CASTLE BIOSCIENCES

The Skin Cancer Diagnostics Company

DecisionDx® DiffDx-Melanoma

Improving diagnostic resolution for the benefit of patient care

October 28, 2020

NASDAQ: CSTL

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 our anticipated milestones, including the timing of expected local coverage determinations for our products, estimated total addressable market attributable to our pipeline products, the advancement of our strategic objectives, the anticipated commercial availability of DecisionDx DiffDx-Melanoma and the ability of DecisionDx DiffDx-Melanoma to add diagnostic clarity and confidence for dermatopathologists and help dermatologists better understand the clinical implications for more informed patient care. 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 and our ability to maintain compliance with the covenants in our debt facility, the timing and amount of revenue we are able to recognize in a given fiscal period, unexpected delays in planned launch of our pipeline products, the level and availability of reimbursement for our products, our ability to manage our anticipated growth and the risks set forth in our Annual Report on Form 10-K for the year ended December 31, 2019, 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.

Wednesday, October 28, 2020	*Welcome and Company Overview* 4:30pm-4:45pm	Derek Maetzold, President & CEO
	Difficult-to-Diagnose Lesions & DecisionDx DiffDx-Melanoma 4:45pm-4:55 pm	Sarah I. Estrada, MD, FCAP Laboratory Director, Affiliated Dermatology®
	DecisionDx DiffDx-Melanoma 4:55pm-5:05pm	Matthew Goldberg, MD Medical Director
	Summary 5:05pm-5:15pm	Derek Maetzold
	Q & A 5:15pm-5:30pm	Castle Management & Dr. Estrada

