CASTLE BIOSCIENCES

Transforming the management of dermatologic conditions

Wells Fargo 2021 Healthcare Conference

September 9, 2021

Disclaimers

FORWARD-LOOKING STATEMENTS

The information in this presentation contains forward looking statements and information 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 the effects of the COVID 19 pandemic on our business and our efforts to address its impact on our business, statements concerning the estimated size of our total addressable market or our existing and pipeline products, statements concerning trends in sales report volume growth, the number of test reports delivered, expectations regarding future order flow, and our prospects and plans and the objectives of management. The words "anticipates," "believes," "estimates," "expects," "intends," "may," "plans," "projects," projects," "will," "would" 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, the effects of the COVID 19 pandemic on our business and our efforts to address its impact on our business, subsequent study results and findings that contradict earlier study results and findings, our tests including DecisionDx Melanoma, DecisionDx SCC, DecisionDx DiffDx Melanoma and myPath Melanoma, their ability to provide the aforementioned benefits to patients, and the risks set forth in our Quarterly Report on Form 10 Q for the quarter ended June 30, 2021, 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.

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Leading Dermatologic Diagnostics Company

Transforming the management of skin cancer and other dermatologic diseases with high unmet clinical need

Culture of Teamwork and Innovation

Suite of Dermatologic Prognostic And Diagnostic Tests

Expansive Body of Evidence

Strong Financial Position

Robust Pipeline

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Financial Summary 2Q 2021

	2Q21	2Q20
Revenue	**$22.8M**	$12.7M
Adj. Revenue[1]	**$22.9M**	$10.4M
Total GEP test reports[2]	**7,007**	3,314
Total Derm test reports[2]	**6,539**	3,008
Operating Cash Flow	**$(6.4)M**	$13.5M
Adj. Operating Cash Flow[1]	**$(4.3)M**	$3.3M
Gross Margin	**83%**	83%
Adj. Gross Margin[1]	**84%**	79%
Cash & Cash Equivalents	**$368M** as of 6/30/2021	$180M as of 6/30/2020

[1]See Non-GAAP reconciliations at the end of this presentation.
[2]Castle had two commercially available GEP tests as of 6/30/2020.

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Estimated ~$5.5B U.S. Total Addressable Market[1]

In market and pipeline tests, leveraging established dermatologic sales channels

Indication/ Test outcome	Trade Name	Reimbursement Status	Peer-Reviewed Publications	Primary Customers	Initial Launch Targets	Initial addressable market, patients[2]	Estimated U.S. TAM
Cutaneous melanoma/ Risk of metastasis	DecisionDx MELANOMA	MCR, MCRA Commercial – in process	30+	Derms (including Mohs), Surgeons	—	***~130k patients*** classified as Stage I, II or III	~$540M
Cutaneous squamous cell carcinoma/ Risk of metastasis	DecisionDx-SCC	Expected draft LCD in 2021 Commercial – in process	5	Derms (including Mohs)	~4,709 current customers[3]	***~200k*** w/ high-risk features	~$820M
Suspicious pigmented lesions/ Melanoma status	myPath Melanoma DecisionDx DiffDx-Melanoma	MCR, MCRA Commercial – in process Expected draft LCD in 2021 Commercial – in process	9 2	Dermpaths, Derms	~1,778 current dermpath customers[4]	***~300k patients*** w/indeterminant biopsy	~$600M
Pipeline Test-Inflammatory	Target launch anticipated by the end of 2025	N/A	N/A	Expected to utilize existing dermatologic sales channels	~4,709 current customers[3]	***~450k patients*** eligible for systemic therapies	~$1.9B
Other Pipeline Tests	Target launches anticipated by the end of 2025	N/A	N/A	Expected to utilize existing dermatologic sales channels	To be announced	To be announced	~$1.7B

[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 indeterminant biopsy.
[3]Clinicians who ordered DecisionDx-Melanoma in last twelve months (as of 6/30/2021).
[4]Pathologists who provided clinical specimens for DecisionDx-Melanoma in last twelve months (as of 6/30/2021).
-MCR = Medicare. MCRA = Medicare Advantage; current customer estimates based on last twelve months.

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COVID Variant Update

Positive trends continue despite the impact of variants in some geographies

- In the second quarter of 2021, we delivered 70% growth in DecisionDx-Melanoma test reports, compared to the second quarter of 2020
  - We believe this is reflective of gains in both diagnoses of melanoma compared to 2020 as well as significant gains in market penetration
- Although in certain geographies, some providers, mostly academic institutions, have stopped allowing in-person visits by our sales team, overall, in-person sales calls QTD remain consistent with what we saw in Q2
- Positive trends in year-over-year test order volume growth that we saw in the second quarter of 2021 continued in July and August
- We can't predict any potential future impacts due to variants
- According to our analysis of third-party diagnoses data for dermatology, trends in diagnoses of cutaneous melanoma remained below 2019 levels in 2Q2021 compared to 2Q2019, and we saw similar, but slightly improving trends in July and August

