

# › Empowering people, informing care decisions



February 2026

**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 ability to advance penetration of our tests with clinicians and payers; our ability to carry out our commercial strategies; our future approach to capital allocation; pipeline opportunities to expand screening and diagnostic support for patients; our test volume growth strategy and expectations; our ability to maintain strong adjusted gross margin and a strong balance sheet; 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 or developed through collaborations; 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 conflicts in the Middle East 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, 2025, and our subsequent Quarterly Reports on Form 10-Q, 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 (loss) income: 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 (loss) income 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, AdvanceAD-Tx, TissueCypher, DecisionDx-UM, DecisionDx-PRAME and DecisionDx-UMSeq are trademarks of Castle Biosciences, Inc.

## 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



# Fourth Quarter and Full-Year 2025 Results Highlights



1

Total test reports for our core revenue drivers (DecisionDx-Melanoma, TissueCypher) increased 42% in Q4 2025 year over year, driving 37% growth for full year 2025

2

Achieved provided guidance of high single-digit percentage volume growth at 9% for DecisionDx-Melanoma for full year 2025 over 2024

3

Entered into a collaboration and license agreement with SciBase and completed the acquisition of Previs

4

Announced launch of AdvanceAD-Tx, the Company's test designed to guide systemic therapy decision making in patients ages 12 and older with moderate-to-severe atopic dermatitis

5

Net cash provided by operations in 2025 was \$64.3 million, compared to \$64.9 million in 2024

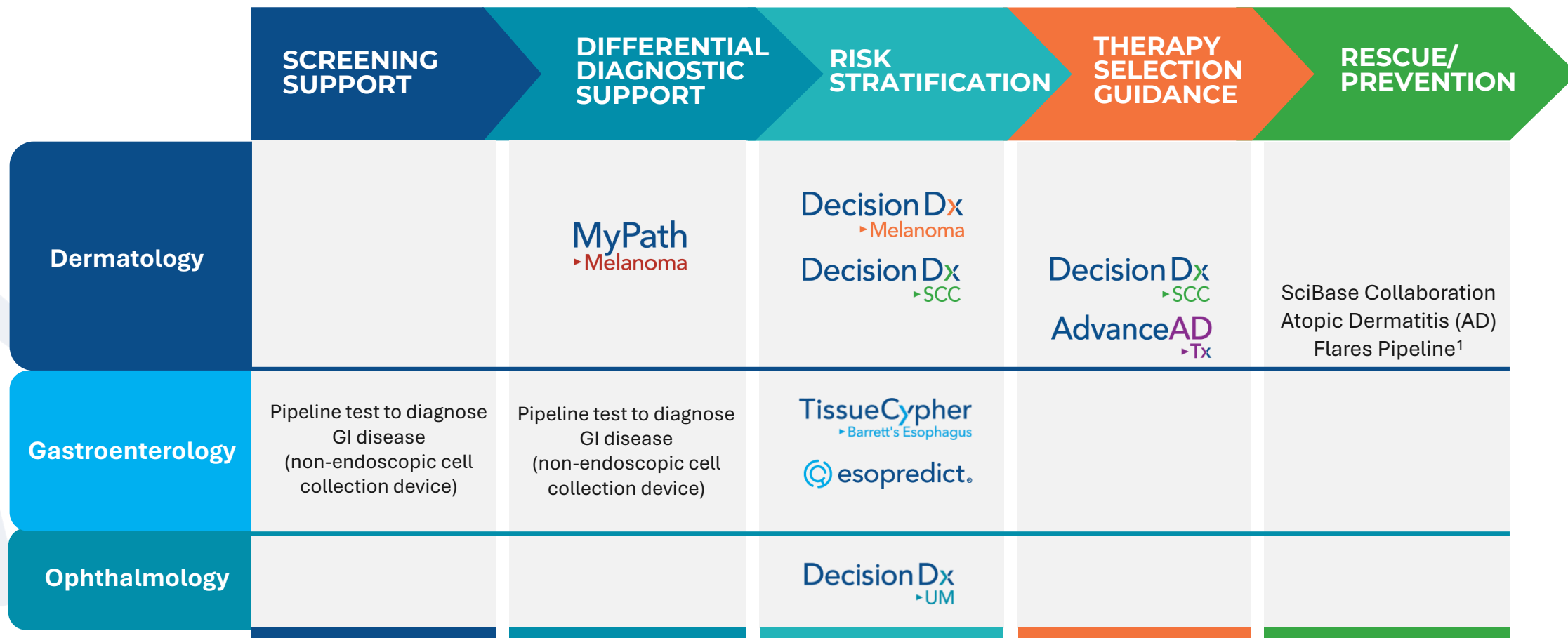
6

As of December 31, 2025, cash, cash equivalents and marketable investment securities totaled \$299.5 million