CASTLE BIOSCIENCES
The Skin Cancer Diagnostics Company

Derek Maetzold
Founder, President & CEO

Welcome and Company Overview

CASTLE BIOSCIENCES
The Skin Cancer Diagnostics Company

Castle Biosciences Attendees

Name	Prior Experience
Derek Maetzold ***Founder, Director, President and CEO***	Derek J. Maetzold founded Castle Biosciences in September 2007 and has served as our President and Chief Executive Officer and as a member of our board of directors since inception. Previously, Mr. Maetzold held leadership roles at Encysive Pharmaceuticals, Schering-Plough Corporation (now Merck), Integrated Communications, Amylin Pharmaceuticals and Sandoz Pharmaceuticals (now Novartis).
Frank Stokes ***Chief Financial Officer***	Frank Stokes has served as our Chief Financial Officer since December 2017. From January 2017 to December 2017, Mr. Stokes served as Chief Financial Officer of Hammock Pharmaceuticals. From May 2011 to December 2016, Mr. Stokes served as a Managing Director of Leerink Swann (now SVB Leerink). Mr. Stokes also held positions as a Managing Director at Robert W. Baird & Co. Incorporated and Wachovia Securities, LLC. While at SVB Leerink and Robert W. Baird & Co., Mr. Stokes led life sciences, tools and diagnostics sector investment banking efforts, and managed financings and mergers and acquisitions transactions.
Bernhard Spiess ***Chief Business Officer***	Bernhard E. Spiess has served as our Chief Business Officer since September 2019, previously serving as our Chief Operating Officer from May 2016 to September 2019. From April 1997 to April 2016, Mr. Spiess held various positions with Beckman Coulter, Inc., a manufacturer of biomedical testing instrument systems, tests and supplies, including as Vice President, Strategic Marketing, Blood Virus & Infectious Diseases from February 2015 to April 2016, and as Vice President, Marketing, Molecular Diagnostics from April 2008 to February 2015.
Toby Juvenal ***Chief Commercial Officer***	Toby Juvenal has served as our Senior Vice President, Sales since January 2018, previously serving as our Vice President of Sales & Marketing since October 2008, when he joined the Company as one of three initial employees. Mr. Juvenal has over 28 years of sales, sales management, and managed care experience in the pharmaceutical, biotechnology and diagnostics industries.
Kristen Oelschlager, RN, CHC ***Chief Operations Officer***	Kristen Oelschlager has served as our Senior Vice President, Clinical Operations since January 2018, previously serving as our Vice President, Clinical Operations from 2013 to 2018, and as our Executive Director of Operations, when she joined the company in 2008 as one of three initial employees. Ms. Oelschlager brought more than 15 years of experience in clinical nursing, clinical operations services, and clinical research to her position.
Robert Cook, PhD ***Senior Vice President, Research & Development***	Bob Cook has served as our Vice President, Research & Development since July 2019, and previously served as our Vice President, Medical Affairs and R&D from April 2018 to July 2019, Executive Director, R&D from June 2015 to April 2018, and Manager of Scientific Relations from February 2011 to June 2015. Dr. Cook joined Castle Biosciences following a postdoctoral fellowship at Baylor College of Medicine where he focused on the genetic regulation of rare ovarian granulosa cell tumors. In his current position, Dr. Cook oversees research and development at Castle. He previously completed his doctoral work in Biochemistry, Molecular Biology and Cellular Biology at Northwestern University,
Alice Izzo ***Vice President, Marketing***	Alice Izzo has served as our Vice President, Marketing since March 2018, previously serving as our Executive Director, Marketing since joining the company in September 2013. Prior to Castle, Ms. Izzo held various leadership positions at Amylin Pharmaceuticals, including Vice President of Corporate Affairs.
Matthew Goldberg, MD ***Medical Director***	Dr. Matthew Goldberg has served as our Medical Director since August 2020. Prior to joining Castle, Dr. Goldberg was an Assistant Professor in Dermatology and Pathology at the Icahn School of Medicine at Mount Sinai in New York and retains his affiliation as an Assistant Clinical Professor of Dermatology. Before joining the Mount Sinai Dermatology faculty, Dr. Goldberg directed Dermatopathology education for the MedStar Georgetown/Washington Hospital Center dermatology residency program. Dr. Goldberg is board certified in dermatology and dermatopathology.
Camilla Zuckero ***Executive Director, Investor Relations***	Camilla Zuckero has served as our Executive Director, Investor Relations, since October 2019. Prior to joining Castle, Ms. Zuckero was responsible for Global Investor Relations and External Communications at Sysco Corporation. Prior to that, she led Investor Relations and Corporate Communications at Opexa Therapeutics.

Sarah I. Estrada, M.D., FCAP

Dr. Estrada is a native of Phoenix and works as a dermatopathologist and Laboratory Director at Affiliated Dermatology in Scottsdale. She attended medical school at Tulane University Medical Center, where she graduated in the top 10 percent of her class. She then completed an Anatomic and Clinical Pathology residency at St. Joseph's Hospital and Medical Center in Phoenix, followed by a dermatopathology fellowship at the Medical University of South Carolina. She has been practicing dermatopathology for 14 years and has developed a special interest in melanocytic lesions. She has personally diagnosed over 300,000 skin biopsies, including over 10,000 melanomas and difficult melanocytic lesions. In addition, through her work with Castle Biosciences, Inc., she has reviewed approximately 30,000 cases of melanoma from institutions across the country. As such, she is passionate about diagnostic accuracy in melanocytic pathology and has long supported the use of emerging technologies to increase diagnostic concordance.

