

# › Empowering people, informing care decisions



## First Quarter 2025

May 5, 2025

**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, including with regard to our acquisition of Previs; 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 ability to advance penetration of our tests with clinicians and payers; our ability to carry out our commercial strategies; 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 products and subsequent coverage decisions; Novitas’ local coverage determination signifying non-coverage by Medicare of our DecisionDx-SCC test; our estimated total addressable markets for our products and product candidates; the expenses, capital requirements and potential needs for additional financing, the anticipated cost, timing and success of our product candidates; our plans to research, develop and commercialize new tests; 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, tariffs and disruptions to trade, 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; the possibility that 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; our planned installation of additional equipment and supporting technology infrastructures and implementation of certain process efficiencies may not enable us to increase the future scalability of our TissueCypher Test; the possibility that actual application of our tests may not provide the anticipated benefits to patients; the possibility that our newer gastroenterology and mental health franchises may not contribute to the achievement of our long-term financial targets as anticipated; and the risks set forth under the heading “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2024, and our Quarterly Report on Form 10-Q for the three months ended March 31, 2025, each filed or to be filed with the SEC, 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 income (loss): interest income, interest expense, income tax expense (benefit), depreciation and amortization expense, stock-based compensation expense and change in fair value of trading securities.

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 income (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.

# Registered Trademarks

DecisionDx-Melanoma, DecisionDx-CMSeq, i31-SLNB, i31-ROR, DecisionDx-SCC, MyPath Melanoma, DiffDx-Melanoma, TissueCypher, IDgenetix, DecisionDx-UM, DecisionDx-PRAME and DecisionDx-UMSeq are trademarks of Castle Biosciences, Inc.

# Proven strategy designed to drive value creation for our stakeholders





# Key Q1 2025 and recent results



1

The Company announced its achievement of surpassing a significant milestone of 200,000 DecisionDx-Melanoma test orders

2

Q1 2025 total test reports for our core revenue drivers (DecisionDx®-Melanoma, DecisionDx®-SCC, TissueCypher®) increased 33% over Q1 2024; Q1 2025 revenue increased 21% over Q1 2024 to \$88 million

3

Gross Margin for Q125 was 49%, and Adjusted Gross Margin was 81%, compared to 78% and 81% respectively for the same periods in 2024

4

Net cash used in operations in Q125 was \$6.0 million, compared to \$6.8 million net cash used in operations in Q124

5

As of March 31, 2025, cash, cash equivalents and marketable investment securities totaled \$275.2 million

6

Net loss for Q125 was \$25.8 million and Adjusted EBITDA for Q125 was \$13.0 million

7

Received a 2025 Top Workplace USA award for an exceptional workplace culture, our fourth year in a row to receive this national distinction

# Castle to acquire Previs



*Potential to combine the power of methylation with spatialomics for greater impact on patient care*

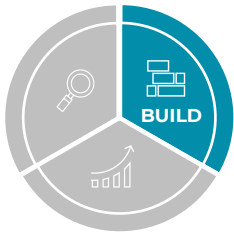
## About Previs

- Gastrointestinal (GI) health company with a commercial stage methylation-based Barrett's esophagus biomarker technology (Esopredict®) discovered at Johns Hopkins University in Dr. Steven Meltzer's lab
- >20 years of research and \$20M in NIH funding led to development of technology
- Pipeline of diagnostics for upper GI diseases and cancers

## Transaction Background

- Castle signed definitive agreement to acquire Previs
- Transaction expected to close in the coming weeks
- Financial details of the transaction not disclosed
- Transaction in alignment with our growth and capital allocation strategies

# Data from the DecisionDx-Melanoma prospective, multicenter CONNECTION study was successful at predicting which patients with T1 tumors have a low risk of SLN positivity



DecisionDx-Melanoma correctly identified a population of patients with low risk of SLN positivity who could have avoided a sentinel lymph node biopsy

