

# › Empowering people, informing care decisions



May 2024

**C/STLE**  
BIOSCIENCES

# 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 positioning for continued growth and value creation; our estimated U.S. total addressable market for our commercially available tests; our ongoing studies generating data and their impact on driving adoption of our tests; study observations and interpretations of study data, including conclusions about the benefits and impact of our tests on treatment decisions and patient outcomes; our expected 2024 catalysts; and our ability to be net operating cash flow positive by the end of 2025; our future approach to capital allocation; our expected launch of our pipeline expansion by the end of 2025; and the timing and achievement of program milestones. 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; 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 and geopolitical events (such as the ongoing Israel-Hamas War and 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, 2023, 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.

# Disclaimers

## Financial Information; Non-GAAP Financial Measures

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 GAAP net revenues to exclude net positive and/or net negative revenue adjustments recorded in the current period associated with changes in estimated 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. 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 loss reported in accordance with GAAP; should be considered in conjunction with our financial information presented in accordance with GAAP; have no standardized meaning prescribed by GAAP; are unaudited; and are not prepared under any comprehensive set of accounting rules or principles. In addition, from time to time in the future, there may be other items that we may exclude for purposes of these non-GAAP financial measures, and we may in the future cease to exclude items that we have historically excluded for purposes of these non-GAAP financial measures. Likewise, we may determine to modify the nature of adjustments to arrive at these non-GAAP financial measures. Because of the non-standardized definitions of non-GAAP financial measures, the non-GAAP financial measure as used by us in this press release and the accompanying reconciliation tables have limits in their usefulness to investors and may be calculated differently from, and therefore may not be directly comparable to, similarly titled measures used by other companies. 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 tables at the end of this presentation.

### Industry and Market Data

This presentation includes certain information and statistics obtained from third-party sources. The Company has not independently verified the accuracy or completeness of any such third-party information.

## OUR MISSION

**Improving health**  
through **innovative tests**  
that guide patient care

## OUR VISION

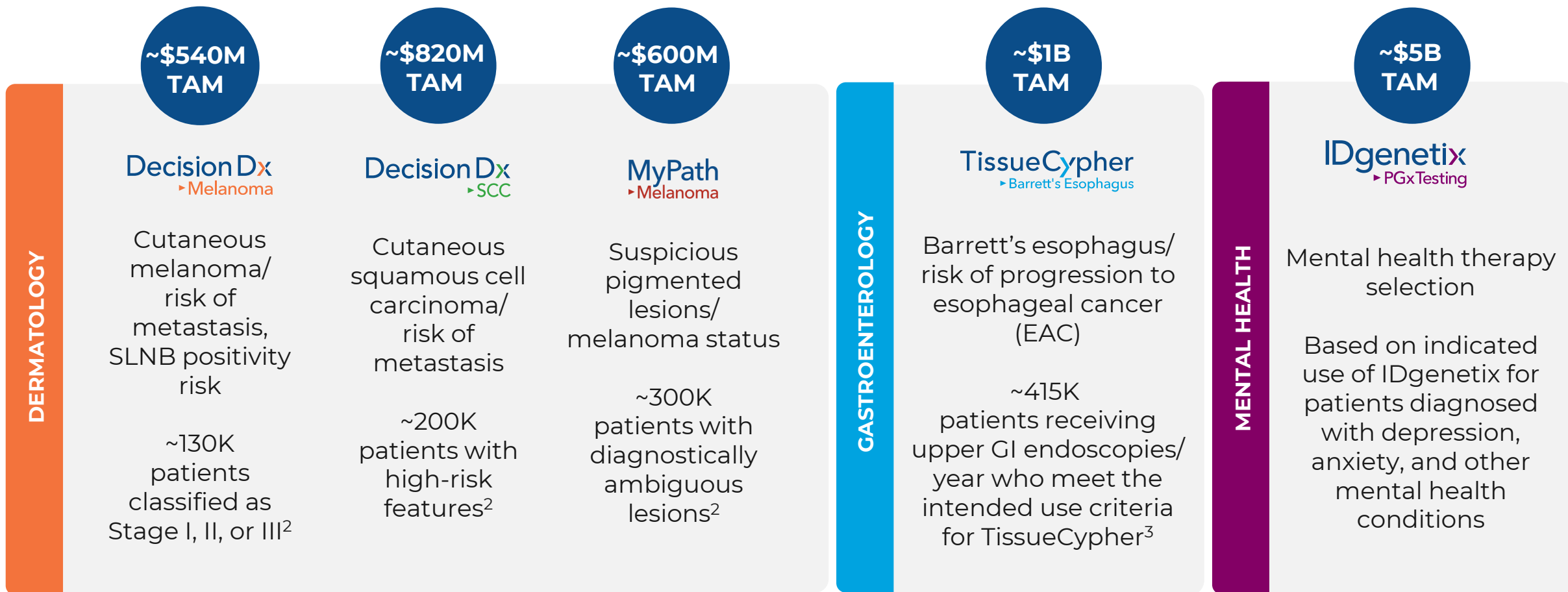
**Transforming** disease  
management by keeping  
people first: patients, clinicians,  
employees, and investors