Recent Achievements And Expected Future Milestones

2021 milestones on track

- ✓ **Dec 2018:** Initial LCD effective for DecisionDx-Melanoma
- ✓ **Feb 2019:** Expanded outside sales territories to 23
- ✓ **July 2019:** IPO
- ✓ **Aug 2019:** Expanded draft LCD for DecisionDx-Melanoma posted
- ✓ **Dec 2019:** Expanded outside sales territories to 32
- ✓ **Sept 2020:** Launch of DecisionDx-SCC
- ✓ **3Q2020:** Commercial team expansion
- ✓ **4Q2020:** Launch of DecisionDx DiffDx-Melanoma
- ✓ **Oct 2020:** LCD expansion finalized for DecisionDx-Melanoma, effective date 12/6/20
- ✓ **2H2020:** Initiation of work on additional dermatology pipeline products
- ✓ **1H2021:** Planned commercial team expansion to mid-60s
- ✓ **2021:** Acquired myPath® Melanoma
- ✓ **2021:** Planned announcement of pipeline indications
- **2021:** Potential draft LCD for DecisionDx-SCC and DecisionDx DiffDx-Melanoma
- **2021+:** Continued development of dermatologic pipeline products; potential launches in 2025
- **2021+:** Continued evidence development for all commercialized products
- **2022:** Potential effective LCD for DecisionDx-SCC and DecisionDx DiffDx-Melanoma

2018 | 2019 | 2020 | 2021 | 2022

✓ = Achieved

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THANK YOU

Use Of Non-GAAP Financial Measures (Unaudited)

In this presentation, we use the metrics of Adjusted Revenue, Adjusted Gross Margin and Adjusted Operating Cash Flow, which are non-GAAP financial measures and are not calculated in accordance with generally accepted accounting principles in the United States (GAAP). Adjusted Revenue and Adjusted Gross Margin reflect adjustments to net revenues to exclude changes in variable consideration related to test reports delivered in previous periods. Adjusted Gross Margin also excludes acquisition-related intangible asset amortization. Adjusted Operating Cash Flow excludes the effects of cash activity associated with COVID-19 government relief payments to healthcare providers.

We use Adjusted Revenue, Adjusted Gross Margin and Adjusted Operating Cash Flow internally because we believe these metrics provide useful supplemental information in assessing our revenue and cash flow performance, respectively. We believe Adjusted Revenue and Adjusted Gross Margin are also useful to investors because they provide additional information on current-period performance by removing the effects of revenue adjustments related to tests delivered in previous periods and acquisition-related intangible asset amortization, which we believe may facilitate revenue and gross margin comparisons to historical periods. We believe Adjusted Operating Cash Flow is also useful to investors as a supplement to GAAP measures in the assessment of our cash flow performance by removing the effects of COVID-19 government relief payments, which we believe are not indicative of our ongoing operations. 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 substitutes for net revenues or net cash (used in) provided by operating activities reported in accordance with GAAP and should be considered in conjunction with our financial information presented on GAAP basis. 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 next slide.

Reconciliation Of Non-GAAP Financial Measures (Unaudited)

The table below presents the reconciliation of adjusted revenue and adjusted gross margin, which are non-GAAP measures. See "Use of Non-GAAP Financial Measures (UNAUDITED)" on the previous slide for further information regarding the Company's use of non-GAAP financial measures.

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
(in thousands)				
Adjusted revenue				
Net revenues (GAAP)	$ 22,758	$ 12,715	$ 45,571	$ 30,133
Revenue associated with test reports delivered prior periods	166	(2,291)	(5,092)	(1,048)
Adjusted revenue (Non-GAAP)	$ 22,924	$ 10,424	$ 40,479	$ 29,085
Adjusted gross margin				
Gross margin (GAAP)[1]	$ 18,805	$ 10,569	$ 38,590	$ 25,596
Amortization of acquired intangible asset	256	—	256	—
Revenue associated with test reports delivered prior periods	166	(2,291)	(5,092)	(1,048)
Adjusted gross margin (Non-GAAP)	$ 19,227	$ 8,278	$ 33,754	$ 24,548
Gross margin percentage (GAAP)[2]	82.6 %	83.1 %	84.7 %	84.9 %
Adjusted gross margin percentage (Non-GAAP)[3]	83.9 %	79.4 %	83.4 %	84.4 %

1. Calculated as net revenues (GAAP) less the sum of cost of sales (exclusive of amortization of acquired intangible asset) and amortization of acquired intangible asset.
2. Calculated as gross margin (GAAP) divided by net revenues (GAAP).
3. Calculated as adjusted gross margin (Non-GAAP) divided by adjusted revenue (Non-GAAP).

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Reconciliation Of Non-GAAP Financial Measures (Unaudited)

The table below presents the reconciliation of adjusted operating cash flow, which is a non-GAAP measure. See "Use of Non-GAAP Financial Measures (UNAUDITED)" on the previous slide for further information regarding the Company's use of non-GAAP financial measures.

(in thousands)	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020
Adjusted operating cash flow				
Net cash used in operating activities (GAAP)	$ (6,438)	$ 13,501	$ (10,069)	$ 13,250
Medicare advance payment[1]	2,173	(8,350)	2,173	(8,350)
HHS provider relief funds[2]	—	(1,882)	(1,882)	(1,882)
Adjusted operating cash flow (Non-GAAP)	$ (4,265)	$ 3,269	$ (9,778)	$ 3,018

1. In April 2020, we received an advance payment of $8.3 million from the Centers for Medicare & Medicaid Service (CMS), for which recoupment has commenced in April 2021. We recorded the receipt of the payment as a liability on our balance sheet and, in accordance with GAAP, it is included in net cash provided by operating activities in the period received. We have excluded receipt of the advance payment from adjusted operating cash flow, but as claims are submitted for reimbursement and applied against this balance, we include the advance payment in adjusted operating cash flow to the extent that Medicare claims submitted for reimbursement have been applied to the balance.

2. In April 2020, we received a one-time payment of $1.9 million in relief funds automatically allocated to Medicare providers under the Coronavirus Aid, Relief and Economic Security Act (CARES Act) from the U.S. Department of Health and Human Services (HHS).

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