Castle Biosciences

Innovators in Proprietary Gene Expression Profile Tests for Dermatologic Cancers

Innovative Products

Evidence Development

Strong Financials

Improving Health Outcomes Of Patients With Skin Cancer Through Innovative, Clinically Actionable, Cost-Effective Diagnostics

2Q2020: Strong Financials

	2Q20	2Q19	**Six months ended 6/30/20**	Six months ended 6/30/19
Revenue	**$12.7M**	$10.7M	**$30.1**	$19.5M
DecisionDx-Melanoma reports	**3,008**	3,691	**7,582**	6,923
DecisionDx-UM reports	**306**	376	**667**	736
Operating Cash Flow	**$13.5M**	$0.5M	**$13.3M**	$1.8M
Adj. Operating Cash Flow[1]	**$3.3M**	$0.5M	**$3.0M**	$1.8M
Gross Margin	**83.1%**	81.4%	**84.9%**	81.5%
Cash & Cash Equivalents			**$179.8M (as of 6/30/20)**	$17.5M (as of 6/30/19)

[1]See Non-GAAP reconciliations at the end of this presentation.

Castle's 2020 dermatological cancer products target an estimated $2.0B U.S. total addressable market[1]

	MELANOMA	SQUAMOUS CELL CARCINOMA	SUSPICIOUS PIGMENTED LESIONS
INITIAL CASTLE ADDRESSABLE MARKET[2]	**~130,000 patients** classified as Stage I, II or III **~$540M Estimated U.S. TAM**	**~200,000 patients** present with high-risk features **~$820M Estimated U.S. TAM**	**~300,000 patients** with an indeterminant biopsy **~$600M Estimated U.S. TAM**
CSTL's PROPRIETARY GENE EXPRESSION PROFILE TEST:	DecisionDx MELANOMA	DecisionDx-SCC	DecisionDx® DiffDx-Melanoma

[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.

Our main focus is serving the skin cancer market

DecisionDx-SCC is being launched into existing relationships

Indication / Test outcome	Trade Name	Commercial Status	Reimbursement Status	Peer-Reviewed Publications	Primary Customers	Initial Launch Targets
Cutaneous Melanoma / Risk of metastasis	DecisionDx MELANOMA	Available	MCR, MCRA Commercial – in process	26	Derms (including Mohs), Surgeons	
Cutaneous Squamous Cell Carcinoma / Risk of metastasis	DecisionDx·SCC	Available	Expected draft LCD in 2021	4	Derms (including Mohs)	~4,200 current customers[1]
Suspicious Pigmented Lesions / For difficult-to-diagnose pigmented lesions	DecisionDx® DiffDx-Melanoma	Expected November 2020	Expected draft LCD in 2021	2*	Dermpaths, Derms	~1,900 current dermpath customers[2]

[1]Clinicians who ordered DecisionDx-Melanoma in LTM (as of 6/30/2020)
[2]Pathologists who provided clinical specimens for DecisionDx-Melanoma in LTM (as of 6/30/2020)
*Two manuscripts accepted.
MCR = Medicare. MCRA = Medicare Advantage; current customer estimates based on LTM.

Sarah I. Estrada, M.D., FCAP
Laboratory Director, Affiliated Dermatology®

Difficult-to-Diagnose Lesions & DecisionDx DiffDx-Melanoma

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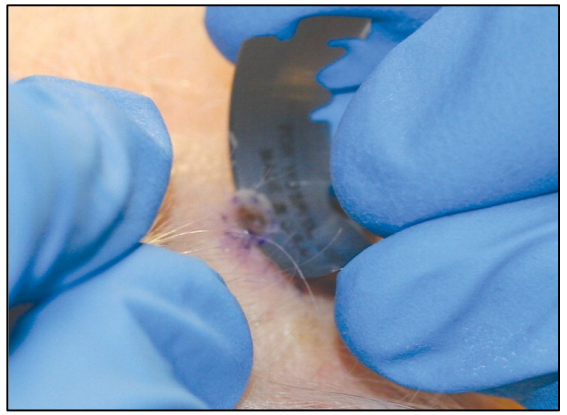
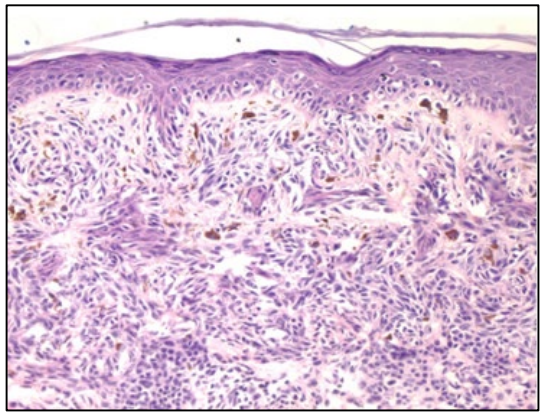
Dermatopathologists and dermatologists work together to diagnose melanoma