# Proven strategy designed to drive value creation for our stakeholders



# Answering clinical questions to guide care along the patient journey





# 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 58 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 forgo 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 December 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>

**~231,900**

patients with a clinical DecisionDx-Melanoma order from ~16,700 clinicians<sup>4</sup>

**~\$540M**

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

# 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

+

+

Ulceration  
 Age  
 Breslow thickness  
 Mitotic rate  
 SLN status  
 Tumor location

i31-ROR

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.”**

# 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 low SLNB positive outcomes**

3

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

# 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 17 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>

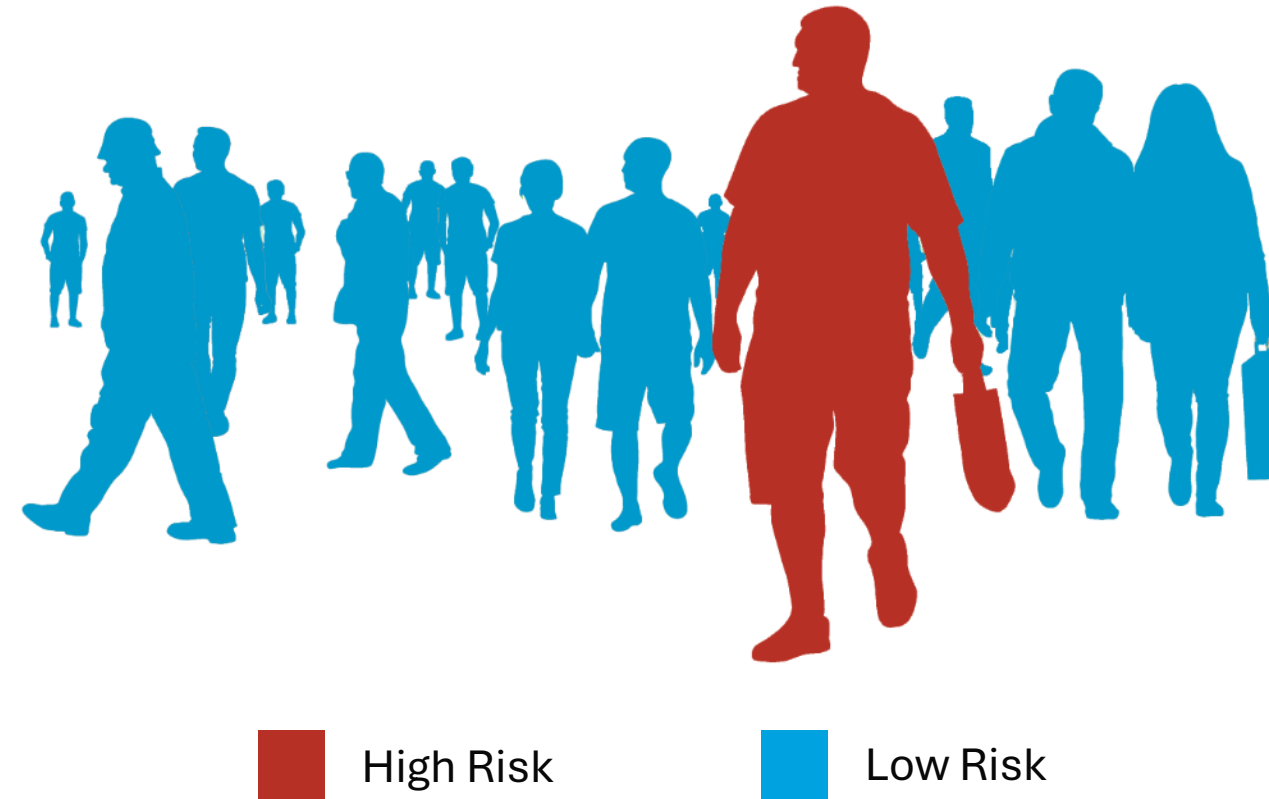
~\$1B

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

# TissueCypher provides individualized 5-year risk of progression to HGD or EAC

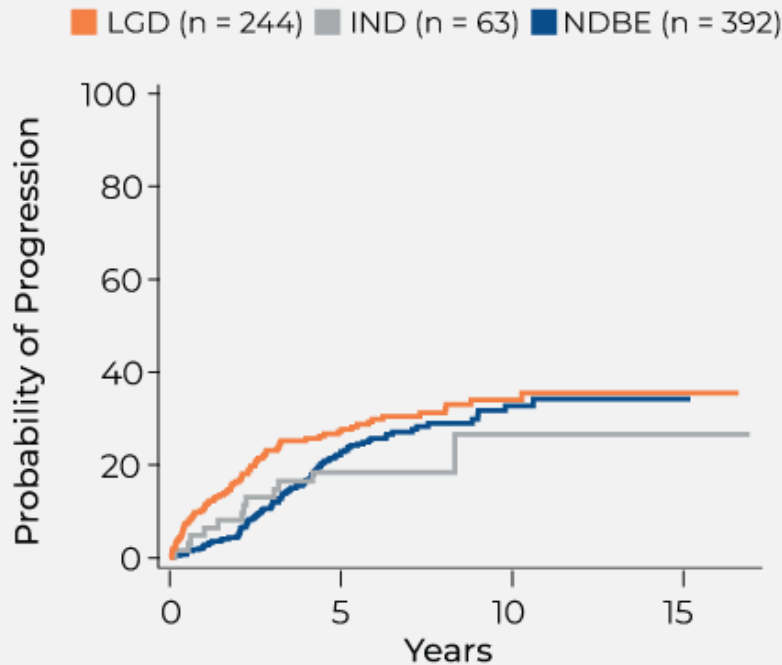
Indicated for NDBE, IND, and LGD

- **High Risk** score enables increased surveillance or early intervention to prevent cancer<sup>1</sup>