# Proven strategy designed to drive value creation for our stakeholders

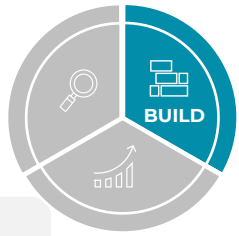


# Estimated ~\$8B U.S. total addressable market<sup>1</sup> for commercially available tests



1. U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors. 2. Annual U.S. incidence for Stage I, II or III melanoma estimated at 130,000; annual U.S. incidence for squamous cell carcinoma estimated at 1,000,000 with addressable market limited to carcinomas with one or more high risk features; annual U.S. incidence for suspicious pigmented lesion biopsies estimated at 2,000,000 with addressable market limited to the 15% with an indeterminate biopsy. 3. 415,000 upper GI endoscopies/year with confirmed dx of BE (ND, IND, LGD, excluding HGD).

# Building evidence showing the value of our tests



## DecisionDx

► Melanoma

Studies<sup>1</sup> show clinical use of our test is associated with improved melanoma specific outcomes, which means the test guides appropriate decisions and patients live longer. The test provides significantly better risk stratification than AJCC8 staging in patients with stage I cutaneous melanoma

## DecisionDx

► SCC

Studies<sup>2</sup> demonstrating that DecisionDx-SCC can improve risk stratification when used in conjunction with staging, to help predict responsiveness to adjuvant radiation therapy (ART) and when used in conjunction with clinicopathologic factors in considering use of ART, can potentially lead to net annual Medicare healthcare savings of up to approximately \$972 million

## TissueCypher

► Barrett's Esophagus

Ablation has been shown to stop progression to EAC but use is generally limited to clinicopathologically identified higher-risk patients.<sup>3</sup> New pooled analysis<sup>4</sup> and SRMA studies<sup>5</sup> show that our test is a stronger identifier of higher risk disease compared to all clinicopathologic factors

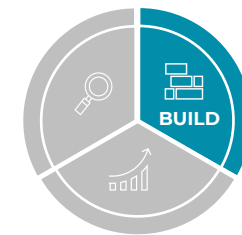
## IDgenetix

► PGx Testing

Randomized controlled study shows integrating drug-gene, drug-drug and lifestyle factors provides 75%<sup>6</sup> more guided information compared to traditional gene-drug interactions alone

1. Podlipnik S, Martin BJ, Morgan-Linnell SK et al., Dhillon et al. *Archives of Derm Research* 2023 and Bailey et al. *JCO PO*, 2023; 2. Wysong A, Newman JG, Covington KR, et al., Gopal R, Marquardt M, Singh G, et al., Somani SK, Ibrahim SF, Tassavor M, et al., and Newman et al. *Head & Neck* 2021; Ruiz et al. *JAAD* 2022; Moody et al. accepted and Castle Biosciences data on file; 3. Cotton CC, et al. *Gastroenterology*. 2017; 4. Davison et al. *Clin Transl Gastroenterol* 2023; 5. Castle Biosciences data on file (Systematic Review and Meta-Analysis of TissueCypher's predictive performance in five completed clinical validation studies); 6. Cao et al., Psych Congress Annual Meeting 2023  
EAC=esophageal adenocarcinoma

# DecisionDx-Melanoma provides precise, personalized risk prediction for two critical clinical questions



Clinical use of DecisionDx-Melanoma is associated with improved patient survival



Individual risk of SLNB positivity

Individual risk of recurrence

31-GEP Class Score

i31-SLNB

Ulceration  
Breslow thickness  
Age  
Mitotic rate

i31-ROR

Ulceration  
Age  
Breslow thickness  
Mitotic rate  
SLN status  
Tumor location

Collaborative study with the National Cancer Institute's SEER Program Registries is the largest real-world study of GEP testing in melanoma (n=4,687):

- SEER cohort of **unselected, prospectively** tested patients shows improved survival for patients tested with DecisionDx-Melanoma compared to untested patients with **29% lower 3-year melanoma-specific and 17% lower 3-year overall mortality**, and
- DecisionDx-Melanoma provided **significant, independent risk stratification** of patients with cutaneous melanoma

**SLN- patients with a high-risk DecisionDx-Melanoma result had routine imaging surveillance added to their treatment plan. These patients:**

- Had their recurrence detected **~10 months earlier**, with **62% lower tumor burden**
- Were more likely to **start immunotherapy** when offered (76.3% vs 67.9%)
- Saw **improved overall survival** outcomes at 45 months (86.8% vs 75%)

**“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.”**

# DecisionDx-Melanoma significantly improves risk stratification in stage I melanoma compared to AJCC staging



DecisionDx-Melanoma compared to American Joint Committee on Cancer Staging Manual 8th Edition (AJCC8) staging for stage I cutaneous melanoma (CM) patients (n=6,883) in 2 cohorts analyzed recurrence-free survival and melanoma-specific survival. Study results demonstrated:

- DecisionDx-Melanoma **significantly improved patient risk stratification**, independent of AJCC8 staging in patients
- DecisionDx-Melanoma **provided greater separation** between high-risk (Class 2B) and low risk (Class 1A) groups than seen between AJCC8 stage IA and IB

## COHORT 1 – Combined

Combined cohort of stage I CM patients enrolled in previous retrospective and prospective studies from multiple centers (n=1,261)

## COHORT 2 – NCI-SEER

Large, unselected real-world cohort of stage I CM patients from the SEER registry (n=5,651)

# Advancing penetration of our tests with clinicians and payers



## Expert Consensus & Guidelines<sup>1</sup>

- DecisionDx-Melanoma: 2023 National Society for Cutaneous Medicine recommends use of GEP testing (DecisionDx-Melanoma) in the clinical assessment and management of CM
- DecisionDx-SCC: 2023 Expert consensus panel report recommends considering the test for SCC cases with at least one high-risk feature to maximize prognostic accuracy and utility
- TissueCypher: 2022 AGA Clinical Practice Update states that the test may be beneficial for risk-stratification of patients with non-dysplastic BE

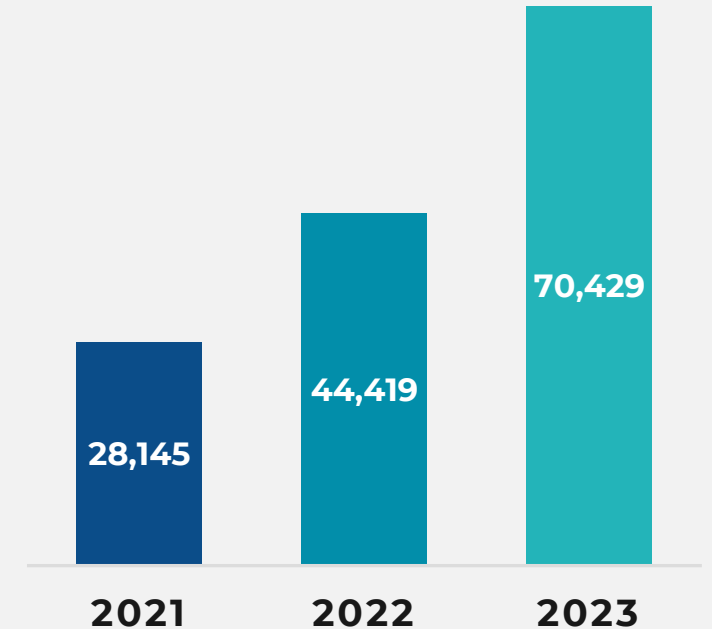
## Reimbursement Strategy

- Increased total number of ADLTs to 5 by obtaining approval from CMS for DecisionDx-SCC
- Increased the CLFS payment rate for 2024 on 4 of our tests through the CLFS and PAMA rate-setting process, while maintaining value-based rates for our remaining tests
- Secured positive medical policies across all four therapeutic areas in 2024 (i.e., dermatology, gastroenterology, mental health and UM)

## Castle Commercial Playbook

- Optimizing commercial team
- Continuing provider education
- Evolving our white glove go-to-market strategy
- Comprehensive digital strategy
- Robust patient advocacy strategy across all therapeutic areas

## Total Test Report Volume



# Expected 2024 Catalysts

1

Full year impact of studies showing patients who receive DecisionDx-Melanoma as part of their clinical management have improved survival compared to those who are not tested

2

Commercial expansion in alignment with Castle principles and servant leadership culture

3

DecisionDx-SCC patient outcomes benefits and cost savings in use of adjuvant radiation therapy highlighted in three peer-reviewed publications since the start of 2024

4

Additional development updates on our inflammatory disease pipeline program in the second half of 2024



