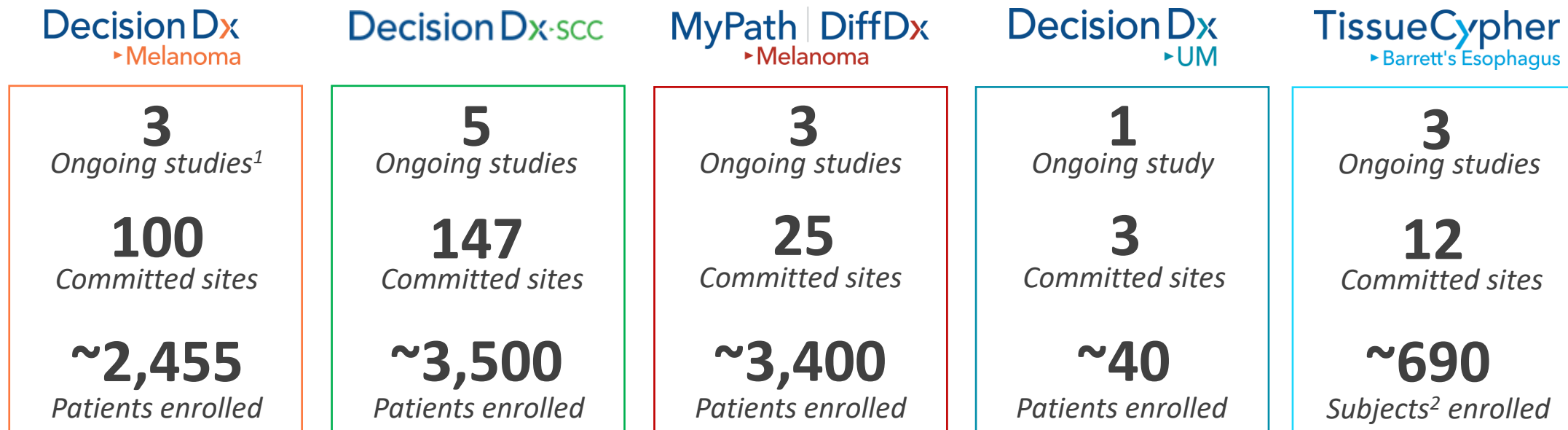
## Strategic Opportunities



- Significant opportunities where early reimbursement wins have been achieved and we can utilize our commercial success
- Potential to create a suite of tests in a single call point

## Accelerating Investments in Clinical Development

Ongoing studies to generate data that supports the clinical value of our tests and provider and payer adoption



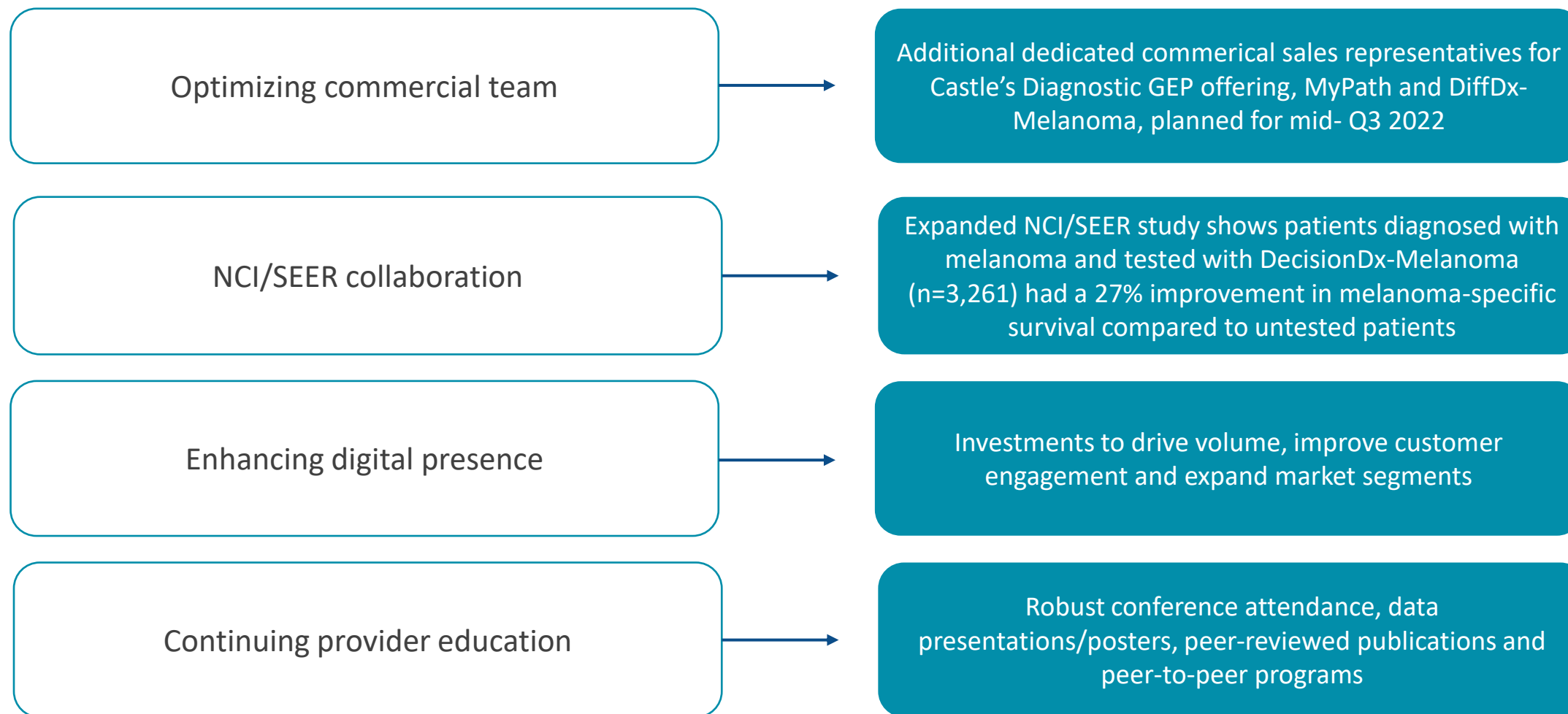
**Ongoing collaboration with NCI/SEER has allowed for studies with 5,200+ patients clinically tested with DecisionDx-Melanoma to date<sup>3</sup>**

Our Core Derm Business  
is Strong

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## Strong Core Derm Business Pillar of Growth



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

## Diagnostic Support



## Risk Stratification



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



**Strong provider growth and continued adoption with ~2,280 new ordering clinicians and ~6,960 unique ordering clinicians for our dermatologic tests over the last 12 months<sup>2</sup>**

# DecisionDx-Melanoma: Precision Risk Stratification Based on an Individual Patient’s Tumor Biology Informs Treatment Plans

Market Snapshot	Clinical Questions <i>(post-melanoma diagnosis)</i>	Clinical Utility	Transforming Disease Management
<p><b>~\$540M</b> revenue opportunity<sup>1</sup></p> <p><b>~130k patients</b> classified as Stage I, II or III<sup>2</sup></p>	<p>Is the risk of SLN-positivity high enough to warrant referral for the SLNB surgery?</p>	<p>Accurately identifies those at <b>low and high risk for a positive SLN</b><sup>3</sup></p>	<p>DecisionDx-Melanoma <b>could result in 74% fewer SLNB surgeries</b><sup>4</sup>, potentially saving the U.S. healthcare system \$250M<sup>5,6</sup> due to <b>more precise risk stratification</b><sup>3</sup></p>
	<p>What is the individual risk of recurrence?</p>	<p>Provides <b>personalized risk of recurrence</b> to give guidance for patient follow-up and treatment intensity decisions</p>	<p><b>Only melanoma prognostic test shown to be associated with improved survival</b>; patients diagnosed with cutaneous melanoma and tested with DecisionDx-Melanoma had a <b>27% improvement in melanoma-specific survival</b> compared to untested patients<sup>7</sup></p> <hr/> <p>In clinical utility studies, <b>45% of patients were re-stratified</b> and <b>~50% of clinicians changed patient management</b> based on DecisionDx-Melanoma results<sup>8</sup></p>

SLN = sentinel lymph node; SLNB = sentinel lymph node biopsy. Source: NCCN Guidelines for Cutaneous Melanoma v3.2020 <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.