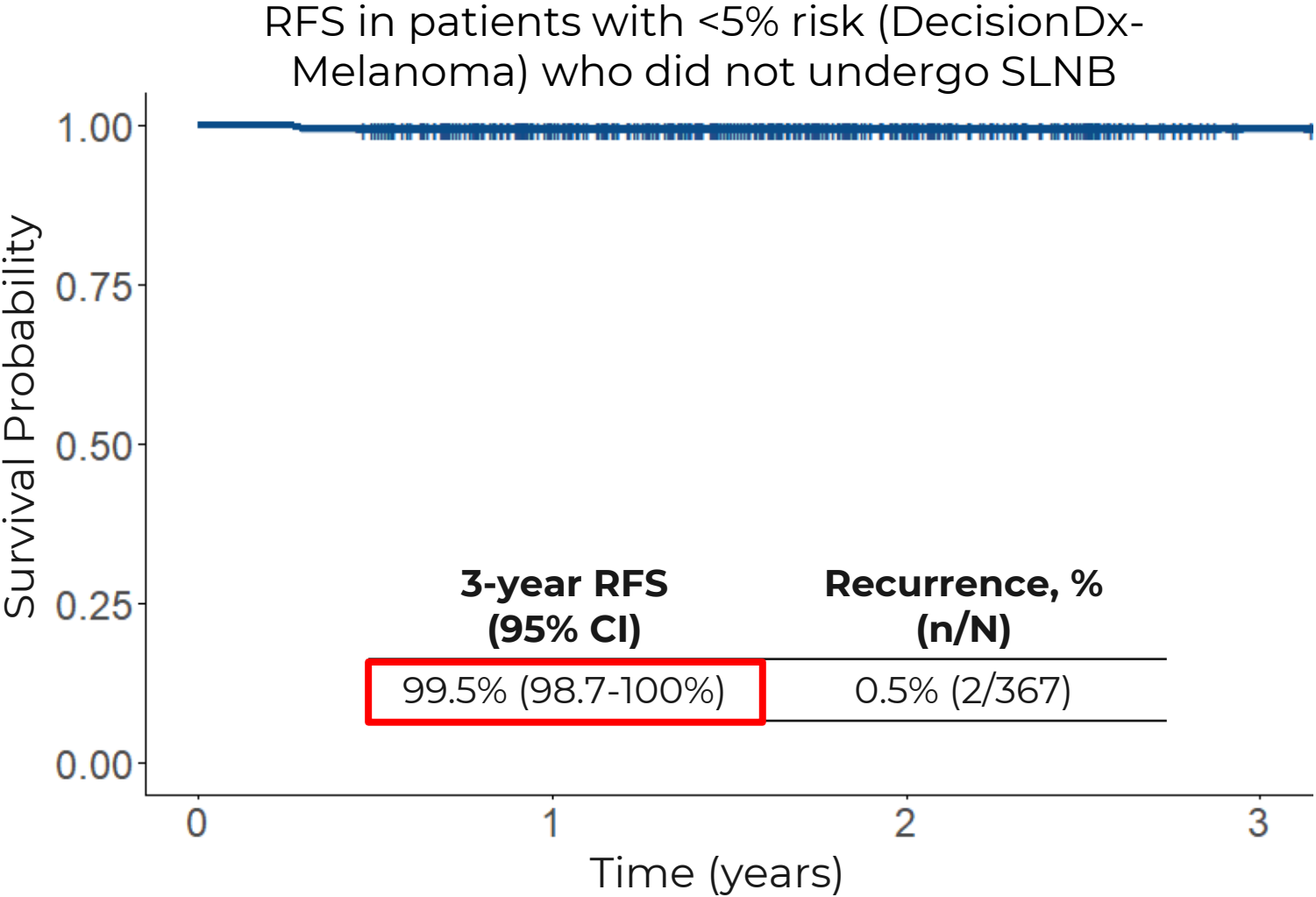
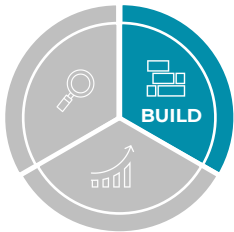
## SLN positivity rates among those with T1 tumors

	<b>DecisionDx-Melanoma Predicted &lt;5% Risk Group</b>	<b>DecisionDx-Melanoma Predicted ≥5% Risk Group</b>
T1	1.6%	5.7%

If DecisionDx-Melanoma was used in these patients to direct SLNB decisions, there could have been a 64% reduction in SLNB surgical procedures

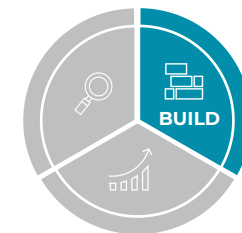


# Patients with low-risk DecisionDx-Melanoma test results who did not undergo SLNB have high recurrence-free survival (RFS) (three-year recurrence free survival rate of 99.5%)



— <5% risk of SLN positivity by i31-GEP who did not undergo SLNB

# Evidence from prospective studies supporting DecisionDx-Melanoma demonstrates:



1

Physicians are using DecisionDx-Melanoma to inform clinical decisions about sentinel lymph node biopsy (SLNB) and **performing fewer SLNBs**