# > Financials



# Well positioned for continued value creation



Drive robust test volume growth



Maintain strong Adjusted Gross Margin



Goal to achieve operating cash flow positivity by the end of 2025



Maintain strong balance sheet

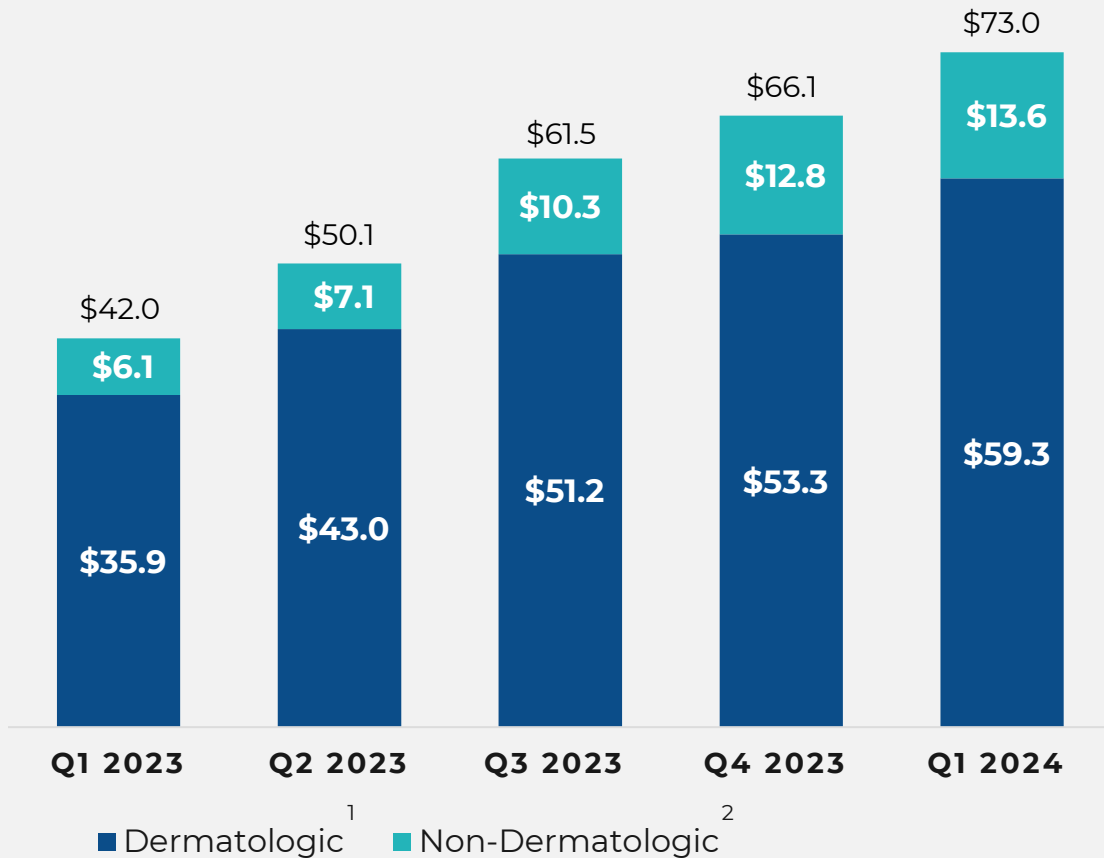