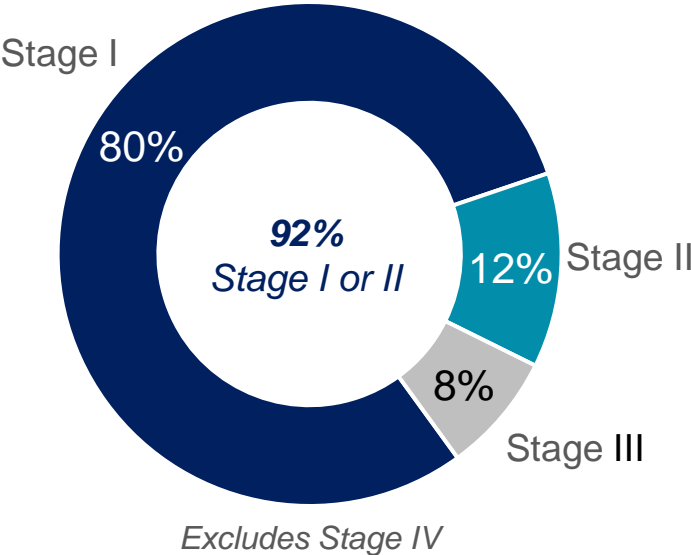
<sup>3</sup>Whitman et al. *JCO Precision Oncology* 2021; <sup>4</sup>For patients with melanomas of less than or equal to 2.0 mm thick; <sup>5</sup>Vetto et al. *Future Oncol* 2019. <sup>6</sup>Clearview health economic model, data on file

<sup>7</sup>Kurley et al. Presented at EADO, April 21-23, 2022; <sup>8</sup>Berger et al. *CMRO* 2016; Dillon et al. *Skin J Cutan Med*; Farberg et al. *J Drugs Derm* 2017; Schuitemoerder et al. *J Drugs Derm* 2018; Dillon et al. *CMRO* 2022

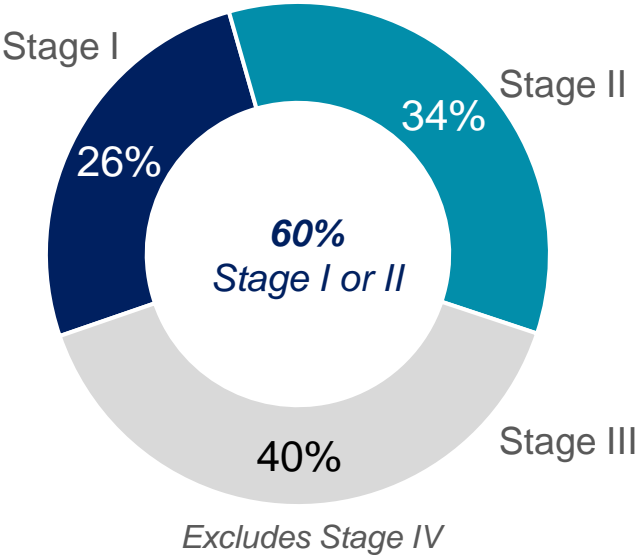


# Current Melanoma Staging Misses Patients with Aggressive Tumor Biology

### Stage at Diagnosis



### Melanoma Deaths by Stage at Diagnosis



The majority of melanoma deaths occur in patients who were diagnosed at Stage I or II



# DecisionDx-Melanoma Is Supported by Significant Scientific Evidence

**9,000+**

Total patients included in studies including *independent validation*

**35+**

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

**105,000+**

Patients with a clinical *DecisionDx-Melanoma* order from *10,200+ clinicians*

**1A**

Level 1A evidence\*

**50%**

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

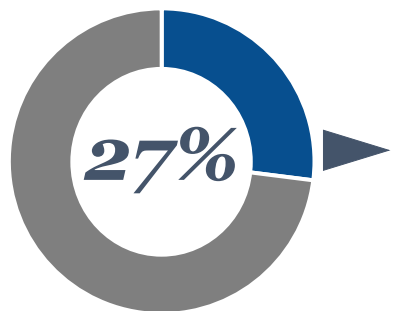
**Medicare+**

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

\*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 June 30, 2022

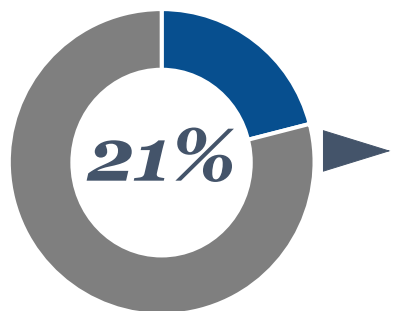
## NCI/SEER Data Linked with DecisionDx-Melanoma Test Results

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



**Benefit in MSS in patients that were tested at 3 years over those that were not tested**

	3-year MSS (95% CI)	Deaths, % (n/N)
31-GEP Tested	97.7% (97.0-98.4%)	1.6% (58/3621)
Matched Untested	96.6% (96.2-97.1%)	2.2% (238/10863)
<b>Hazard ratio<sup>‡</sup></b>	<b>0.73 (0.54-0.97)</b>	<b>P=0.03</b>



**Benefit in OS in patients that were tested at 3 years over those that were not tested**

	3-year OS (95% CI)	Deaths, % (n/N)
31-GEP Tested	93.1% (92.0-94.2%)	4.8% (174/3621)
Matched Untested	91.2% (90.4-91.9%)	6.1% (658/10863)
<b>Hazard ratio<sup>‡</sup></b>	<b>0.79 (0.67-0.93)</b>	<b>P=0.006</b>

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

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

## Sentinel lymph node biopsy (SLNB)

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

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

## Breast Cancer Test\*\*

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

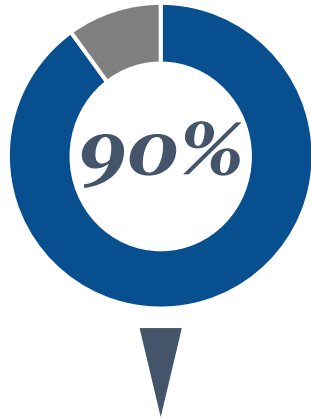
BCSS mortality difference of **0.50% at 3 years** when comparing tested and untested populations

## DecisionDx ▶Melanoma

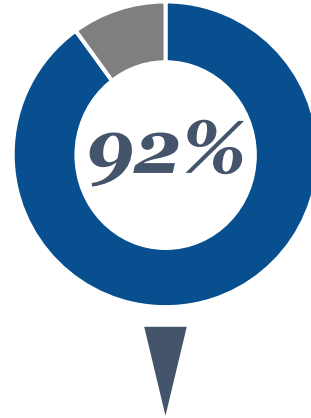
DecisionDx ▶Melanoma	3-yr MSS <sup>3</sup>
DecisionDx-Melanoma	97.7%
Matched Untested	96.6%
Absolute Mortality Difference	<b>1.1% (p&lt;0.05)</b>

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

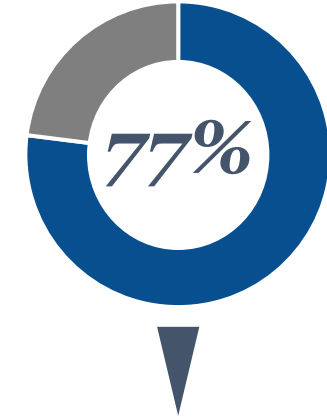
## Patients with Melanoma Desire Testing with DecisionDx-Melanoma



Wanted prognostic information about their melanoma tumors at diagnosis



Felt the testing was useful



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

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

# DecisionDx-SCC: Delivering Precision Patient Classification and Informing Squamous Cell Carcinoma Management Decisions within Established Guidelines

Market Snapshot	Clinical Question <i>(post-SCC diagnosis)</i>	Clinical Utility	Transforming Disease Management
<p><b>~\$820M</b> revenue opportunity<sup>1</sup></p> <p><b>~200k patients</b> with high-risk features<sup>2</sup></p>	<p>Who is really at low risk or high risk for metastasis?</p>	<p><b>Predicts metastatic risk</b> for individual SCC patients with one or more risk factors</p>	<p><b>Strongest independent predictor of SCC metastasis, compared to AJCC8 and BWH staging</b>            (Sensitivity of a DecisionDx-SCC Class 2A or 2B result (77.8%) was significantly higher (p&lt;0.0001) than that of high-stage AJCC8 (38.1%) and BWH (30.2%))<sup>3</sup></p>
		<p>Incorporation of DecisionDx-SCC can <b>improve management decisions within established guidelines</b></p>	<p><b>97% of clinicians would change patient management</b> given DecisionDx-SCC results with 2 risk factors<sup>4</sup></p>
		<p>Proven <b>significant and independent prognostic value</b> for stratifying risk of metastasis in high-risk SCC patients</p>	<p><b>Identifies nearly 80% of tumors</b> traditionally staged as <b>low risk</b> (T1 tumors AJCC8 and/or BWH) <b>that metastasized as biologically high risk</b><sup>5</sup></p>

SCC = squamous cell carcinoma; NCCN = National Comprehensive Cancer Network (NCCN); BWH = Brigham and Women's Hospital; AJCC8 = American Joint Committee on Cancer Eighth Edition

<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 squamous cell carcinoma estimated at 1,000,000 with addressable market limited to carcinomas with one or more high risk features.