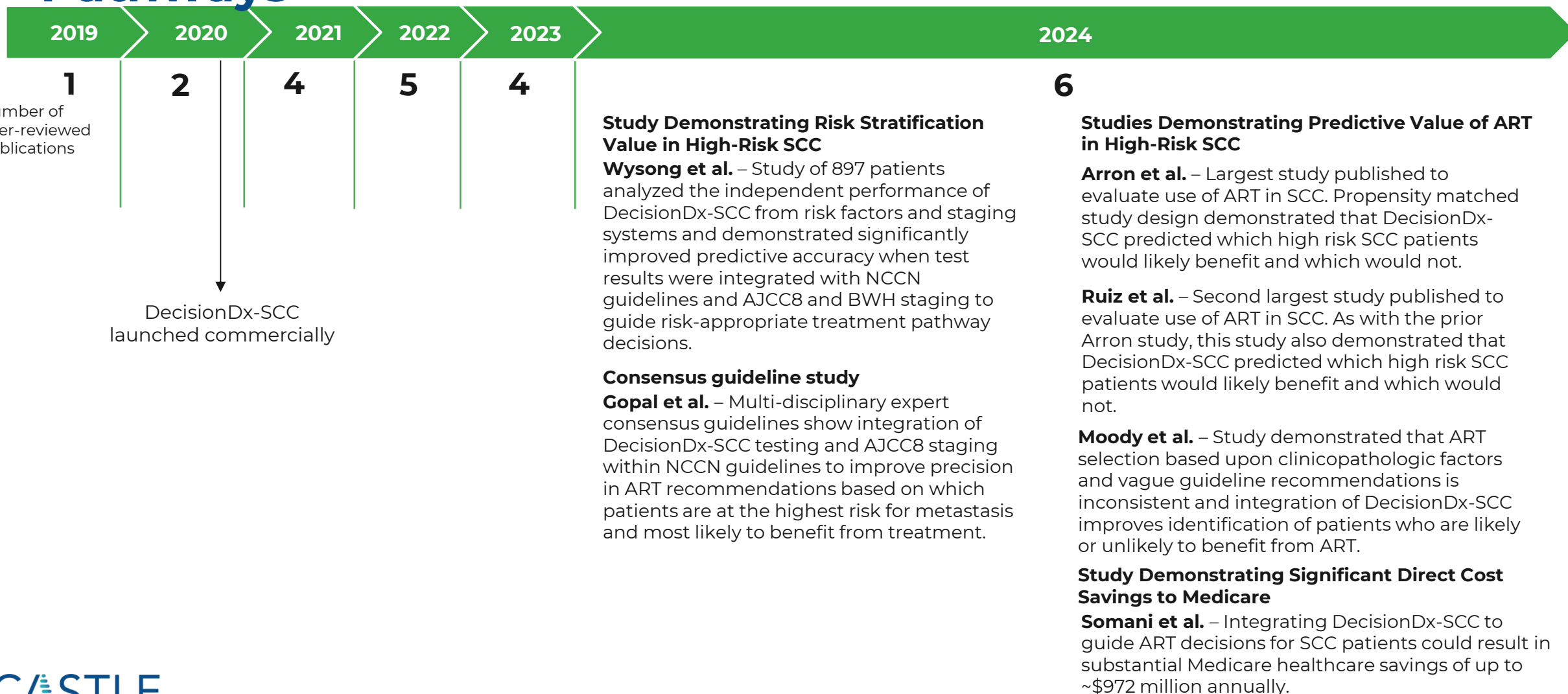
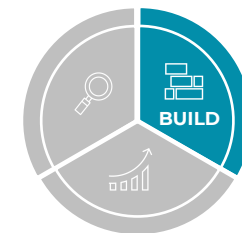
2

DecisionDx-Melanoma low-risk test results are **associated with very low SLNB positive outcomes**

3

DecisionDx-Melanoma low-risk, Class 1A patients who **forego an SLNB have high recurrence-free survival**