- **Low Risk** score minimizes over-treatment and supports extension of surveillance intervals to guideline recommendations<sup>1</sup>



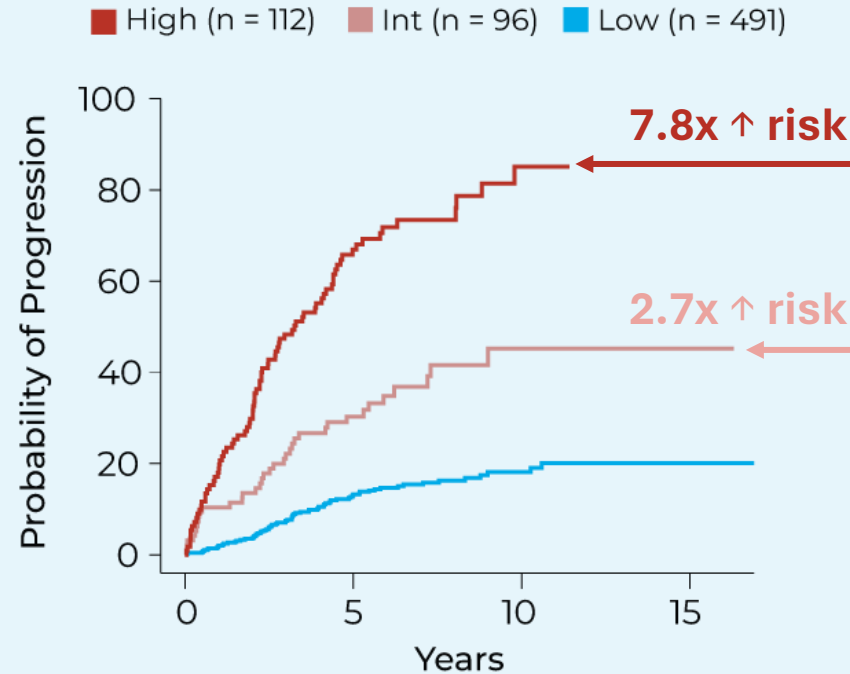
# TissueCypher provides independent prediction of progression

## Real world histologic grading



No significant risk stratification

## TissueCypher risk class



62% progressors detected

n=699 patients<sup>1-6</sup>, 150 incident progressors, 40 prevalent cases, 509 non-progressors

# AdvanceAD-Tx

A non-invasive molecular test that is designed to detect the underlying immune biology of atopic dermatitis (AD) that is driving an individual patient's AD and thus helps to guide systemic treatment decision making in patients with moderate-to-severe AD

## Validated in Real-World Patients

- The AdvanceAD-Tx test has been clinically validated in patients 12 years and older with moderate-to-severe AD. The clinical validation study included both systemic treatment naïve patients and those who were on a systemic treatment but considering a switch in therapy.
- The test can be ordered at any point in the patient's treatment journey and provides valuable molecular insight to help guide therapy-class selection. Ordering the test early may help reduce uncertainty, minimize trial-and-error, and support more timely disease control.