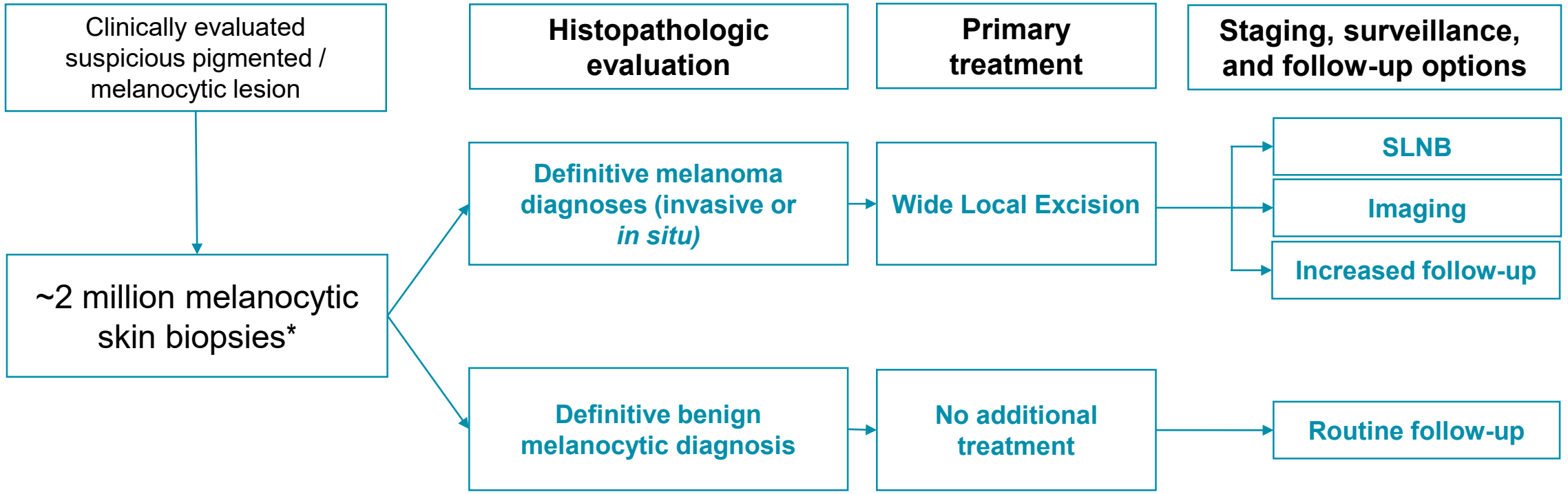
Dermatologist		Dermatopathologist	Dermatologist
A suspicious pigmented lesion is examined by a doctor or dermatologist by visual inspection and/or with a dermatoscope.	If warranted, the lesion is biopsied.	Lesion is examined via microscope by a dermatopathologist or pathologist.	If the lesion contains a malignant melanocytic proliferation, **the diagnosis is melanoma.**