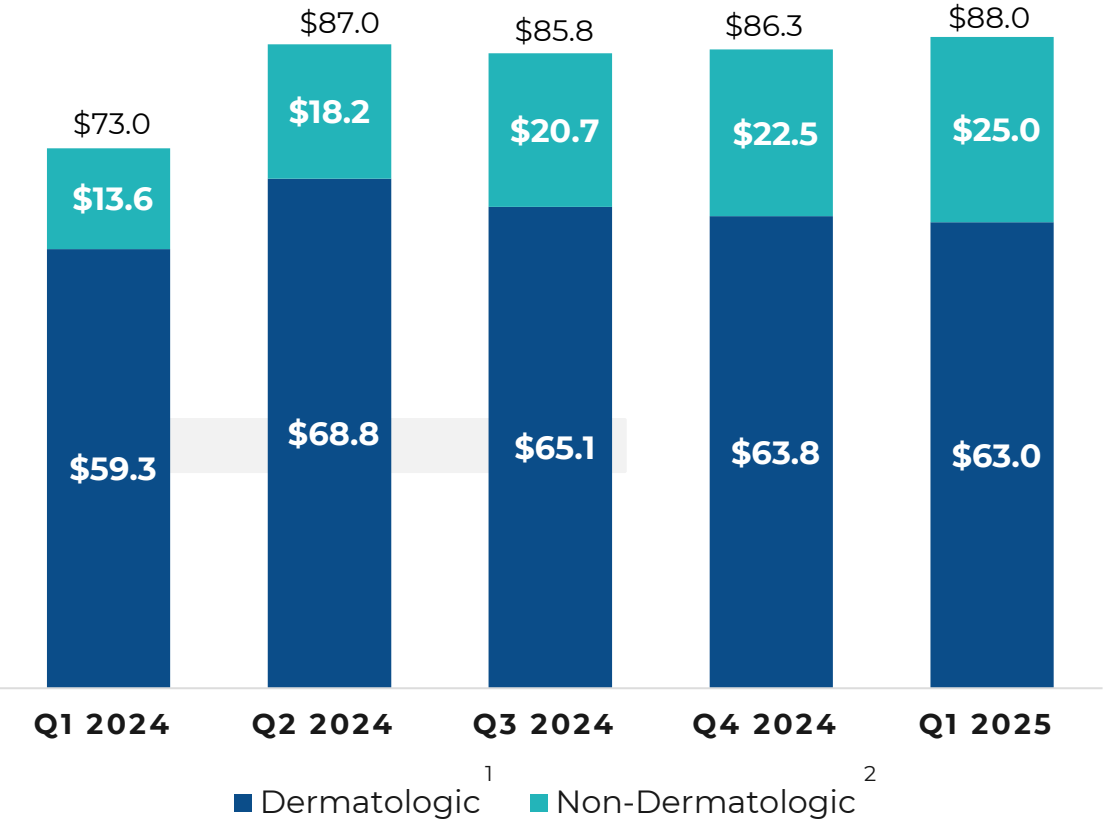
# DecisionDx-SCC Has Consistently Demonstrated High Value for Patients in Guiding SCC Treatment Pathways



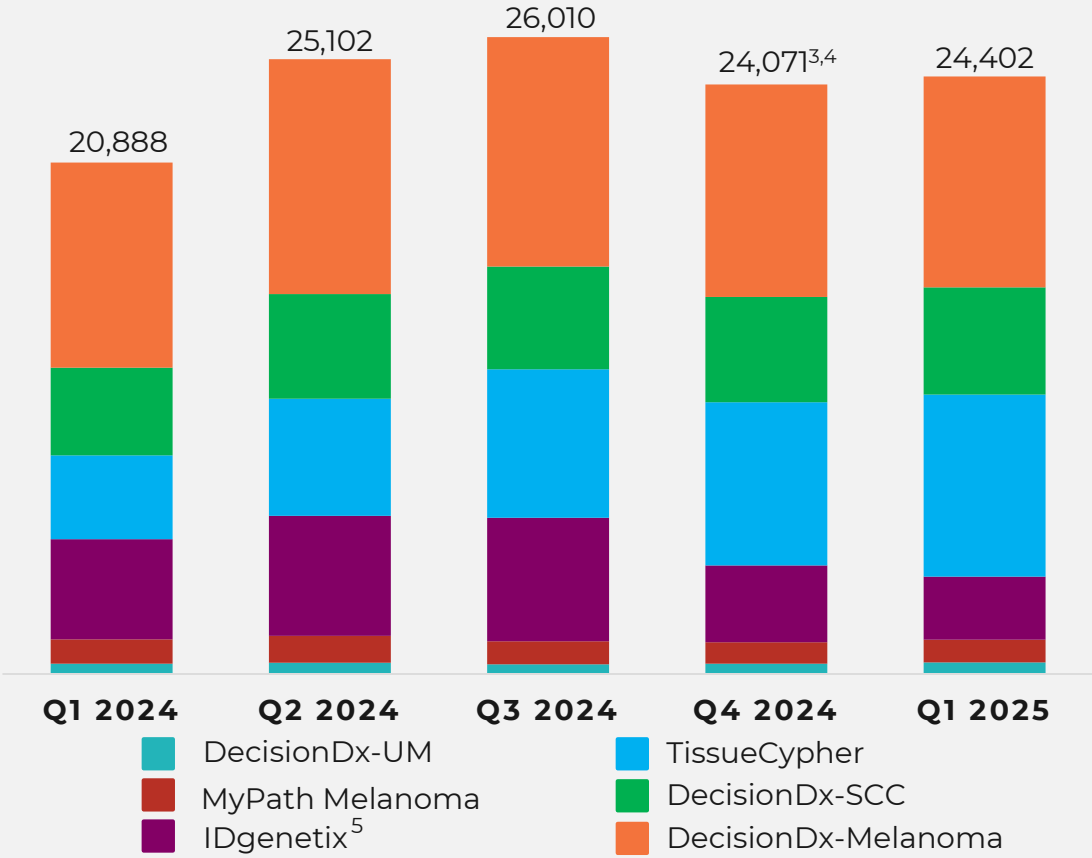


# Drive robust test report volume and revenue growth

NET REVENUE BY QUARTER (\$M)