~10m

patient population of moderate-to-severe AD patients 12+ year of age, based on one-year prevalence<sup>1</sup>

~27%

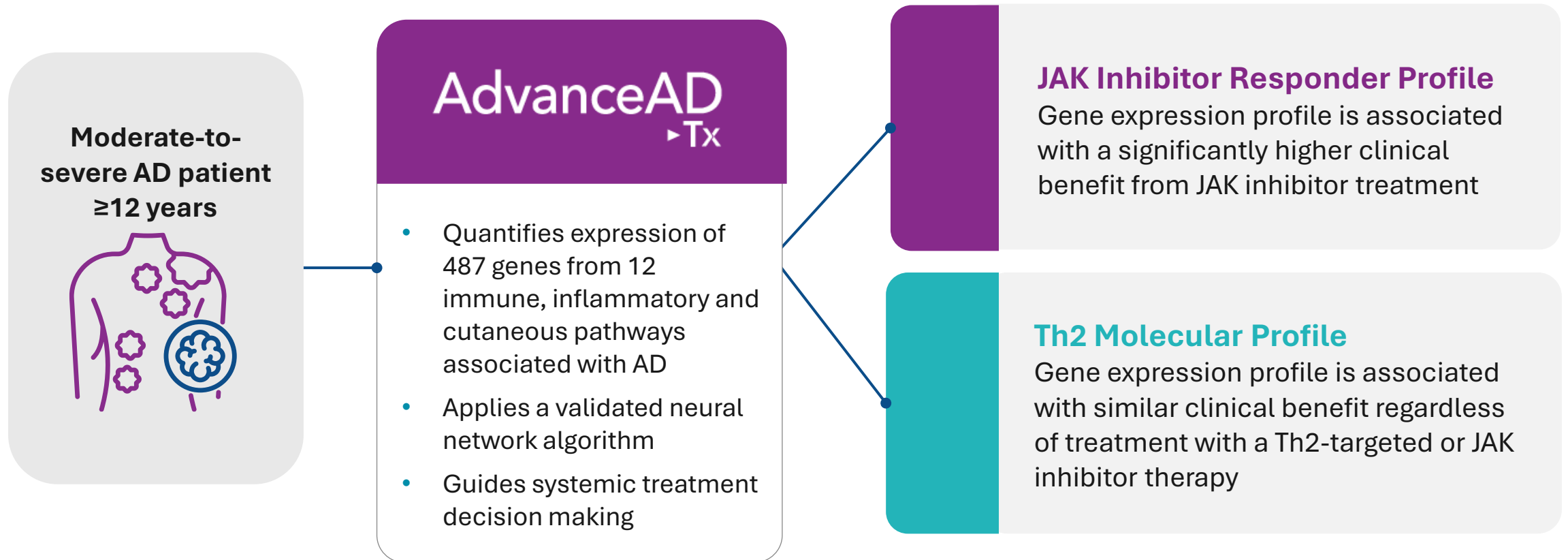
of patients who started on an advanced biologic or JAKi switched to another advanced systemic therapy<sup>2</sup>

~\$33 billion

Estimated U.S. TAM<sup>3</sup>

1. Atopic Dermatitis in America Study: A Cross-Sectional Study Examining the Prevalence and Disease Burden of Atopic Dermatitis in the US Adult Population. DOI:<https://doi.org/10.1016/j.jid.2018.08.028>. Patient burden and quality of life in atopic dermatitis in US adults: A population-based cross-sectional study. DOI:<https://doi.org/10.1016/j.jid.2018.08.028>; <https://www.census.gov/data/tables/time-series/demo/popest/2020s-national-detail.html>  
2. <https://pmc.ncbi.nlm.nih.gov/articles/PMC11904833/pdf/ActaDV-105-41504.pdf>; 3. U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors.

