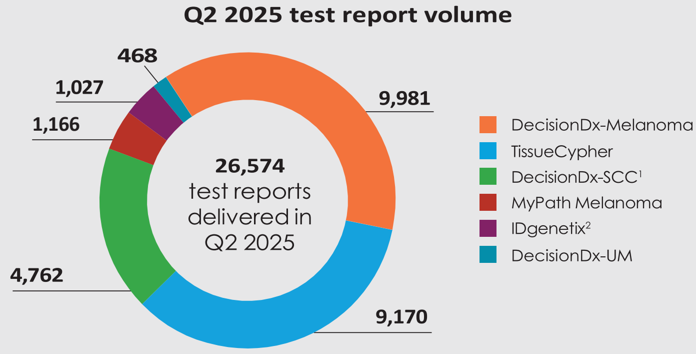
Q2 2025 FACT SHEET

Empowering people, informing care decisions

Q2 2025 Review

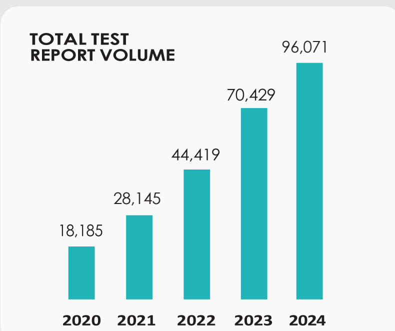
- Q2 2025 total test reports for our core revenue drivers (DecisionDx-Melanoma, TissueCypher) increased 33% over Q2 2024
- Raised 2025 revenue guidance to $310-320 million, up from $287-297 million previously reported
- Gross margin for Q2 2025 was 77.3% and Adjusted Gross Margin was 79.5%
- As of June 30, 2025, cash, cash equivalents and marketable investment securities totaled $275.9 million

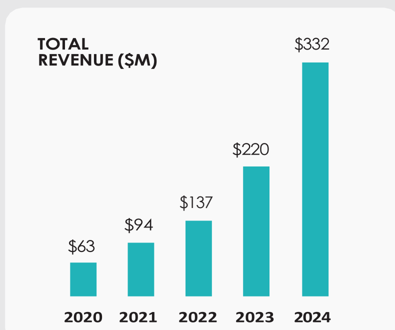
Q2 Test Report Volume



1. The Novitas local coverage determination, or LCD, that included non-coverage language for DecisionDx-SCC, went into effect on April 24, 2025; 2. Effective May 2025, the IDgenetix test was discontinued.

Proven track record of consistent execution (2020-2024)





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	OPHTHALMOLOGY	GASTROENTEROLOGY
DecisionDx Melanoma	DecisionDx UM	TissueCypher Barrett's Esophagus
DecisionDx SCC		esopredict
MyPath Melanoma		

Following a strong first quarter, our team closed out a very successful second quarter that we believe continued to reflect the clinical value our tests provide to clinicians and their patients. We saw very solid total year-over-year test volume growth in our core revenue drivers, with both DecisionDx-Melanoma and TissueCypher exceeding our volume expectations for the quarter, driving our top-line performance. In alignment with our capital allocation priorities and M&A strategy, we closed the Previse tuck-in acquisition and announced an exciting collaboration and license agreement with SciBase, both of which we believe will support our mid- to long-term value creation goals. At the same time, we remain deeply focused on execution across our current test portfolio, which we believe positions us well for continued near-term success. Our ability to invest in the future while advancing our core franchises reflects the strength of our growth initiatives and commitment to delivering sustainable value to our stakeholders.

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: 2025 total revenue guidance, the continued success of our growth initiatives and our ability to translate growth into profitability; our estimated U.S. total addressable market for our commercially available tests; our continued focus on delivering operational excellence; the potential mid- to long-term value possibly generated from the Previse and SciBase transactions; and our ability to capitalize on strategic opportunities. 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 our 2025 total revenue guidance; 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, labor shortages, liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets; recession risks, tariffs; 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; the possibility that the actual application of our tests may not provide the anticipated benefits to patients; the possibility that our newer gastroenterology 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 quarter ended June 30, 2025, each filed or to be filed with the SEC, and in our other documents and reports filed or to be filed 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.

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Financial Information; Non-GAAP Financial Measures

In this presentation, we use the metrics of Adjusted Revenues and Adjusted Gross Margin, 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 and DecisionDx-SCC related expenses that were post-revenue.

We use Adjusted Revenues and Adjusted Gross Margin 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 and DecisionDx-SCC related expenses that were post-revenue 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. 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-CM*Seq*, i31-SLNB, i31-ROR, DecisionDx-SCC, MyPath Melanoma, TissueCypher, DecisionDx-UM, DecisionDx-PRAME and DecisionDx-UM*Seq* are trademarks of Castle Biosciences, Inc.

Non-GAAP Reconciliations

The table below presents the reconciliation of Adjusted Revenues and Adjusted Gross Margin, which are non-GAAP financial measures.

(in thousands)	**Three months ended June 30 2025**
Adjusted Revenues	
Net revenues (GAAP)	$86,188
Revenue associated with test reports delivered in prior periods	(6)
Adjusted revenues (Non-GAAP)	**$86,182**
Adjusted Gross Margin	
Gross margin (GAAP)[1]	$66,601
Amortization of acquired intangible assets	1,961
Revenue associated with test reports delivered in prior periods	(6)
Adjusted Gross Margin (Non-GAAP)	**$68,556**
Gross Margin percentage (GAAP)[2]	77.3%
Adjusted gross margin percentage (Non-GAAP)[3]	79.5%

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).

USEFUL LINKS

Q2 2025 Earnings Press Release

Corporate Presentation

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