TOTAL TEST VOLUME BY QUARTER

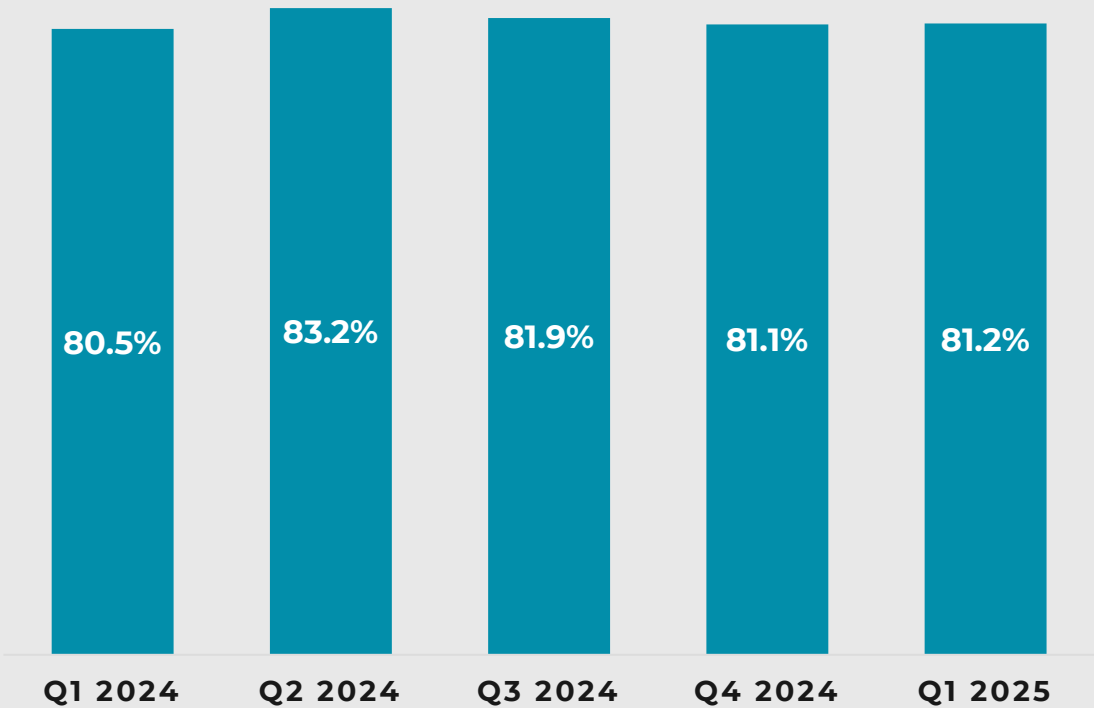


1. Consists of DecisionDx-Melanoma, DecisionDx-SCC and our Diagnostic Gene Expression Profile offering (MyPath Melanoma and DiffDx-Melanoma)  
2. Consists of TissueCypher Barrett's Esophagus Test, DecisionDx-UM and IDgenetix  
3. Q4 2024 DecisionDx-Melanoma volume reflects typical seasonality, with the fourth quarter historically having the fewest workdays compared to the other three quarters, and specifically Q4 2024 had two less working days than Q3 2024; further, the overlap of Christmas and Hanukkah led to additional dermatology practice closures  
4. In late 2024, we revised our commercial strategy for our IDgenetix test, reallocating resources to inside sales and non-personal promotions  
5. Effective May 2025, IDgenetix will be discontinued