# AdvanceAD-Tx guides systemic treatment choice for patients with moderate-to-severe atopic dermatitis



## Data from the IDENTITY Study

Patients with JAKi Responder Profile who are treated with a JAK inhibitor therapy, compared to those treated with a Th2-targeted therapy achieve the following by 3 months:

Achieved a higher rate of EASI-90 (45.5% vs 8.3%,  $p=0.021$ )

More likely to achieve a validated investigator global assessment score of clear (vIGA-AD 0, 36.4% vs 0%,  $p=0.006$ )

More likely to remain flare-free during treatment (54.5% vs. 16.7%,  $p=0.041$ )

More likely to report “no itch” by three months (45.5% vs. 8.3%,  $p=0.021$ )

Reached EASI-90 3.8 times faster ( $p=0.049$ )

# > Financials



# Fourth Quarter and Year-end 2025 Financial Highlights

*Track record of consistent execution and strong business fundamentals*

	Total Revenue	Total Report Volume	Adjusted Gross Margin <sup>1,2</sup>	Adjusted EBITDA <sup>3</sup>	Operating Cash Flow	Cash Position <sup>4</sup>
4Q25	\$87.0M	27,236	77.6%	\$11.5M	\$26.9M	\$299.5M
2025	\$344.2M	105,053	79.8%	\$44.0M	\$64.3M	\$299.5M

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. 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. As of December 31, 2025; includes Cash, Cash Equivalents & Marketable Investment Securities

# Fourth Quarter and Year-end 2025 Test Volume Results

	4Q25	4Q24	2025	2024
<b>Total Test Reports</b>	<b>27,236</b>	24,071	<b>105,053</b>	96,071
DecisionDx-Melanoma	<b>10,022</b>	8,672	<b>39,083</b>	36,008
TissueCypher	<b>11,803</b>	6,672	<b>39,014</b>	20,956
DecisionDx-SCC <sup>1</sup>	<b>3,971</b>	4,299	<b>17,294</b>	16,348
MyPath Melanoma	<b>1,045</b>	879	<b>4,288</b>	3,909
DecisionDx-UM	<b>395</b>	424	<b>1,769</b>	1,699
IDgenetix <sup>2</sup>	<b>0</b>	3,125	<b>3,605</b>	17,151