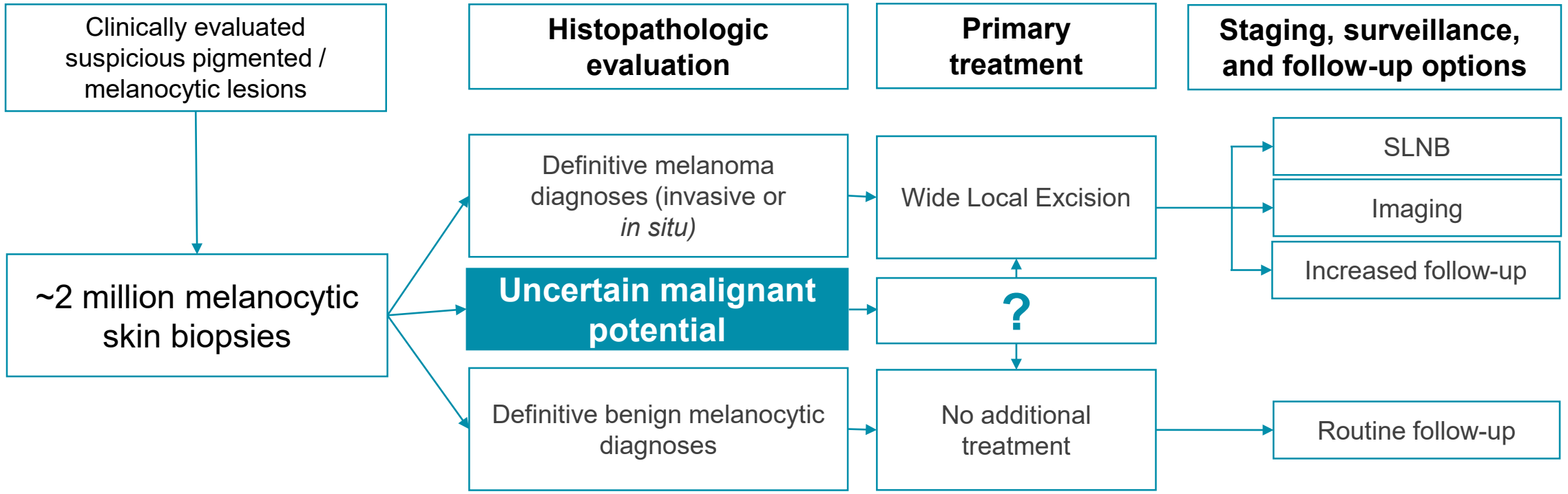
Of the approximately 2 million annual pigmented biopsies, Castle estimates approximately 300,000 are difficult-to-diagnose

A definitive diagnosis of melanoma or a benign melanocytic lesion directs specific treatment plans