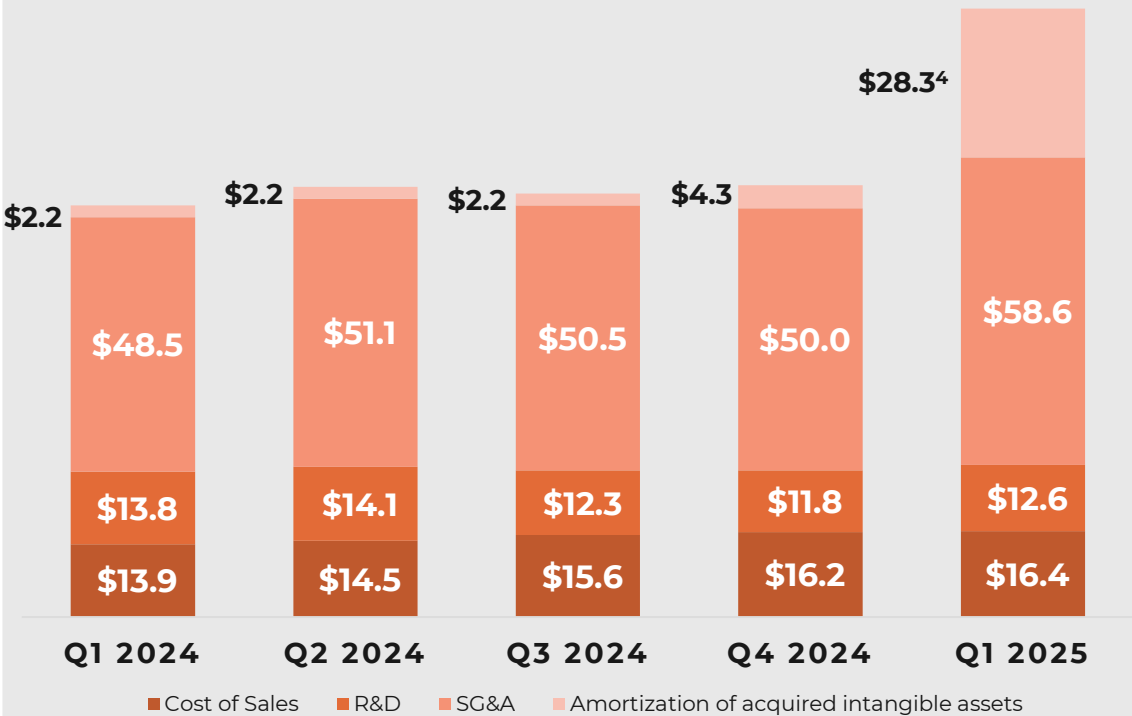


# Maintain strong Adjusted Gross Margin

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



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



1. Adjusted Gross Margin is a non-GAAP measure. See Non-GAAP reconciliations at the end of this presentation for a reconciliation of Adjusted Gross Margin to its most closely comparable GAAP measure.  
2. Calculated as Adjusted Gross Margin (Non-GAAP) divided by Adjusted Revenues (Non-GAAP)  
3. Total operating expenses, including cost of sales  
4. During the first quarter of 2025, we made the decision to discontinue our IDgenetix test offering, effective May 2025. As a result of this decision, we further revised the estimated useful life of the asset and determined that the intangible asset should be fully amortized as of March 31, 2025. This change resulted in an acceleration of amortization expense of approximately \$20.1 million during the three months ended March 31, 2025.