# A disciplined approach to capital allocation

**Commercial optimization**

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

**Strategic opportunities, including within our current therapeutic areas**

# Well positioned for continued value creation



Drive robust test volume growth



Maintain strong Adjusted Gross Margin



Maintain strong balance sheet



Follow disciplined capital allocation

# > Appendix

# 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 24 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.

**~77%**

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

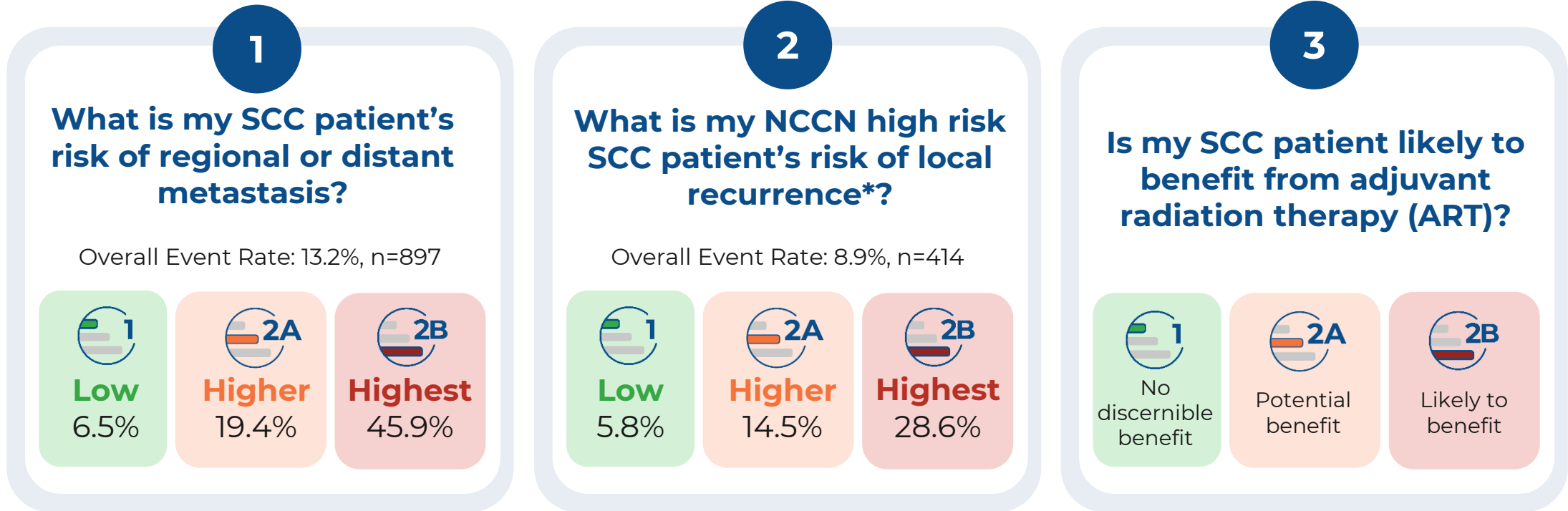
**~\$820M**

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

**~59,250**

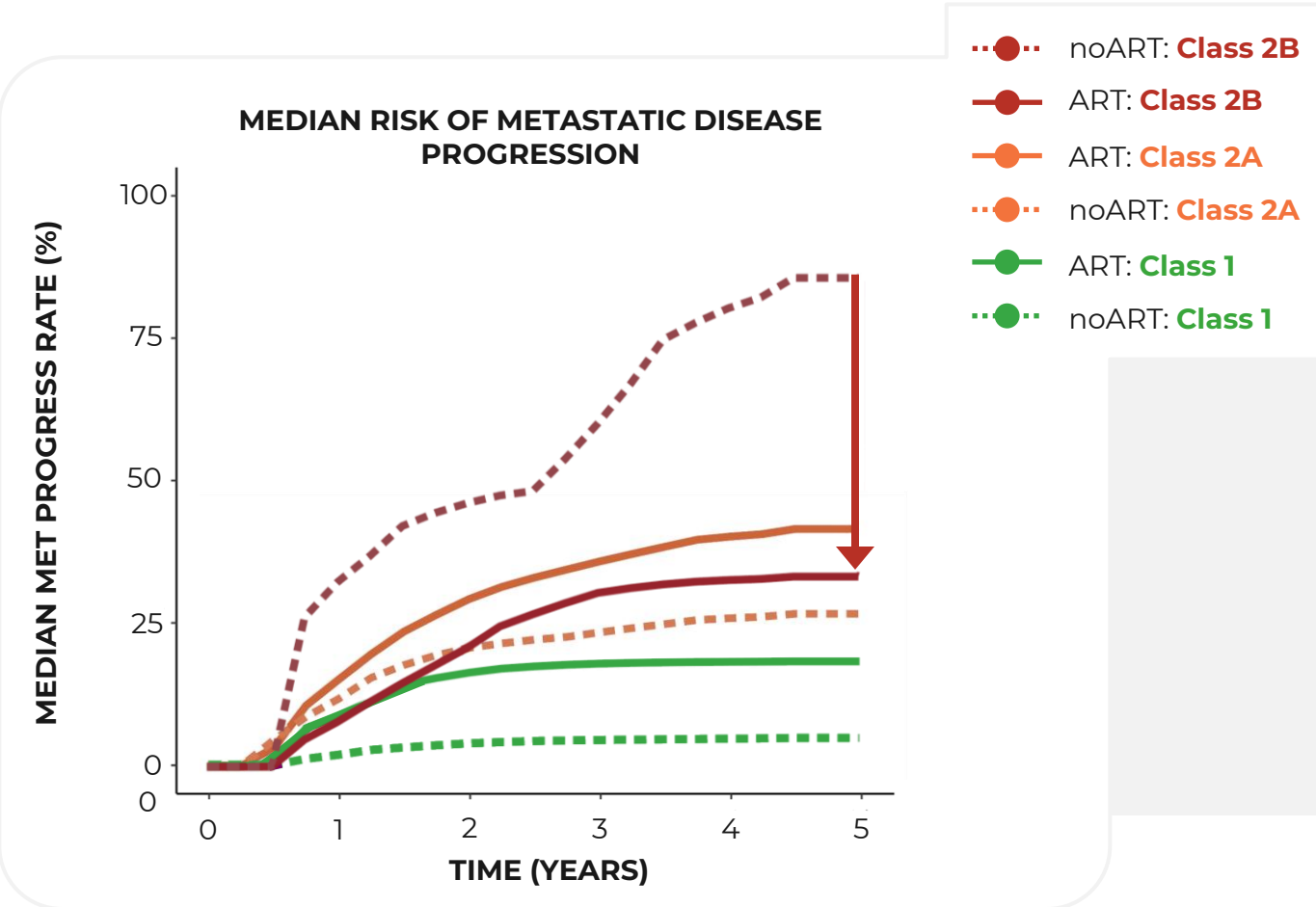
patients with a clinical DecisionDx-SCC order from ~7,380 clinicians<sup>5</sup>