NCCN Guidelines for Squamous Cell Skin Cancer v1 2022

<sup>3</sup>Ibrahim et al., *Future Oncology* 2021; <sup>4</sup>Goldberg et al., *Presented at Winter Clinical Dermatology*, January 14-19, 2022

<sup>5</sup>Farberg et al., *Presented at American Academy of Dermatology Summer Meeting 2021*; Ibrahim et al., *Future Oncology* 2021

# DecisionDx-SCC Can Inform Risk-Appropriate Management to Guide Patient Care

## 1 or more

Validated to determine the biological risk of metastasis *for SCC patients with 1 or more high risk factors*

## 40

*Quantifies expression of 40 genes from primary tumor* using RT-PCR

## 1,010+

Validated across 2 independent studies *spanning 1,018 patients*<sup>1</sup>

## 10

*Peer-reviewed publications* to date

## 2,100+

*Clinicians have ordered* DecisionDx-SCC

## ~3,500

*Patients* are currently enrolled in *ongoing studies* from **147 centers**



# Castle's Diagnostic GEP Offering Can Aid in the Diagnosis and Inform Management Decisions for Patients with Ambiguous Melanocytic Lesions

Market Snapshot	Clinical Question	Clinical Utility	Transforming Disease Management
<p>~\$600M revenue opportunity<sup>1</sup></p> <p>~300k patients with an indeterminate biopsy<sup>2</sup></p> <p><i>After melanoma diagnosis, clinicians can order DecisionDx-Melanoma using the same tissue sample</i></p>	<p>Is the melanocytic lesion malignant or benign?</p>	<p>Designed to classify lesions <b>objectively and accurately</b> as benign, intermediate or malignant when the distinction cannot be made confidently by histopathology alone</p>	<p>When the potential for malignancy cannot be excluded, the <b>most appropriate treatment plan for a patient is unclear</b>; clinicians typically recommend a treatment plan consistent with melanoma which <b>may result in overtreatment</b> of some patients<sup>4</sup></p>
		<p><b>Can adds diagnostic clarity and confidence</b> for more informed patient care</p>	<p><b>Proven utility in reducing ambiguous diagnoses (by ~43%)<sup>5</sup></b> by dermatopathologists and <b>reducing surgical re-excisions (by ~77%)</b> by dermatologists <b>in patients with benign GEP results<sup>6</sup></b></p>
		<p><b>Guidelines support ancillary diagnostic testing in ambiguous melanocytic lesions</b>, including NCCN, the American Academy of Dermatology and the American Society of Dermatopathology<sup>3</sup></p>	<p>By leveraging a second GEP test, <b>more than 99% of patients tested will receive a clinically actionable result<sup>7</sup></b></p>

<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 suspicious pigmented lesion biopsies estimated at 2,000,000 with addressable market limited to the 15% with an indeterminate biopsy

<sup>3</sup>NCCN Guidelines Version 2.2022 Melanoma: Cutaneous; Fung et al. *J Cutan Pathol*. E-pub 18 Sept. 2021; 1-15.

<sup>4</sup>Ensslin et al. *Dermatol Surg* 2018; <sup>5</sup>Cockerell et al. *Medicine* 2016; <sup>6</sup>Farberg et al. *SKIN J Cutaneous Med* 2020; <sup>7</sup>Goldberg et al. *J Dermatol Physician Assist* 2022

## Castle's Diagnostic GEP Tests Provide Objective and Accurate Information for More Informed Patient Care

**41,000+**

Lesions clinically tested

**2**

*Independently validated GEP tests* to aid in diagnosis and guide patient management

**8+**

Years of *clinical testing* experience

**12**

*Peer-reviewed publications*, including prospective studies

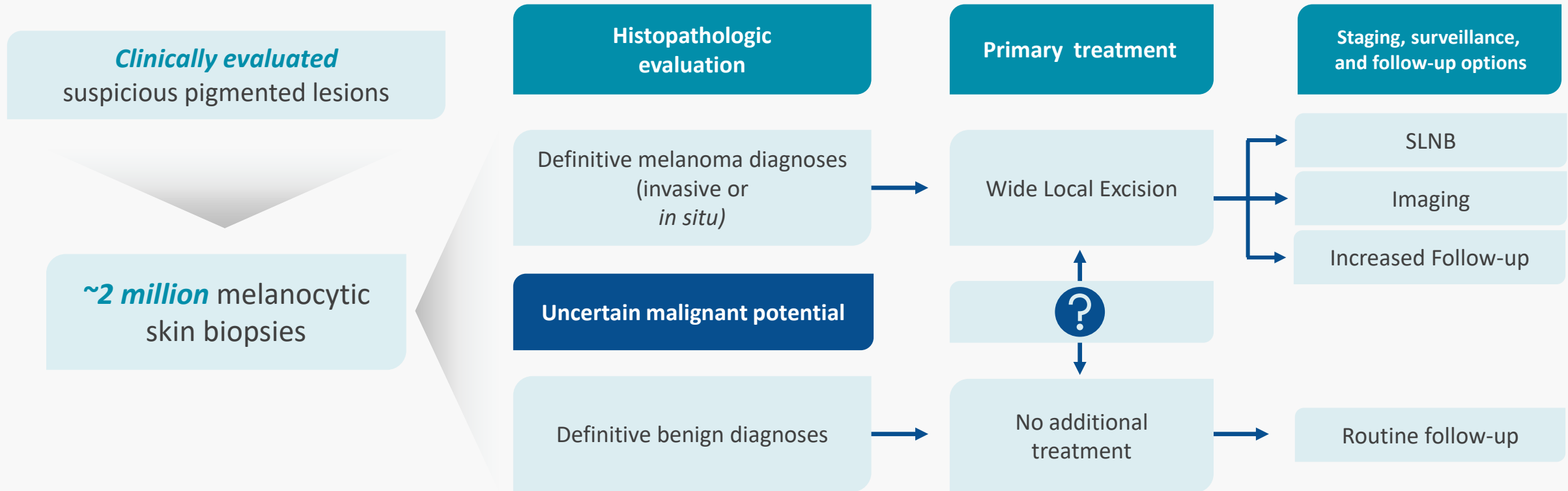
**3**

*GEP testing is supported by 3 national guidelines* to aid in diagnosing ambiguous lesions