Follow disciplined capital allocation

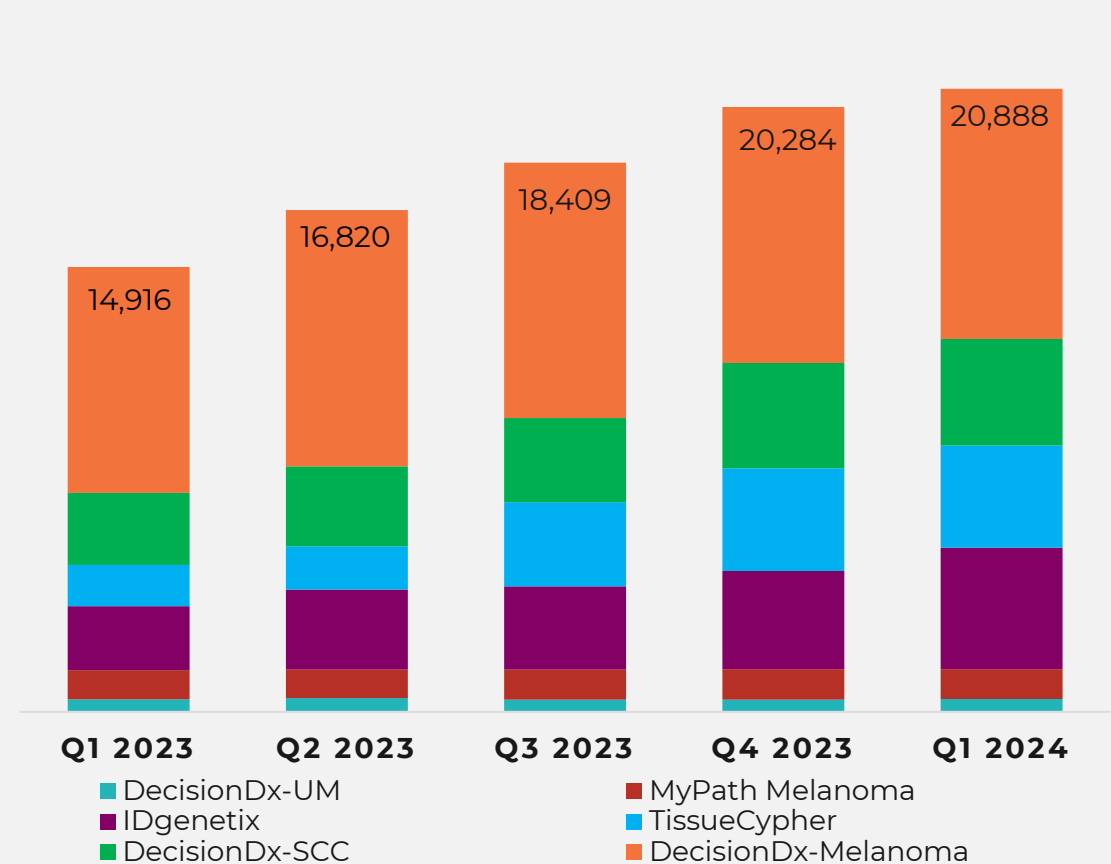


# Drive robust test report volume and revenue growth

### TOTAL REVENUE BY QUARTER (\$M)



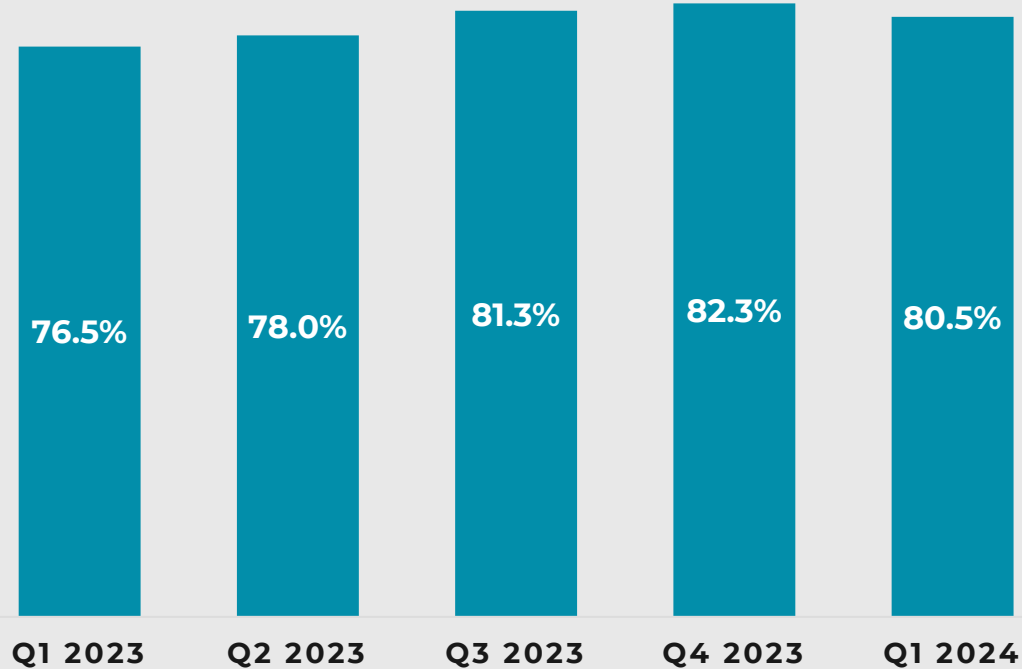
### TOTAL TEST VOLUME BY QUARTER



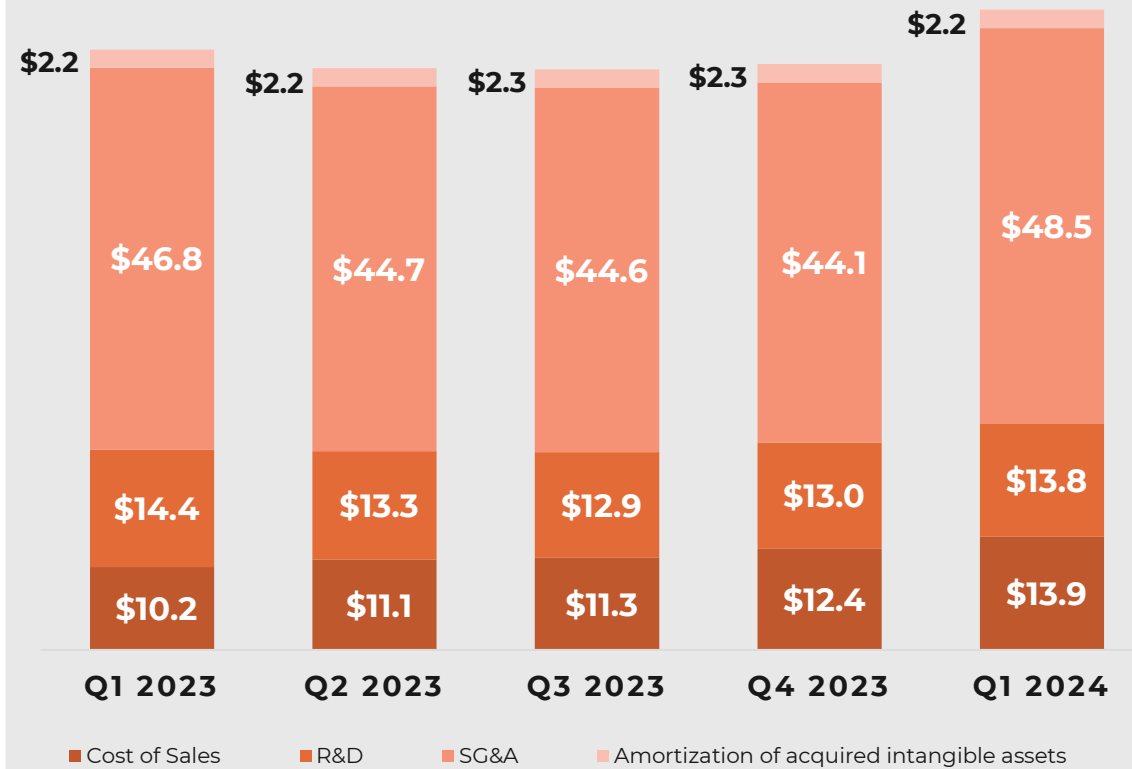


