CASTLE BIOSCIENCES

Transforming the management of dermatologic cancers and other dermatologic diseases with unmet clinical need

Baird 2021 Healthcare ESG Symposium

June 17, 2021

DISCLAIMERS

FORWARD-LOOKING STATEMENTS

The information in this press release 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 our ability to establish, integrate and implement an ESG program into our governance structure, and the anticipated benefits, as set forth in this presentation, that it would have on our business. The words “anticipates,” “believes,” “estimates,” “expects,” “intends,” “may,” “plans,” “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, our ability to establish, integrate and implement an ESG program into our governance structure, and the risks set forth in our Quarterly Report on Form 10-Q for the quarter ended March 31, 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.

Leading Dermatologic Diagnostics Company

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

CULTURE OF TEAMWORK, OF INNOVATION

SUITE OF DERMATOLOGIC PROGNOSTIC AND DIAGNOSTIC TESTS

EXPANSIVE BODY OF EVIDENCE

STRONG FINANCIAL POSITION

ROBUST PIPELINE

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	4	Derms (including Mohs)	~4,365 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	~1,740 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	~4,365 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 o r 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 3/31/2020)
[4]Pathologists who provided clinical specimens for DecisionDx-Melanoma in last twelve months (as of 3/31/2020)
-MCR = Medicare. MCRA = Medicare Advantage; current customer estimates based on last twelve months.

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Financial Summary 1Q 2021

	1Q21	1Q20
Revenue	**$22.8M**	$17.4M
Adj. Revenue[1]	**$17.5M**	$14.3
Total GEP test reports[2]	**5,142**	4,935
Total Derm test reports[2]	**4,805**	4,574
Operating Cash Flow	**$(3.6)M**	$(0.3)M
Adj. Operating Cash Flow[1]	**$(5.5)M**	$(0.3)M
Gross Margin	**87%**	86%
Adj. Gross Margin[1]	**83%**	83%
Cash & Cash Equivalents[3]	**$407M**	$99M

[1]See Non-GAAP reconciliations at the end of this presentation.
[2]Castle had two commercially available GEP tests in 1Q2020.
[3] As of 3/31/2021

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Our culture and operations were built on ESG principles

As a young public company, we are now implementing a formal ESG program

Helps mitigate risks and create opportunities

Helps progress our vision to transform patient management of dermatologic diseases with high unmet clinical need

Builds employee engagement and retention

Uncovers potential financial opportunities

Advances sustainable long-term value creation for our stockholders

First Steps

Building our ESG Program

We conducted a materiality assessment, peer benchmarking analysis and conducted SME interviews to develop our initial ESG disclosure roadmap

Leveraging SASB

We leverage the Sustainability Accounting Standards Board (SASB) accounting standards to focus on the ESG risks and opportunities most relevant to our long-term financial sustainability, our investors and other stakeholders

Engaging with Stakeholders

We are laying the groundwork to meet current and future stockholder and stakeholder expectations on managing ESG risks and opportunities and regularly engage to understand their perspective

Oversight of ESG

Strategy is supported by Executive Management and the Board of Directors

A cross-functional **Management Committee** is developing a platform to integrate ESG risk management and strategy throughout the organization

Review and oversight of our ESG program resides with the **Audit Committee** of the Board

Governance Highlights

Board Diversity

- Our Board of Directors consists of 28% female directors
- As we make changes to our board, we look for opportunities to increase the diversity through outreach in new channels and diverse slates

Business Ethics & Compliance

- Our Compliance Program includes our Ethics and Integrity Program, routine process and system audits, reporting requirements, actions for resolution and whistleblower protection
- Mandatory employee training includes ethics, HIPAA regulation and anti-harassment

Data Security & Patient Privacy

- The Audit Committee of the Board has oversight of data security and patient privacy
- Our cybersecurity program incorporates physical security measures, routine user training, secure electronic transmission of Protected Health Information (PHI) and network safeguards such as audit trails to mitigate risk

Environment Highlights

Environmental Risk

- We minimize environmental risk by employing safe operating procedures and technology, and we maintain crisis management plans
- Our Disaster Emergency Management Plan includes action planning and training for all laboratory staff

Waste Management

- We responsibly treat and dispose of hazardous and non-hazardous waste in partnership with third-party vendors

Grassroots Employee Initiatives

- An employee-driven effort at our HQ gathers recyclable materials, including aluminum and cardboard for deposit at collection facility

Human Capital Highlights

Talent Development

- We provide a continuing education program for clinical laboratory scientists and sponsor relevant certifications
- Our Manager Leadership Learning & Development Program includes resource guides, a subscription to an online learning platform and development exercises

Diversity, Equity and Inclusion

- As of December 31, 2020, our employee base was approximately 63% female and 37% male
- We are building on our existing diversity and inclusion strengths through additional opportunities and related initiatives

Employee Engagement

- Employee engagement surveys are administered to new hires within the first 90 days of employment
- Over 600 virtual cards have been sent to date by employees acknowledging each other through our “Thank You Card “program, first launched in Q32020

Social Capital Highlights

Access & Affordability

- We believe a patient's ability to pay for our tests should not affect care; and therefore, have put a generous Patient Assistance Program in place for those who need it