**Medicare+**

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

# Diagnosing Melanoma, the Clinical Issue: Uncertainty Creates an Over- or Under-Treatment Dilemma





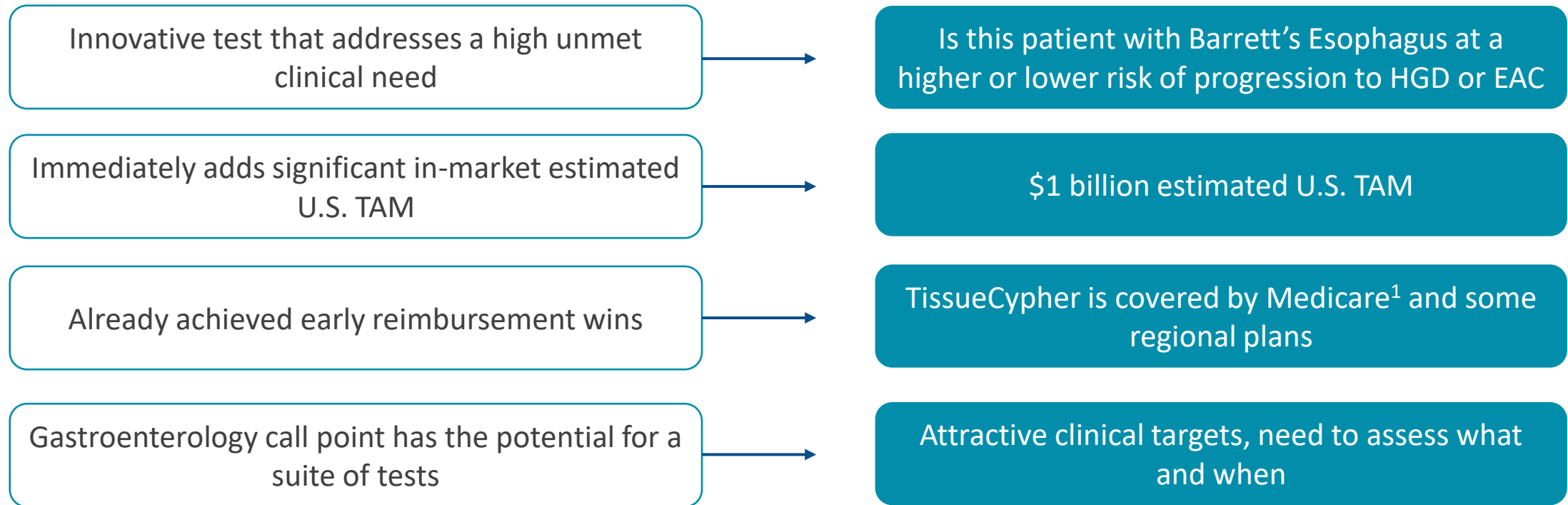
## Strategic Opportunities

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# Cernostics Acquisition Aligns with Our Strategic Opportunities Goals

Integration expected to be a meaningful revenue contributor in 2024



***Our capital allocation priorities include strategic acquisitions with potential for mid- to long-term value creation and revenue and earnings growth***

# TissueCypher: Designed to Independently Predicts Development of Esophageal Cancer in Patients with Barrett's Esophagus (BE)

Market Snapshot	Clinical Decision Point	Clinical Utility	Transforming Disease Management
<p><b>~\$1B</b> revenue opportunity<sup>1</sup></p> <p><b>~384k patients</b> receiving upper GI endoscopies/year w/ confirmed Dx of BE<sup>2</sup></p>	<p>Which BE patients will progress to HGD or esophageal cancer?</p>	<p>Provides a <b>5-year individual risk of progression to high-grade dysplasia or esophageal adenocarcinoma</b> for patients with confirmed BE</p>	<p><b>Strongest predictor of progression to esophageal cancer (risk-stratification)</b>            TissueCypher hazard ratio of 7.7 compared to GI expert pathologist diagnosis of 3.9 (p&lt;0.0001); pooled analysis<sup>3-7</sup></p>
		<p>Identifies patients:</p> <ol style="list-style-type: none"> <li>1) At risk for future progression and patients harboring prevalent HGD/EAC</li> <li>2) At low risk of progression who may be able to avoid unnecessary treatment or surveillance</li> </ol>	<p>Patients receiving a high-risk TissueCypher score are <b>9.4 times more likely to progress</b> within 1–5 years<sup>3</sup></p> <hr/> <p>Clinical use study demonstrates <b>55% change in patient management</b><sup>9</sup></p>

HGD = high-grade dysplasia; EAC = esophageal adenocarcinoma; BE = Barrett's esophagus

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

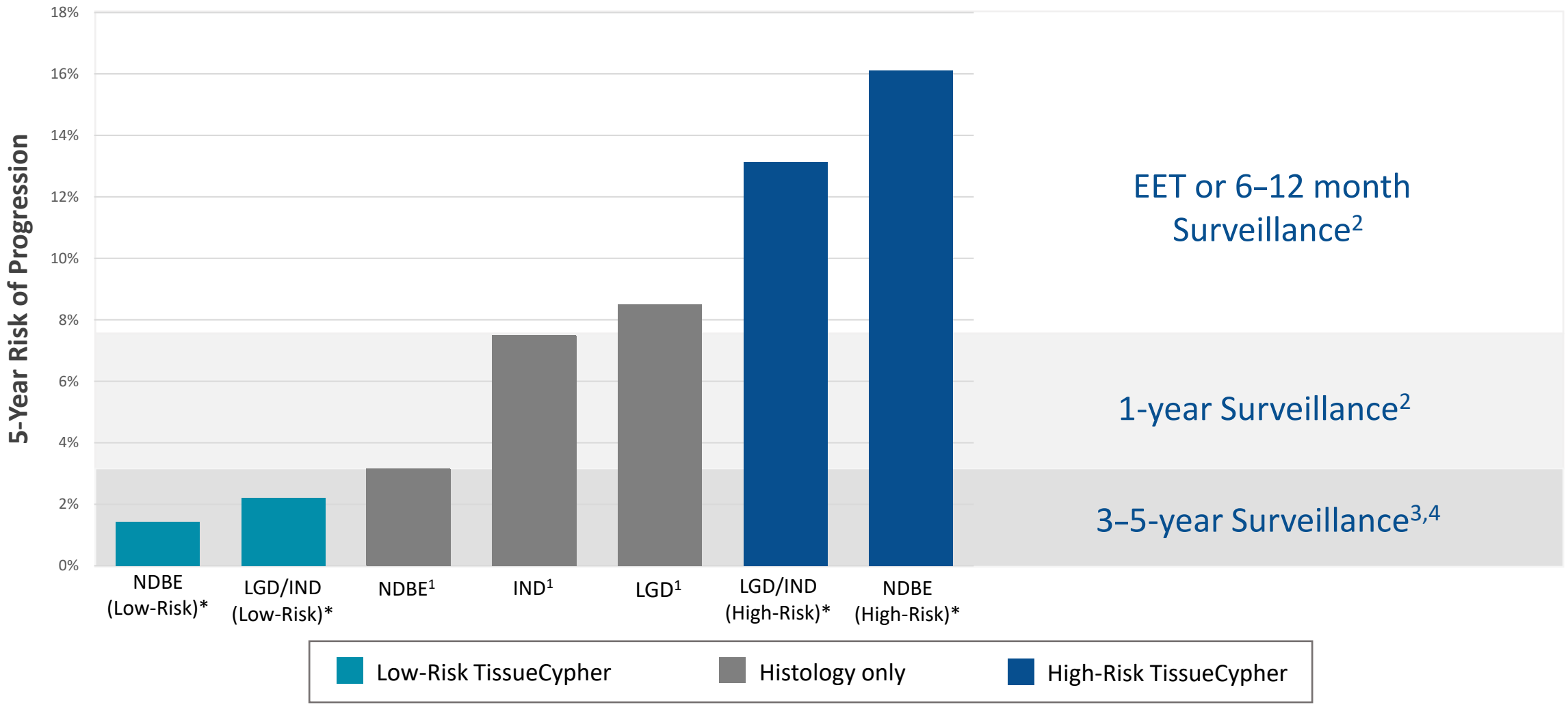
<sup>2</sup>384,000 upper GI endoscopies/year with confirmed dx of BE (ND, IND, LGD) x \$2,513 = U.S. only TAM of ~\$1 billion

<sup>3</sup>Critchley-Thorne et al. Cancer Epidemiol Biomarkers Prev 2016.

<sup>4</sup>Critchley-Thorne, et. al. Cancer Epidemiol Biomarkers Prev. Feb 2017 <sup>5</sup>Davison, et. al. Am J Gastroenterol. Feb 2020

<sup>6</sup>Frei, et. al. Clin Transl Gastroenterol. Oct 2020; <sup>7</sup>Frei, et. al. Am J Gastroenterol. Apr 2021; <sup>9</sup>Diehl, et.al. Endoscopy International Open, 2021, Mar; 9(3): E348-E355

# TissueCypher Can Contribute Significant Improvements in Risk Prediction Over Pathology Alone



1 Progression rates: Rastogi et al. *Gastrointest Endosc* 2008; Krisnamoorthi et al. *Gastrointest Endosc* 2020; Singh et al. *Gastrointest Endosc* 2014; Wani et al. *Clin Gastroenterol Hepatol* 2011. 2 Consensus guidelines from ACG (2015), AGA (Medical Position Statement, 2011) and ASGE (2019); 3 Shaheen et al. *Am J Gastroenterol* 2022. 4 Komanduri et al. *Clin Gastroenterol Hepatol* 2022. \*Data on file, Castle Biosciences. Data from pooled analysis of TissueCypher's risk stratification performance reported in 5 clinical validation studies.