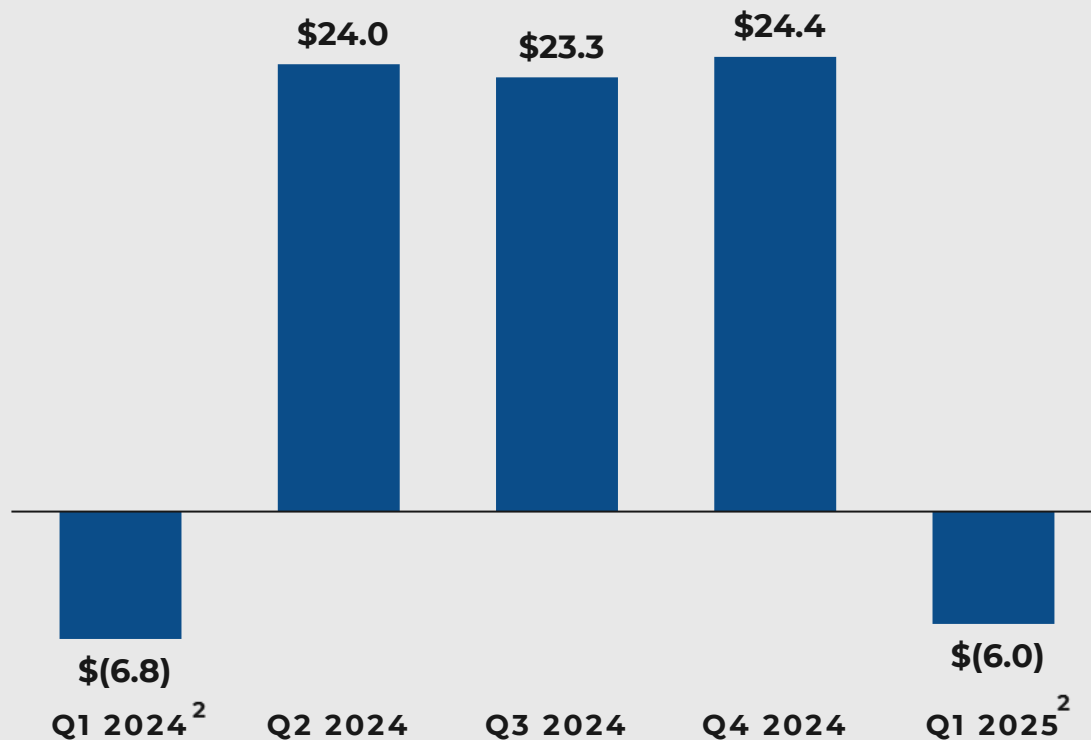




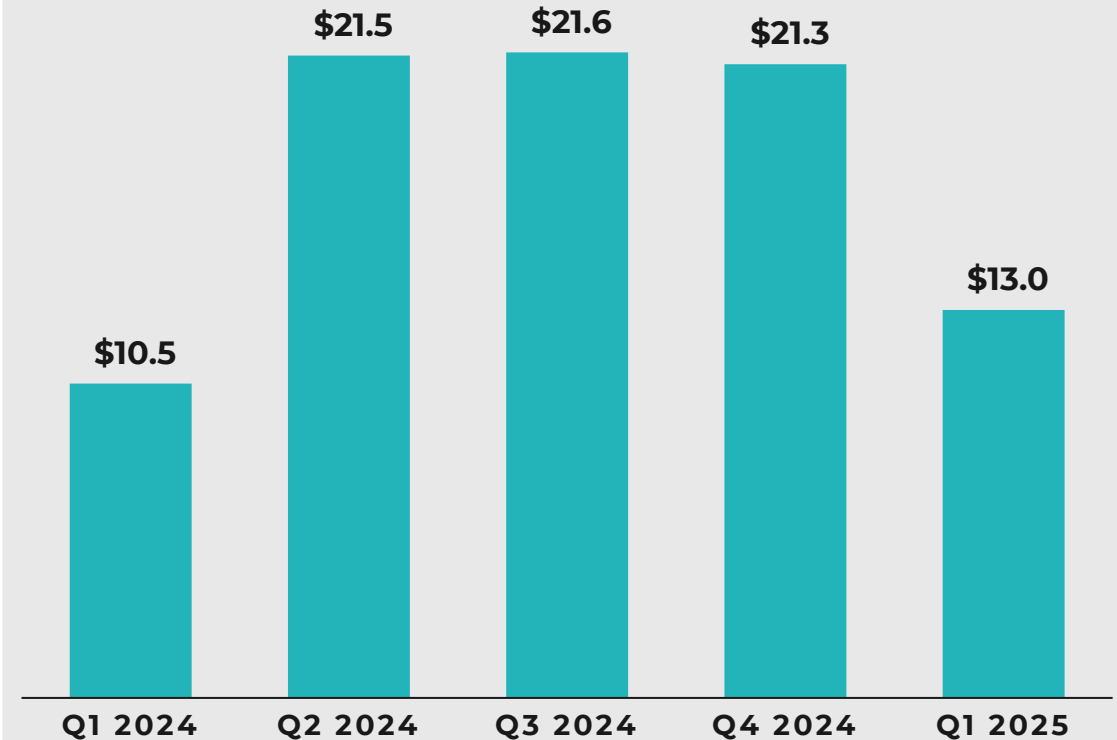
# Improving operating cash flow and Adjusted EBITDA

*Cash position of ~\$275M<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, 2025; includes Cash, Cash Equivalents & Marketable Investment Securities

2. Net cash used in operating activities in Q1 2025 and Q1 2024 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 income (loss), interest income, interest expense, income tax expense (benefit), depreciation and amortization expense, stock-based compensation expense and changes in fair value of trading securities

# > 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 53 peer-reviewed publications, including two publications (Bailey et al. 2023 and Dhillon et al. 2023) demonstrating an association with testing and improved patient outcomes

## SLNB Guidance and Patient Outcomes<sup>1,2</sup>

DecisionDx-Melanoma successfully identified patients with T1 tumors with a low risk of SLN positivity who can safely forego SLNB while maintaining high survival rates in a prospective multicenter study and can reduce SLNB-associated complications and healthcare costs.

1. Marks, The i31-GEP identifies patients with T1 cutaneous melanoma who can safely avoid sentinel lymph node biopsy: Results from a prospective, multicenter study. Video abstract presented at: 2024 American Society for Dermatologic Surgery (ASDS) Annual Meeting; 2. Guenther JM, et al. Patients who forego sentinel lymph node biopsy after 31-GEP testing are not harmed: A prospective, multicenter analysis. Poster presented at: 20th European Association of Dermato-Oncology (EADO) Congress; 3. Dillon et al. 2022; 4. Data as of March 31, 2025 ; 5. U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors.

SLN(B)=sentinel lymph node (biopsy)

**50%**

demonstrated change in management for 1 of 2 patients tested<sup>3</sup>

**~200,000**

patients with a clinical DecisionDx-Melanoma order from ~15,000 clinicians<sup>4</sup>

**~\$540M**

Estimated U.S. TAM<sup>5</sup>

# 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 22 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

Several published studies in 2024 supported the use of DecisionDx-SCC to predict likelihood of benefit from adjuvant radiation therapy (ART); two of these studies represent the largest<sup>1</sup> and second largest<sup>2</sup> studies completed to date to evaluate the effectiveness of ART in SCC



**~200,000**

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

**~52%**

of clinicians ordering DecisionDx-SCC also ordered DecisionDx-Melanoma<sup>3</sup>

**~\$820M**

Estimated U.S. TAM<sup>4</sup>

**Up to ~\$972M**

net annual Medicare savings that could be realized by using DecisionDx-SCC to guide adjuvant radiation therapy decisions<sup>5</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 20 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

1. as of March 31, 2025; 2. U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors.

