

Q4 & FULL YEAR 2025 FACT SHEET

Empowering people, informing care decisions

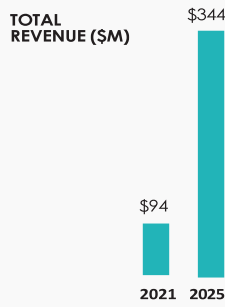
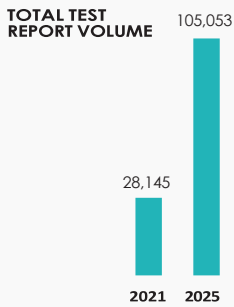


Fourth Quarter and Year-End 2025 Financial Highlights

| | TOTAL REVENUE | TOTAL REPORT VOLUME | ADJUSTED GROSS MARGIN ^{1,2} | ADJUSTED EBITDA ³ | OPERATING CASH FLOW | CASH POSITION ⁴ |
|------|---------------|---------------------|--------------------------------------|------------------------------|---------------------|----------------------------|
| 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 gross margin (GAAP) divided by net revenues (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.

Proven track record of consistent execution (2021-2025)



Proven strategy enables 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 payors

Portfolio of innovative tests designed to guide patient care

DERMATOLOGY

- DecisionDx
•Melanoma
- DecisionDx
•SCC
- MyPath
•Melanoma
- AdvanceAD
•Tx

GASTROENTEROLOGY

- TissueCypher
• Barrett's Esophagus
- esopredict®

OPHTHALMOLOGY

- DecisionDx
•UM

“ We closed out an outstanding year with a strong fourth quarter, reflecting the strength of our innovative test portfolio, disciplined execution and the dedication of the entire Castle team who continue to deliver meaningful impact for patients and clinicians every day. We exited 2025 with clear leadership across our core dermatologic and gastrointestinal franchises, highlighted by continued momentum in TissueCypher, which achieved 86% test report growth over 2024. In 2025, we also delivered an important milestone with the limited access launch of AdvanceAD-Tx™, which materially expanded our total addressable market and reinforced our commitment to providing clinical answers to dermatology clinicians and their patients. As we look ahead to 2026 and beyond, we believe we are well positioned to continue delivering stockholder value and capitalize on our near- and long-term opportunities, supported by continued test adoption growth for our core tests, a robust pipeline and a strong balance sheet.



DEREK MAETZOLD, FOUNDER, PRESIDENT, AND CEO



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
Excitement, Collaboration, Integrity, Innovation, Trust and Excellence

Forward-looking statements

Certain statements made herein are 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 expectations regarding: our ability to continue delivering stockholder value, capitalize on our near- and long-term opportunities, a robust pipeline, a strong balance sheet and continued test adoption growth. The words "anticipates," "believe," "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 our future revenues and test adoption; our estimated 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, labor shortages, disruptions in the banking system or financing markets, recession risks, supply chain disruptions, tariffs, 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 any impacts on our business; the possibility that subsequent study or trial results and findings may contradict earlier study or trial results and findings; the possibility that actual application of our tests may not provide the anticipated benefits to patients or clinicians; 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.

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 benefit or expense, depreciation and amortization expense, stock-based compensation expense and changes in fair value of equity 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. 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 nonstandardized 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 release.

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.

Non-GAAP Reconciliations

The tables below present the reconciliation of Adjusted Revenues, Adjusted Gross Margin and Adjusted EBITDA, which are non-GAAP financial measures.

| (in thousands) | Three months ended December 31, 2025 | Twelve months ended December 31, 2025 |
|---|---|--|
| Adjusted Revenues | | |
| Net revenues (GAAP) | \$87,010 | \$344,229 |
| Revenue associated with test reports delivered in prior periods | (5,134) | 7,592 |
| Adjusted Revenues (Non-GAAP) | \$81,876 | \$351,821 |
| Adjusted Gross Margin | | |
| Gross margin (GAAP) ¹ | \$66,419 | \$238,363 |
| Amortization of acquired intangible assets | 2,276 | 34,838 |
| Revenue associated with test reports delivered in prior periods | (5,134) | 7,592 |
| Adjusted Gross Margin (Non-GAAP) | \$63,561 | \$280,793 |
| Gross Margin percentage (GAAP) ² | 76.3% | 69.2% |
| Adjusted Gross Margin percentage (Non-GAAP)³ | 77.6% | 79.8% |

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 December 31, 2025 | Twelve months ended December 31, 2025 |
|---|---|--|
| Adjusted EBITDA | | |
| Net (loss) income | \$(2,332) | \$(24,158) |
| Interest income | (2,896) | (11,772) |
| Interest expense | 24 | 86 |
| Income tax (benefit) expense | (382) | (5,356) |
| Depreciation and amortization expense | 3,777 | 40,771 |
| Stock-based compensation expense | 11,406 | 45,893 |
| Net losses (gains) on equity securities | 1,855 | (1,466) |
| Adjusted EBITDA (Non-GAAP) | \$11,452 | \$43,998 |