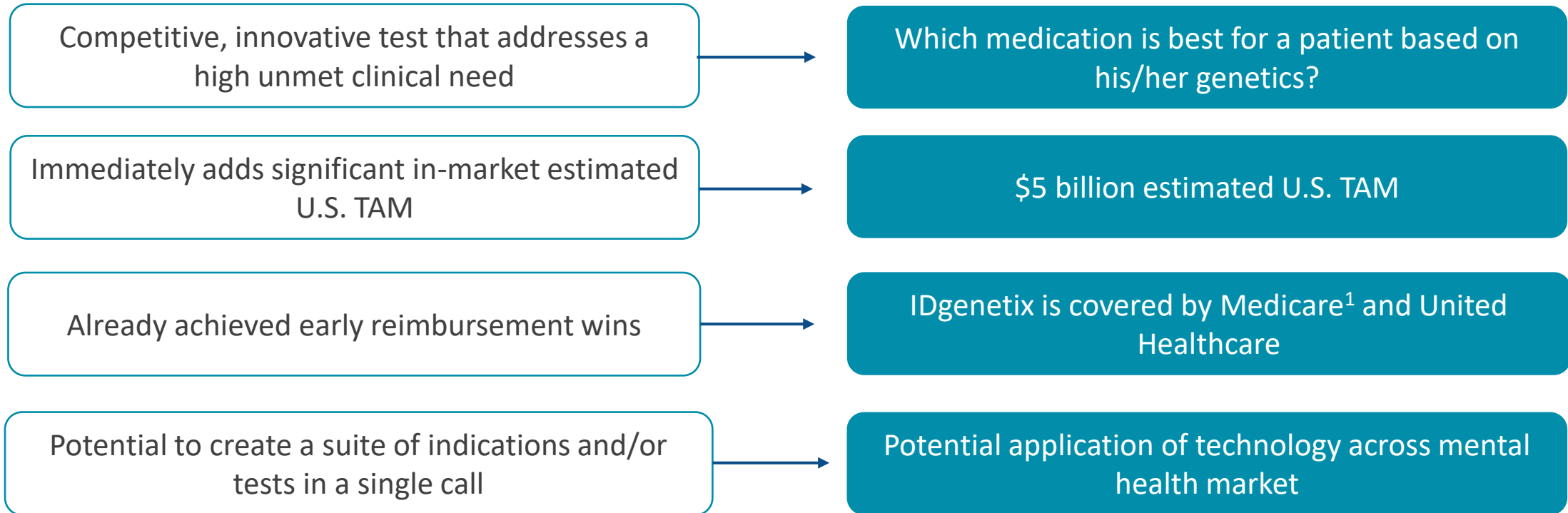
# TissueCypher: Significant 2022 Milestones Already Achieved, Integration On Track

Early TissueCypher performance exceeding our expectations



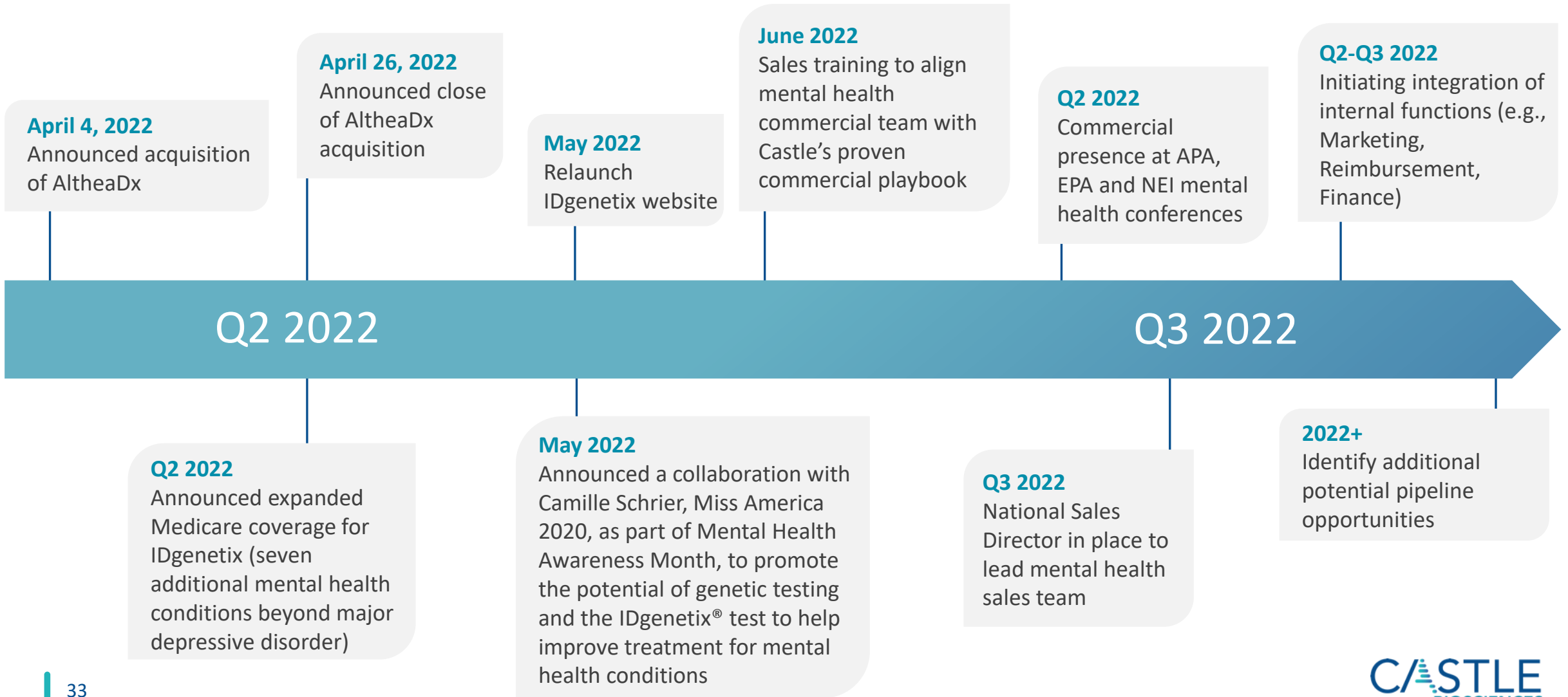
## AltheaDx Acquisition Aligns with Our Strategic Opportunities Goals

Early feedback consistent with pre-deal work, expect IDgenetix to be a meaningful revenue contributor in 2024



***Our capital allocation priorities include strategic acquisitions with potential for mid- to long-term value creation and revenue and earnings growth***