# Maintain strong Adjusted Gross Margin

### ADJUSTED GROSS MARGIN BY QUARTER<sup>1,2</sup>



### OPERATING EXPENSES BY QUARTER (\$M)<sup>3</sup>

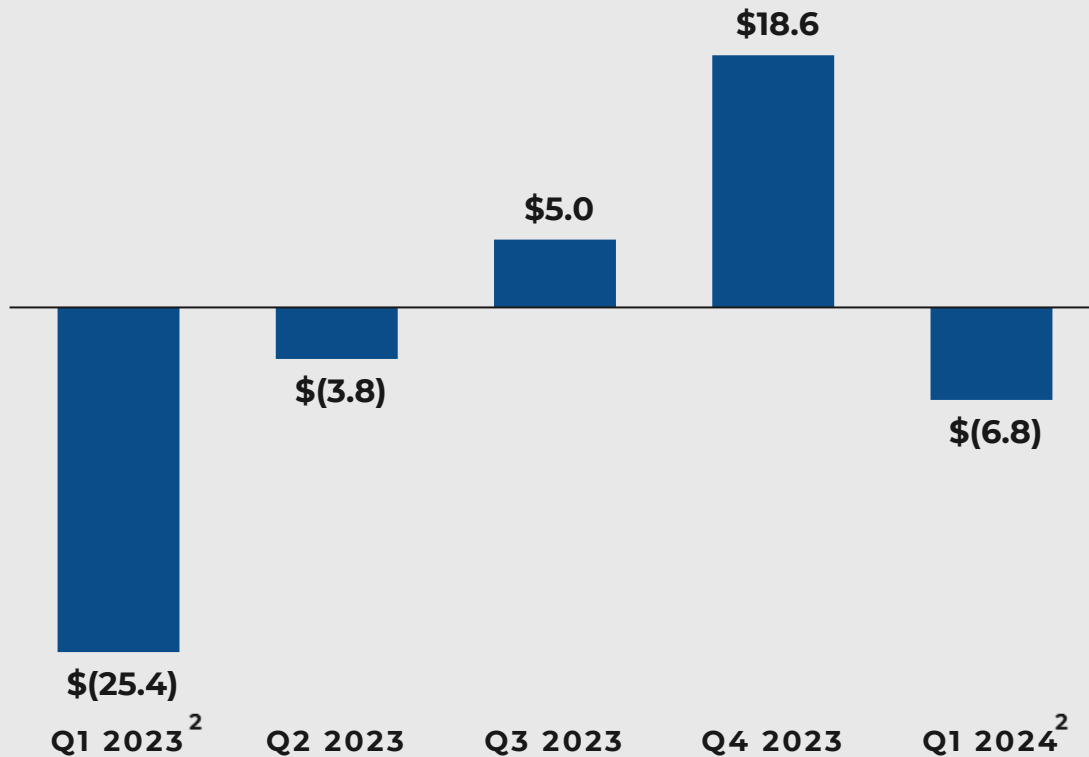




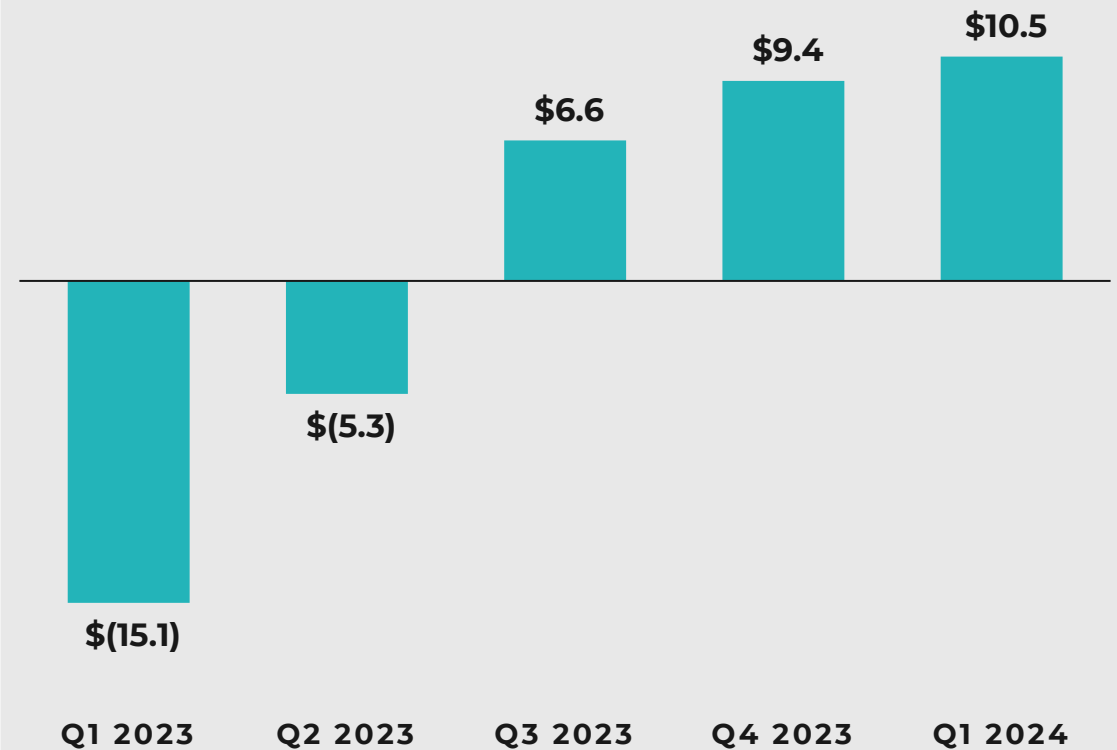
# Improving operating cash flow and Adjusted EBITDA