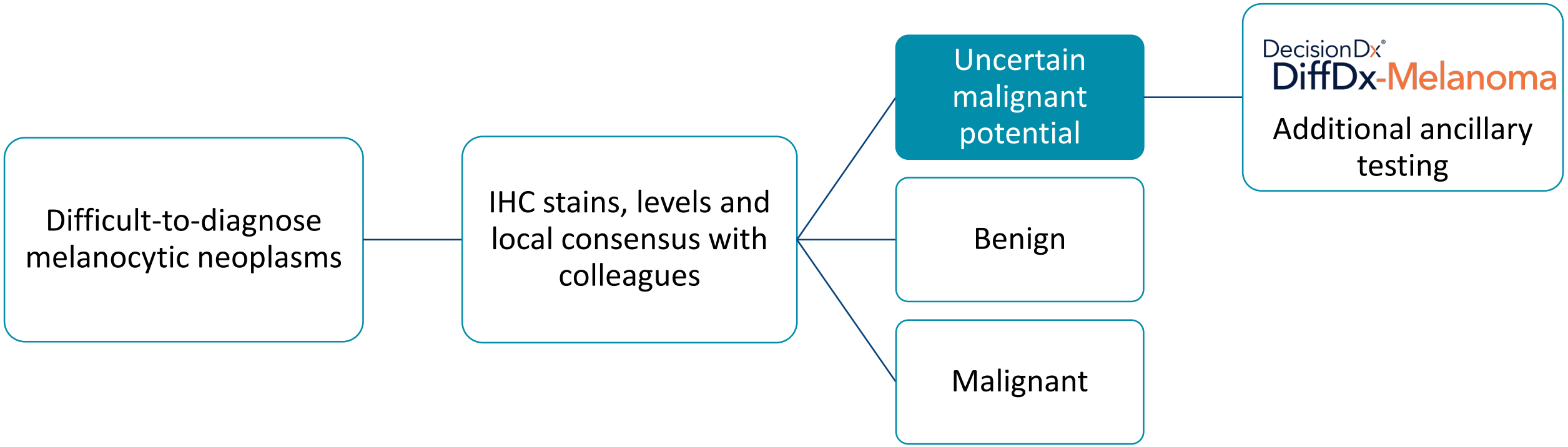


* In the U.S. annually

The Clinical Issue: Uncertainty creates an over- or under-treatment dilemma



DecisionDx DiffDx-Melanoma is designed for use following immunohistochemistry (IHC), levels and local consensus



The unmet need in patients with a difficult-to-diagnose pigmented lesion

The Clinical Problem

A clinical hurdle for dermatopathology is the accurate diagnosis of difficult-to-diagnose melanocytic neoplasms.

Of the estimated 2 million suspicious pigmented lesions biopsied annually in the U.S., approximately 300,000 of those cannot be classified with confidence as either benign tissue or melanoma through traditional histopathology methods.

These difficult-to-diagnose lesions are commonly sent for second opinions to expert dermatopathologists who have more experience with challenging cases; however, the nature of many lesions remains ambiguous with discordant rates of lesions in this category of 25-43% (Elmore et al., 2017).

Undertreatment can lead to tumor recurrence or spread and increase of melanoma specific mortality. Overtreatment can impact patient quality of life (adverse events / increased morbidity) and create unnecessary healthcare costs.

DecisionDx DiffDx-Melanoma

Designed to improve diagnostic resolution for the benefit of patient care

Addressing the Clinical Problem

DecisionDx DiffDx-Melanoma is designed to provide a highly accurate, object result in order to aid dermatopathologists in characterizing difficult-to-diagnose melanocytic lesions. Sensitivity= 99.1%, Specificity= 94.3%

Utilizing machine-learning (AI) to obtain improved accuracy metrics and substantially reduced intermediate-risk zone, DecisionDx DiffDx-Melanoma has been demonstrated to provide a definitive result in ≥96% of lesions submitted for testing with a 96% technical success rate.

DecisionDx DiffDx-Melanoma classifies these lesions as: benign (gene expression profile suggestive of benign neoplasm), intermediate-risk (gene expression profile cannot exclude malignancy) or malignant (gene expression profile suggestive of melanoma) and includes more of the difficult-to-diagnose melanocytic lesion subtypes.

Interpreted in the context of other clinical, laboratory and histopathologic information, DecisionDx DiffDx-Melanoma is designed to add diagnostic clarity and confidence for dermatopathologists, while helping dermatologists deliver more informed patient management plans.

Estrada et al. (2020, in press) *J Cut Med SKIN*

Matthew Goldberg, MD
Medical Director

DecisionDx®
DiffDx-Melanoma

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DecisionDx DiffDx-Melanoma development goals

Leveraging our artificial intelligence-based development process

Applied deep learning	Utilized neural networks to refine the pattern recognition-based algorithm with the final gene set

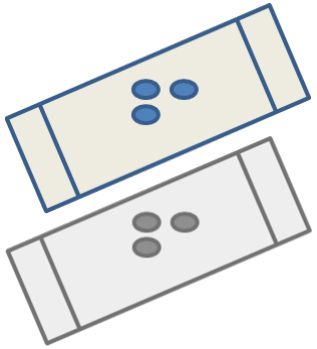
With the goal of maintaining or improving accuracy while doing the following:

Lowering the rate of unactionable results	Lowering the technical failure rate	Including more subtypes of lesions with uncertain malignant potential

Our results:

Demonstrated as an objective test with a high level of accuracy, high technical success rate, low intermediate-risk and inclusion of a variety of lesions with uncertain malignant potential

Castle's discovery to validation approach



Archival benign and malignant samples with concordant diagnoses

200
Benign

216
Malignant

Quantitative RT-PCR performed on training set samples to evaluate gene expression levels.