# IDgenetiX: Integration Beginning, Significant Milestones Already Achieved

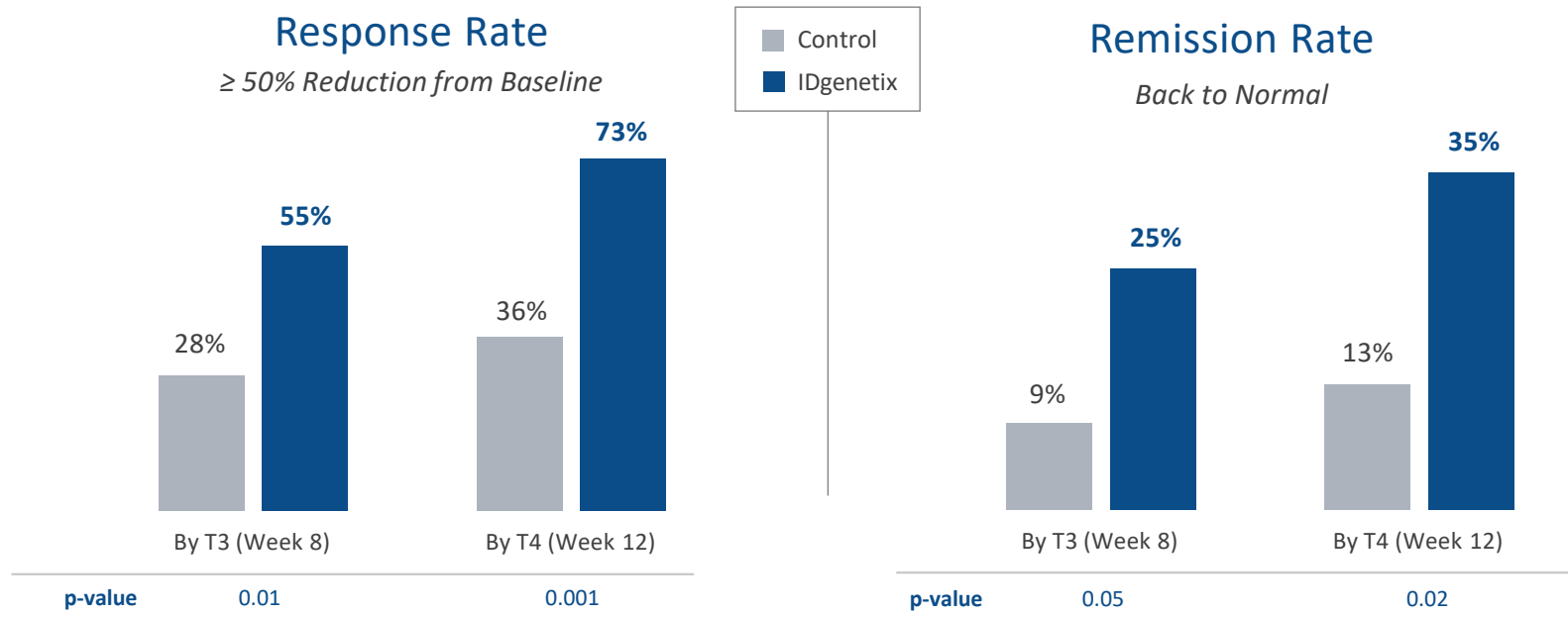


# IDgenetix: Designed to Guide Timely and Evidence-Based Decisions on the Optimal Drug for Each Patient

Market Snapshot	Clinical Decision Point	Clinical Utility	Transforming Disease Management
<p>~\$5B revenue opportunity<sup>1</sup></p>	<p>Which medication is best for each patient?</p>	<p><i>Provides drug-gene, drug-drug and lifestyle factor interactions</i> to guide tailored treatment recommendations for patients in terms of their prescribed medications</p>	<p>Randomized controlled trial showed <b>a greater than 2.5 times improvement in remission rates for patients with severe depression</b>, who were tested with IDgenetix, compared to those who did not have their genes tested<sup>2</sup></p> <hr/> <p><b>Substantial annual cost savings potential of \$5,962 per patient</b> as a result of testing with IDgenetix<sup>3</sup></p> <hr/> <p>Replacing standard-of-care, trial-and-error prescription practices in mental health with a scientifically-backed genetic test with the potential to:</p> <ul style="list-style-type: none"> <li>• <b>Help patients achieve a faster therapeutic response</b></li> <li>• <b>Reduce adverse events</b></li> <li>• <b>Yield cost savings in the healthcare system</b></li> </ul>

**IDgenetix provides drug-gene, drug-drug and lifestyle factor interactions**

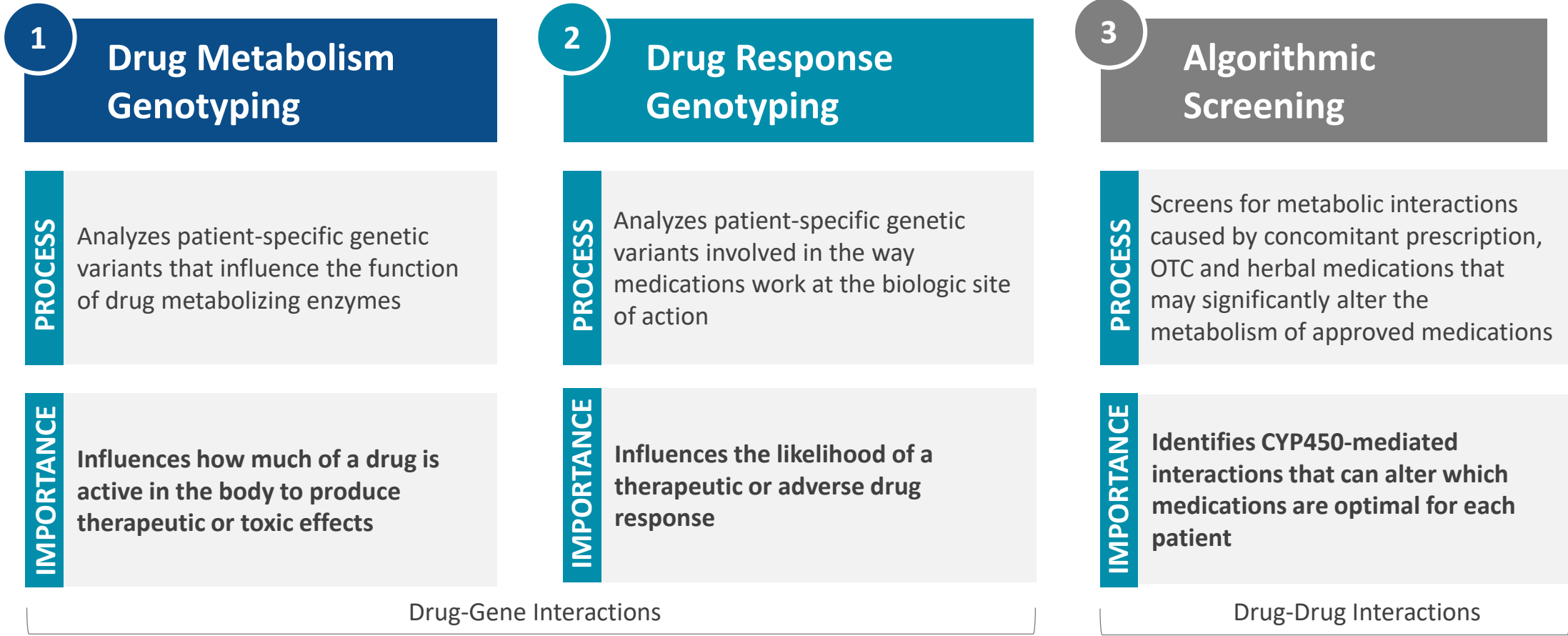
# Enhanced Therapeutic Efficacy vs. Standard of Care



## Clinical Trial Design

- Randomized Controlled Trial (RCT)
- Peer-reviewed and published in the *Journal of Psychiatric Research*
- 685 participants, Depression *and* Anxiety
- Double-blinded
- Treated by a broader group of medical professionals, beyond psychiatrists
- 20 independent clinical sites
- 4, 8 and 12-week efficacy using HAM-A scale

# IDgenetix Testing Process Consists of Three Important Steps



*IDgenetix testing is designed to provide tailored treatment recommendations for each patient by utilizing a bioinformatic algorithm to integrate patient-specific health information with comprehensive genetic results*

# Uveal Melanoma

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

Market Snapshot	Clinical Decision Point	Clinical Utility	Transforming Disease Management
<p><b>More than 90% of U.S. ocular oncology institutions order DecisionDx-Melanoma (1,618 reports issued in 2021)</b></p>	<p>What is the risk that a patient’s uveal melanoma (eye cancer) will spread or recur?</p>	<p>Predicts the <b>likelihood that a patient’s cancer will spread</b> (metastasize) over the next five years <b>to guide surveillance and treatment decisions</b></p>	<p>Key statistics about uveal melanoma:</p> <ul style="list-style-type: none"> <li>• <b>~2,000</b> patients diagnosed in the U.S. annually</li> <li>• <b>~97%</b> of patients – no evidence of metastatic disease at the time of diagnosis</li> <li>• <b>~30%</b> will develop metastases within 5 years</li> </ul> <p>DecisionDx-UM has <b>broad Medicare reimbursement</b><sup>1</sup> (LCD covers patients with a confirmed diagnosis and no evidence of metastatic disease; received payment on ~93% of claims in 2021)</p> <p><b>Included in AJCC and NCCN guidelines</b></p>