Cash position of ~\$239M<sup>1</sup> supports growth initiatives

OPERATING CASH FLOW BY QUARTER (\$M)



ADJUSTED EBITDA BY QUARTER (\$M)<sup>3,4</sup>



1. As of March 31, 2024; includes Cash, Cash Equivalents & Marketable Investment Securities

2. Net cash used in operating activities for Q1 2024 and Q1 2023 includes payout of annual bonuses as well as certain healthcare benefit contributions

3. Adjusted EBITDA is a non-GAAP measure. See non-GAAP reconciliations at the end of this presentation for a reconciliation of Adjusted EBITDA to its most closely comparable GAAP measure

4. Adjusted EBITDA excludes from net loss interest income, interest expense, income tax expense (benefit), depreciation and amortization expense, stock-based compensation expense and change in fair value of contingent consideration



# A disciplined approach to capital allocation

**Commercial optimization**

**Focused R&D efforts to build evidentiary support and develop tests**

**As a lesser priority, strategic opportunities in our current therapeutic areas**

# Proven strategy designed to drive value creation for our stakeholders



## FOCUS

on best/first-in-class tests with high, unmet clinical need and significant market opportunity

## BUILD

robust clinical evidence

## PENETRATE

target markets to further test adoption by clinicians and payers

# > Appendix

# DecisionDx-Melanoma

Provides comprehensive, personalized, genomic tumor information to guide management for patients with cutaneous melanoma

## Clinical Validity, Utility and Demonstrated Patient Outcomes

Demonstrated clinical validity, utility and impact, backed by 50 peer-reviewed publications (as of February 2024), including two publications (Bailey et al. 2023 and Dhillon et al. 2023) demonstrating an association with testing and improved patient outcomes

## Expert Consensus

2023 National Society for Cutaneous Medicine recommends use of GEP testing (DecisionDx-Melanoma) in the clinical assessment and management of cutaneous melanoma



~26%

market penetration<sup>1</sup>

50%

Demonstrated change in management for 1 of 2 patients tested<sup>2</sup>

~164,300

patients with a clinical DecisionDx-Melanoma order from 13,600+ clinicians

# DecisionDx-SCC

Identifies the risk of metastasis in patients with squamous cell carcinoma (SCC) and one or more risk factors

## Clinical Validity and Utility

Demonstrated validity, utility and impact, backed by 16 peer-reviewed publications, including data showing that DecisionDx-SCC can significantly impact patient management plans in a risk-appropriate manner within established guidelines

## Real-World Use Framework

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



**~200,000**

patients diagnosed annually with SCC and classified as high risk in the U.S.

**~55%**

of clinicians ordering DecisionDx-SCC also ordered DecisionDx-Melanoma (Q124)

**Up to ~\$972M**

net annual Medicare savings that could be realized by using DecisionDx-SCC to guide adjuvant radiation therapy decisions<sup>1</sup>

# MyPath Melanoma

Aids in the diagnosis and management for patients with ambiguous melanocytic lesions

## Clinical Validity and Utility

Demonstrated validity, utility and impact, backed by 17 peer-reviewed publications demonstrating the performance and utility of the test in providing objective information to aid in diagnosis in ambiguous melanocytic lesions

## Guideline Support

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



~300,000

patients each year present with a diagnostically ambiguous lesion

>45,000

lesions tested clinically (as of 12/31/2023)

17

peer-reviewed publications

# TissueCypher

A leading risk-stratification test designed to predict risk of progression to esophageal cancer in patients with Barrett's esophagus

## Clinical Validity and Utility

Demonstrated validity, utility and impact, backed by 14 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

## 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

~415,000

patients receiving upper GI endoscopies per year who meet intended use criteria for TissueCypher