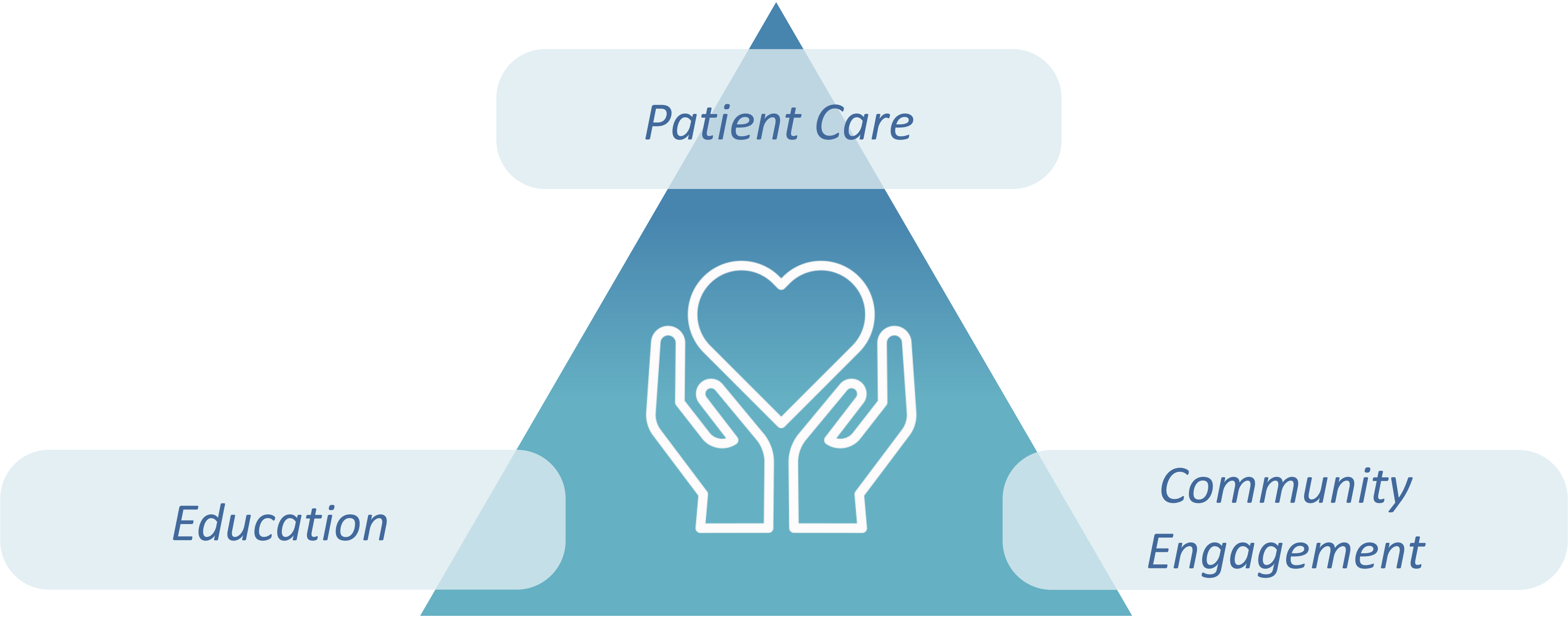
Safety of Clinical Studies

- Our cross-functional development of clinical studies involves R&D, Clinical Research, medical science liaisons, and external physicians and clinicians

Product Quality & Safety

- Our comprehensive Quality Management System and portfolio of SOPs includes quality control, assessment, improvement and planning; monthly and annual audits; and employee education and training
- Our Phoenix laboratory is CLIA-certified and CAP-accredited

Our Giving Philosophy



Next Steps in ESG

Publish inaugural ESG Report	We plan to publish our first ESG report in 2H2021, which will cover relevant ESG factors for our long-term financial sustainability, creating a foundation to build upon as our ESG program evolves
Advance ESG initiatives over time	Leverage our cross-functional management working group to engage with internal stakeholders and identify further opportunities to advance our ESG capabilities, measuring our progress over time
Continued transparency in disclosure	Consider and assess expanded quantitative metrics and the incorporation of expanded capabilities

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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 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, 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)

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)" above for further information regarding the Company's use of non-GAAP financial measures.

	Three Months Ended March 31,	
	2021	**2020**
(in thousands)		
Adjusted revenue		
Net revenues (GAAP)	$ 22,813	$ 17,418
Revenue associated with test reports delivered prior periods	(5,335)	(3,160)
Adjusted revenue (Non-GAAP)	$ 17,478	$ 14,258
Adjusted gross margin ($)		
Gross margin (GAAP)	$ 19,785	$ 15,027
Revenue associated with test reports delivered prior periods	(5,335)	(3,160)
Adjusted gross margin (Non-GAAP)	$ 14,450	$ 11,867
Adjusted gross margin (%)		
Gross margin (GAAP)	86.7 %	86.3 %
Revenue associated with test reports delivered prior periods	(4.0)%	(3.1)%
Adjusted gross margin (Non-GAAP)[1]	82.7 %	83.2 %

1. Calculated by dividing adjusted gross margin by adjusted revenue.

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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)" above for further information regarding the Company's use of non-GAAP financial measures

	Three Months Ended March 31,	
	2021	2020
(in thousands)		
Adjusted operating cash flow		
Net cash used in operating activities (GAAP)	$ (3,631)	$ (251)
HHS provider relief funds[1]	(1,882)	—
Adjusted operating cash flow (Non-GAAP)	$ (5,513)	$ (251)

1. Reflects cash activity in the three months ended March 31, 2021 associated with the HHS provider relief funds.

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