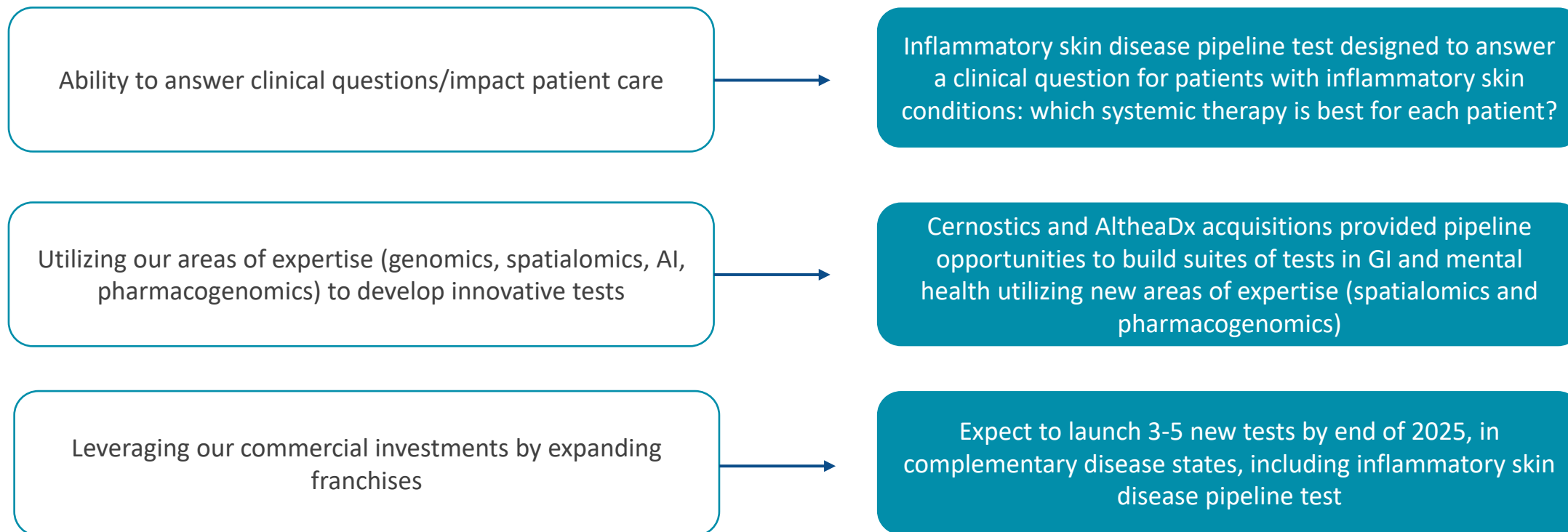


## Pipeline Initiatives

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## Continued Execution on Pipeline Initiatives as a Pillar of Growth



## Targeting 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

Treatments are significantly different for PSO and AD and can be costly  
(e.g., Humira for PSO ~\$68k/year; Dupixent for AD is ~\$38k/year)

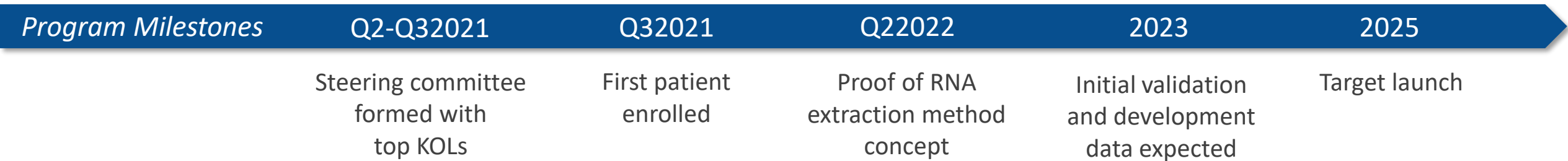
Cutaneous T Cell Lymphoma (CTCL) can mimic clinical presentation of AD and PSO  
~20-30% of patients with PSO will go on to develop psoriatic arthritis, which can produce irreversible joint damage and significant patient morbidity

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

# Castle's Inflammatory Skin Disease Pipeline Test Is Being Developed to Predict Systemic Therapy Response – IDENTITY Study

**54** *Committed Sites*

**303** *Patients Enrolled*



# Environmental, Social and Governance (ESG)

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# ESG Focus Areas for 2022 and Beyond