A woman with brown hair, wearing a dark jacket and a red backpack, is looking out over a landscape under a clear sky.  
**~300,000**

patients each  
year present  
with a  
diagnostically  
ambiguous  
lesion

**50,000+**

lesions tested  
clinically<sup>1</sup>

**~\$600M**

Estimated U.S.  
TAM<sup>2</sup>



# 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 16 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

## Recognition from AGA

2024 Clinical Practice Guideline acknowledges that individuals who may be at increased risk of progression to esophageal cancer might be identified using tissue-based biomarkers, particularly TissueCypher

2022 Recognized in the 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)<sup>1</sup>

**~\$1B**

Estimated U.S. TAM<sup>2</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 27 peer-reviewed publications, which included more than 5,000 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

**27**

peer-reviewed publications

# Atopic Dermatitis Gene Expression Profile Test

Test currently in development for use in patients diagnosed with moderate-to-severe atopic dermatitis (AD) who are seeking systemic treatment

- Pipeline test has shown potential to identify the class of therapy to which a patient with AD is more likely to respond as indicated by an improvement in Eczema Area and Severity Index (EASI) score
- Data from our ongoing validation study for our pipeline test suggests we may be able to improve the standard-of-care 'trial-and-error' treatment approach by identifying patients who are more likely to achieve a greater response to a specific class of therapy based on identification of the immune pathway that is driving their AD

Atopic Dermatitis  
Pipeline Program



## Past and Anticipated Program Milestones

- **Q423:** early discovery data presented
- **Q424:** progress update
- **Assuming successful validation:** expect launch by the end of 2025

# 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 "Use of Non-GAAP Financial Measures (UNAUDITED)" above for further information regarding the Company's use of non-GAAP financial measures.

(In thousands)	Three months ended				
	Mar. 31, 2025	Dec. 31, 2024	Sep. 30, 2024	Jun. 30, 2024	Mar. 31, 2024
<b>Adjusted Revenues</b>					
Net revenues (GAAP)	\$87,988	\$86,311	\$85,782	\$87,002	\$72,974
Revenue associated with test reports delivered in prior periods	(787)	(491)	552	(363)	(1,656)
<b>Adjusted Revenues (Non-GAAP)</b>	<b>\$87,201</b>	<b>\$85,820</b>	<b>\$86,334</b>	<b>\$86,639</b>	<b>\$71,318</b>
<b>Adjusted Gross Margin</b>					
Gross margin (GAAP) <sup>1</sup>	\$43,280	\$65,788	\$67,901	\$70,236	\$56,833
Amortization of acquired intangible assets	28,325	4,340	2,272	2,247	2,247
Revenue associated with test reports delivered in prior periods	(787)	(491)	552	(363)	(1,656)
<b>Adjusted Gross Margin (Non-GAAP)</b>	<b>\$70,818</b>	<b>\$69,637</b>	<b>\$70,725</b>	<b>\$72,120</b>	<b>\$57,424</b>
Gross margin percentage (GAAP) <sup>2</sup>	49.2%	76.2%	79.2%	80.7%	77.9%
<b>Adjusted Gross Margin percentage (Non-GAAP)<sup>3</sup></b>	<b>81.2%</b>	<b>81.1%</b>	<b>81.9%</b>	<b>83.2%</b>	<b>80.5%</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 "Use of Non-GAAP Financial Measures (UNAUDITED)" above for further information regarding the Company's use of non-GAAP financial measures.

(In thousands)	Three months ended				
	Mar. 31, 2025	Dec. 31, 2024	Sep. 30, 2024	Jun. 30, 2024	Mar. 31, 2024
<b>Adjusted EBITDA</b>					
Net income (loss)	\$(25,848)	\$9,590	\$2,269	\$8,920	\$(2,534)
Interest income	(3,099)	(3,372)	(3,404)	(3,144)	(2,996)
Interest expense	17	92	201	270	14
Income tax (benefit) expense	(423)	(1,705)	6,013	(1,034)	45
Depreciation and amortization expense	29,764	5,768	3,541	3,348	3,340
Stock-based compensation expense	11,179	11,439	13,027	13,179	12,675
Changes in fair value of trading securities	1,425	(555)	—	—	—
<b>Adjusted EBITDA (Non-GAAP)</b>	<b>\$13,015</b>	<b>\$21,257</b>	<b>\$21,647</b>	<b>\$21,539</b>	<b>\$10,544</b>



# Thank You