# DecisionDx-SCC addresses *three* critical clinical questions for high-risk SCC patients



**DecisionDx-SCC Class results predict an SCC patient's individual risk of metastasis, local recurrence and individual benefit from adjuvant radiation therapy (ART)**

# DecisionDx-SCC may identify patients who benefit most from ART to control metastatic disease progression



- A **Class 1** or **Class 2A** result did not reflect a significant decrease in median risk of metastatic disease progression between resampled cohorts that did and did not receive ART
- A **Class 2B** result reflects a significant decrease in median risk of metastatic disease progression between resampled cohorts that did and did not receive ART

# 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

**~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>

# DecisionDx-UM

The standard of care for evaluating metastatic risk in uveal melanoma

## Clinical Validity and Utility

Demonstrated validity, utility and impact, backed by 39 peer-reviewed publications, which included more than 5,500 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
- 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

**30+** peer-reviewed publications

# 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.

<i>(In thousands)</i>	Three months ended				
	Dec. 31, 2025	Sep. 30, 2025	Jun. 30, 2025	Mar. 31, 2025	Dec. 31, 2024
<b>Adjusted Revenues</b>					
Net revenues (GAAP)	\$87,010	\$83,043	\$86,188	\$87,988	\$86,311
Revenue associated with test reports delivered in prior periods	(5,134)	(2,498)	(6)	(787)	(491)
<b>Adjusted Revenues (Non-GAAP)</b>	<b>\$81,876</b>	<b>\$80,545</b>	<b>\$86,182</b>	<b>\$87,201</b>	<b>\$85,820</b>
<b>Adjusted Gross Margin</b>					
Gross margin (GAAP) <sup>1</sup>	\$66,419	\$62,063	\$66,601	\$43,280	\$65,788
Amortization of acquired intangible assets	2,276	2,276	1,961	28,325	4,340
Revenue associated with test reports delivered in prior periods	(5,134)	(2,498)	(6)	(787)	(491)
<b>Adjusted Gross Margin (Non-GAAP)</b>	<b>\$63,561</b>	<b>\$61,841</b>	<b>\$68,556</b>	<b>\$70,818</b>	<b>\$69,637</b>
Gross Margin percentage (GAAP) <sup>2</sup>	76.3%	74.7%	77.3%	49.2%	76.2%
<b>Adjusted Gross Margin percentage (Non-GAAP)<sup>3</sup></b>	<b>77.6%</b>	<b>76.8%</b>	<b>79.5%</b>	<b>81.2%</b>	<b>81.1%</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.

<i>(In thousands)</i>	Three months ended				
	Dec. 31, 2025	Sep. 30, 2025	Jun. 30, 2025	Mar. 31, 2025	Dec. 31, 2024
<b>Adjusted EBITDA</b>					
Net (loss) income	\$(2,332)	\$(501)	\$4,523	\$(25,848)	\$9,590
Interest income	(2,896)	(2,833)	(2,944)	(3,099)	(3,372)
Interest expense	24	24	21	17	92
Income tax (benefit) expense	(382)	115	(4,666)	(423)	(1,705)
Depreciation and amortization expense	3,777	3,816	3,414	29,764	5,768
Stock-based compensation expense	11,406	12,100	11,208	11,179	11,439
Net losses (gains) on equity securities	1,855	(3,561)	(1,185)	1,425	(555)
<b>Adjusted EBITDA (Non-GAAP)</b>	<b>\$11,452</b>	<b>\$9,160</b>	<b>\$10,371</b>	<b>\$13,015</b>	<b>\$21,257</b>

➤ Thank You