 Environmental policy

 Environmental metrics

 DEI mission statement

 DEI metrics

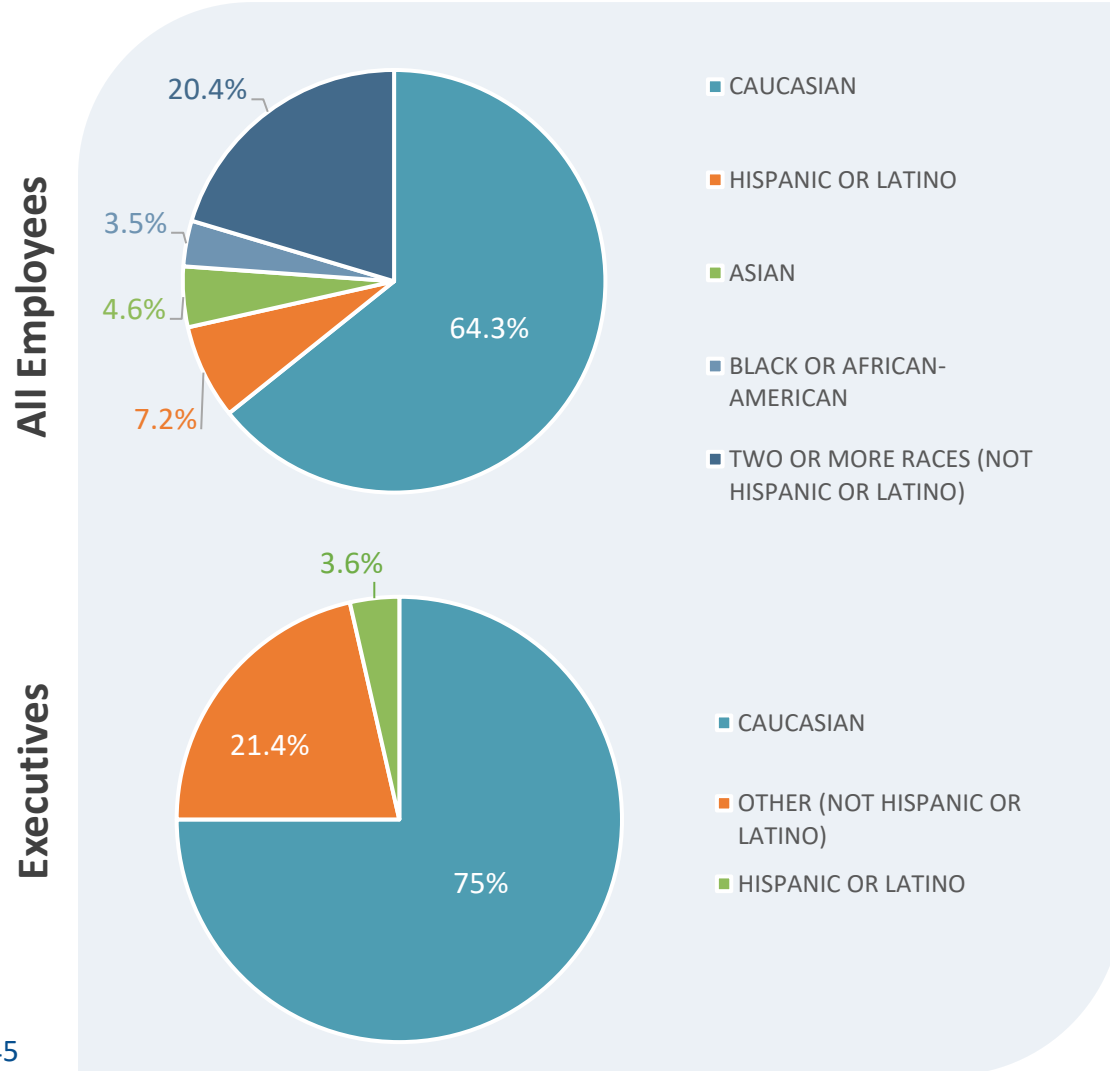
 DEI action plan/roadmap

 Vendor code of conduct/supplier standard

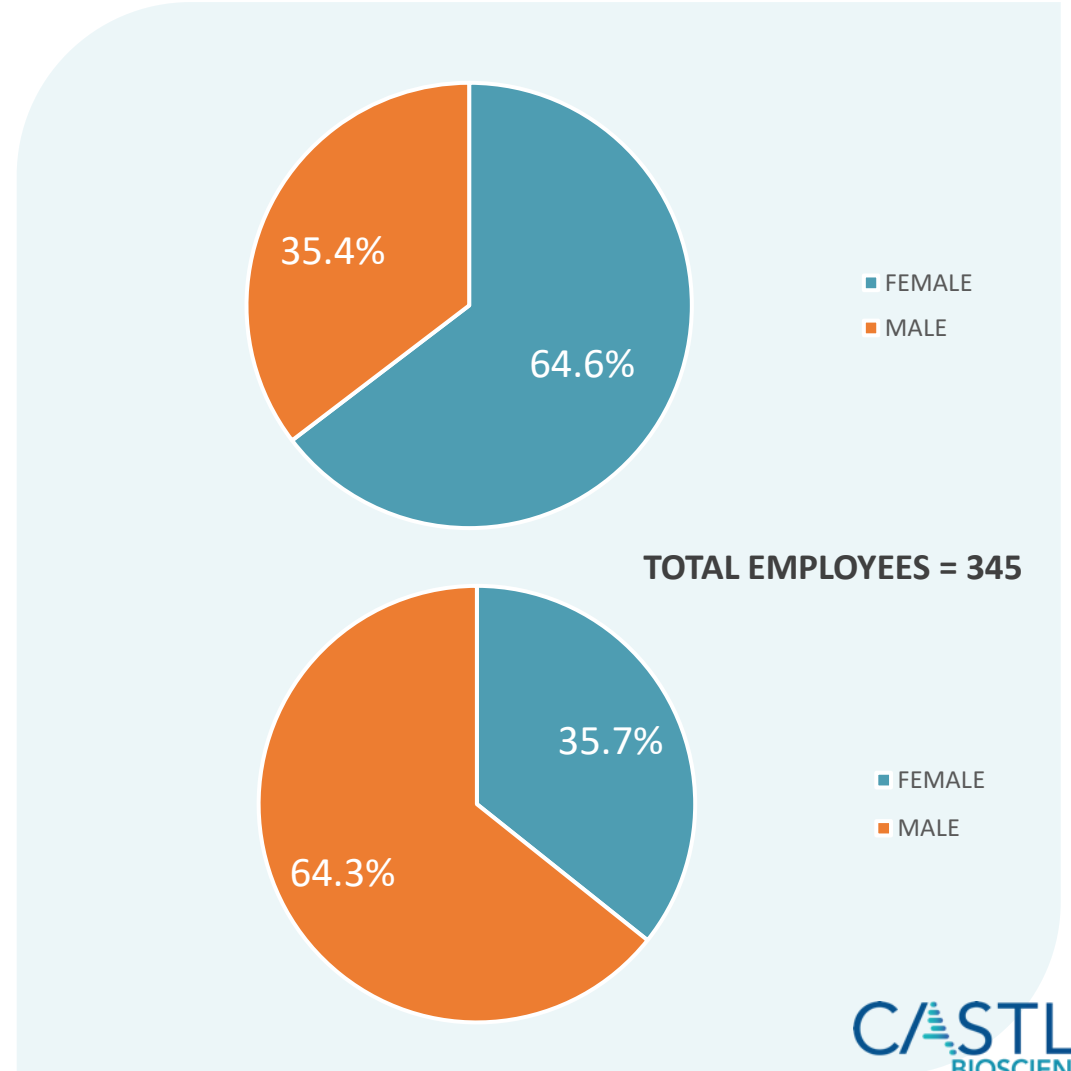


# Commitment to Diversity

## ETHNICITY/RACE



## GENDER



**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 repayments to Medicare of COVID-19 government relief advancements to healthcare providers.

We use Adjusted Revenue, Adjusted Gross Margin and Adjusted Operating Cash Flow internally because we believe these metrics provide useful supplemental information in assessing our revenue and cash flow performance reported in accordance with GAAP, respectively. We believe Adjusted Revenue and Adjusted Gross Margin are also useful to investors because they provide additional information on current-period performance by removing the effects of revenue adjustments related to tests delivered in previous periods and , with respect to Adjusted Gross Margin, acquisition-related intangible asset amortization, which we believe may facilitate revenue and gross margin comparisons to historical periods. We believe Adjusted Operating Cash Flow is also useful to investors as a supplement to GAAP measures in the assessment of our cash flow performance by removing the effects of COVID-19 government relief payments, which we believe are not indicative of our ongoing operations. However, these non-GAAP financial measures may be different from non-GAAP financial measures used by other companies, even when the same or similarly titled terms are used to identify such measures, limiting their usefulness for comparative purposes. These non-GAAP financial measures are not meant to be considered in isolation or used as substitutes for net revenues, gross margin or net cash (used in) provided by operating activities reported in accordance with GAAP and should be considered in conjunction with our financial information presented on a GAAP basis and language from our earnings press release. Accordingly, investors should not place undue reliance on non-GAAP financial measures. Reconciliations of these non-GAAP financial measures to the most directly comparable GAAP financial measures are presented in the slides that follow.

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

The table below presents the reconciliation of adjusted revenue and adjusted gross margin, which are non-GAAP financial measures. See "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 June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
<i>(in thousands)</i>				
<b>Adjusted revenue</b>				
Net revenues (GAAP)	\$ 34,838	\$ 22,758	\$ 61,690	\$ 45,571
Revenue associated with test reports delivered in prior periods	(578)	166	300	(5,092)
Adjusted revenue (Non-GAAP)	<u>\$ 34,260</u>	<u>\$ 22,924</u>	<u>\$ 61,990</u>	<u>\$ 40,479</u>
<b>Adjusted gross margin</b>				
Gross margin (GAAP) <sup>1</sup>	\$ 25,055	\$ 18,805	\$ 44,315	\$ 38,590
Amortization of acquired intangible assets	2,097	256	3,745	256
Revenue associated with test reports delivered in prior periods	(578)	166	300	(5,092)
Adjusted gross margin (Non-GAAP)	<u>\$ 26,574</u>	<u>\$ 19,227</u>	<u>\$ 48,360</u>	<u>\$ 33,754</u>
Gross margin percentage (GAAP) <sup>2</sup>	71.9 %	82.6 %	71.8 %	84.7 %
Adjusted gross margin percentage (Non-GAAP) <sup>3</sup>	77.6 %	83.9 %	78.0 %	83.4 %

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

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

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

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

The table below presents the reconciliation of adjusted operating cash flow, which is a non-GAAP financial measure. See "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 June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
<i>(in thousands)</i>				
<b>Adjusted operating cash flow</b>				
Net cash used in operating activities (GAAP)	\$ (9,001)	\$ (6,438)	\$ (30,431)	\$ (10,069)
Medicare advance payment <sup>1</sup>	—	2,173	—	2,173
HHS provider relief funds <sup>2</sup>	—	—	—	(1,882)
<b>Adjusted operating cash flow (Non-GAAP)</b>	<b>\$ (9,001)</b>	<b>\$ (4,265)</b>	<b>\$ (30,431)</b>	<b>\$ (9,778)</b>

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

# APPENDIX

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Castle Biosciences Is Improving Health through Innovative Tests That Guide Patient Care

 **Dermatology**

Decision Dx  
▶ Melanoma

Decision Dx  
▶ SCC

MyPath | DiffDx  
▶ Melanoma

 **Uveal Melanoma**

Decision Dx  
▶ UM

 **Gastroenterology**

TissueCypher  
▶ Barrett's Esophagus

 **Mental Health**

IDgenetiX

*Portfolio of innovative tests designed to guide patient care*

# Improving Health through Innovative Tests that Guide Patient Care

## Castle Team

**482** Total employees

**154** Sales & marketing team members

**111** Laboratory testing operations team members

**87** Research & development team members

## A Diagnostic Leader

**Strong financial position**, driven by investments in our growth pillars and commercial excellence

**Diversified portfolio** of tests that answer clinical questions and provide actionable information

**Data driven with a robust R&D and clinical research engine** that address areas of unmet clinical need

**Culture of teamwork and innovation**, built on a **patient-centric mindset**

## Robust Data Supporting our Tests

*Peer-reviewed publications*

**35+** Decision Dx  
▶ Melanoma

**10** Decision Dx  
▶ SCC

**12** MyPath | Diff Dx  
▶ Melanoma

**23** Decision Dx  
▶ UM

**9** TissueCypher  
▶ Barrett's Esophagus

# Leadership Team Overview

## MANAGEMENT TEAM

**Derek Maetzold**

*Founder, Director, President and CEO*



**Frank Stokes**

*Chief Financial Officer*



**Toby Juvenal**

*Chief Commercial Officer*



*Stuart Pharmaceuticals*

**Kristen Oelschlager, RN, CHC**

*Chief Operating Officer*



**Robert Cook, PhD**

*Senior Vice President, Research & Development*



Northwestern



**Matthew Goldberg, MD**

*Medical Director*



**Alice Izzo**

*Senior Vice President, Marketing*



## BOARD OF DIRECTORS

Dan Bradbury



Derek Maetzold



Mara Aspinnall



Brad Cole



Tiffany Olson



Miles D. Harrison



Kimberlee Caple



Ellen Goldberg

CHORD Consulting



## Award-Winning Company

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



2019 Technology Innovation in Melanoma Award Winner