1 in 40

patients progress to esophageal cancer within 5 years (among BE patients)

14

peer-reviewed publications

# IDgenetix

Advanced pharmacogenomic (PGx) test designed to guide medication selection and management for patients with neuropsychiatric conditions, such as depression and anxiety

## Advanced PGx

- Demonstrated clinical validity, utility and impact, backed by 19 peer-reviewed publications
- Eliminate trial and error prescribing

## Easy to Use

- 10 mental health and pain conditions in one report
- Collection of DNA sample via simple cheek swab
- 3-5 days to receive test report on average
- Specialized sales and medical science liaison support

IDgenetix  
▶ PGx Testing



**3 in 1 test**

- drug-gene interactions
- drug-drug interactions
- lifestyle factors

**2X**

improved chance of medication response vs. control<sup>1</sup>

**>2.5X**

improved chance of remission of depression symptoms vs. control<sup>1</sup>

# DecisionDx-UM

The standard of care for evaluating metastatic risk in uveal melanoma

## Clinical Validity and Utility

Demonstrated validity, utility and impact, backed by 25 peer-reviewed publications, which included more than 3,600 patients, representing the largest body of evidence for a molecular prognostic test in this field

## Standard of Care

- Utilized in approximately 80% of newly diagnosed patients
- Favorable reimbursement profile – covered by Medicare and more than 100 private insurers
- Included in NCCN Guidelines and considered standard of care

**~8 in 10**

patients diagnosed with UM in the U.S. receive the test as part of their diagnostic workup

**~2,000**

patients diagnosed in the U.S. annually

**25**

peer-reviewed publications

# Inflammatory Skin Disease

Pipeline program to develop a genomic test aimed at guiding systemic therapy selection for patients with moderate-to-severe atopic dermatitis (AD), psoriasis (PSO) and related conditions

- Identified distinct gene expression profiles of super-responders to both AD and PSO therapies, in addition to identifying distinct gene expression profiles for AD, PSO, and mycosis fungoides (MF) lesions
- Test results could empower clinicians to tailor therapy choices for patients by considering their molecular profiles, potentially sparing patients from undergoing numerous ineffective and costly medication trials before discovering an effective treatment to manage their symptoms

## Program Milestones

- **Q423:** early discovery data presented
- **2H2024:** development data expected
- **By end of 2025:** target launch

44

Committed sites<sup>1</sup>

&gt;1,100

Patients enrolled<sup>1,2</sup>

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

(In thousands)	Three months ended				
	Mar. 31, 2024	Dec. 31, 2023	Sep. 30, 2023	Jun. 30, 2023	Mar. 31, 2023
<b>Adjusted Revenues</b>					
Net revenues (GAAP)	\$72,974	\$66,120	\$61,493	\$50,138	\$42,037
Revenue associated with test reports delivered in prior periods	(1,656)	4,086	(883)	88	1,336
<b>Adjusted Revenues (Non-GAAP)</b>	<b>\$71,318</b>	<b>\$70,206</b>	<b>\$60,610</b>	<b>\$50,226</b>	<b>\$43,373</b>
<b>Adjusted Gross Margin</b>					
Gross margin (GAAP) <sup>1</sup>	\$56,833	\$51,426	\$47,902	\$36,832	\$29,633
Amortization of acquired intangible assets	2,247	2,271	2,272	2,248	2,222
Revenue associated with test reports delivered in prior periods	(1,656)	4,086	(883)	88	1,336
<b>Adjusted Gross Margin (Non-GAAP)</b>	<b>\$57,424</b>	<b>\$57,783</b>	<b>\$49,291</b>	<b>\$39,168</b>	<b>\$33,191</b>
Gross margin percentage (GAAP) <sup>2</sup>	77.9%	77.8%	77.9%	73.5%	70.5%
<b>Adjusted Gross Margin percentage (Non-GAAP)<sup>3</sup></b>	<b>80.5%</b>	<b>82.3%</b>	<b>81.3%</b>	<b>78.0%</b>	<b>76.5%</b>

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).

# Reconciliation of Non-GAAP Financial Measures (Unaudited)

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

<i>(In thousands)</i>	Three months ended				
	Mar. 31, 2024	Dec. 31, 2023	Sep. 30, 2023	Jun. 30, 2023	Mar. 31, 2023
<b>Adjusted EBITDA</b>					
Net loss	\$(2,534)	\$(2,580)	\$(6,905)	\$(18,777)	\$(29,204)
Interest income	(2,996)	(3,119)	(2,769)	(2,399)	(2,336)
Interest expense	14	2	2	3	4
Income tax expense	45	39	32	16	14
Depreciation and amortization expense	3,340	3,224	3,174	3,040	2,892
Stock-based compensation expense	12,675	11,802	13,043	12,849	13,525
<b>Adjusted EBITDA (Non-GAAP)</b>	<b>\$10,544</b>	<b>\$9,368</b>	<b>\$6,577</b>	<b>\$(5,268)</b>	<b>\$(15,105)</b>

➤ Thank You