76
Genes

32+3
Genes

76 genes were used in discovery step. As a result of deep learning techniques and neural network modeling, 32 discriminant and 3 control genes were selected.

Test Result

Benign

Intermediate-risk

Malignant

Lock of final 35-GEP assay (training set) with independent validation in a cohort of 503 samples

Workflow for DecisionDx DiffDx-Melanoma:

Identical process to DecisionDx-Melanoma

Diagnostically challenging melanocytic lesion

Dermatopathologist
OR
Dermatology clinician orders

DecisionDx® DiffDx-Melanoma

FFPE tissue

RNA isolation

RT

cDNA generation and amplification

Open array card
32 discriminant gene targets and 3 control genes

qPCR

Analysis of GEP with a proprietary AI algorithm to determine risk

Benign
Suggestive of benign neoplasm

Intermediate-Risk
Cannot exclude malignancy

Malignant
Suggestive of melanoma

Published evidence to support clinician adoption and payor adoption

Discovery and Development

416 subjects

Estrada et al. (2020) *J Cut Med SKIN*

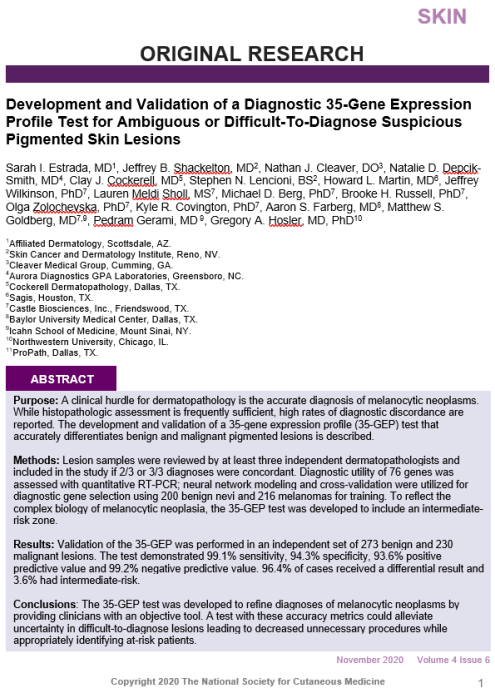
Validation

503 subjects

Estrada et al. (2020) *J Cut Med SKIN*

Utility

Farberg et al. (2020) *J Cut Med SKIN*



SKIN

ORIGINAL RESEARCH

Development and Validation of a Diagnostic 35-Gene Expression Profile Test for Ambiguous or Difficult-To-Diagnose Suspicious Pigmented Skin Lesions

Sarah I. Estrada, MD[1], Jeffrey B. Shackelton, MD[2], Nathan J. Cleaver, DO[3], Natalie D. Depcik-Smith, MD[4], Clay J. Cockerell, MD[5], Stephen N. Lencioni, BS[2], Howard L. Martin, MD[6], Jeffrey Wilkinson, PhD[7], Lauren Meldi Sholl, MS[7], Michael D. Berg, PhD[7], Brooke H. Russell, PhD[7], Olga Zolochevska, PhD[7], Kyle R. Covington, PhD[7], Aaron S. Farberg, MD[8], Matthew S. Goldberg, MD[7,9], Pedram Gerami, MD[9], Gregory A. Hosler, MD, PhD[10]

[1]Affiliated Dermatology, Scottsdale, AZ.
[2]Skin Cancer and Dermatology Institute, Reno, NV.
[3]Cleaver Medical Group, Cumming, GA.
[4]Aurora Diagnostics GPA Laboratories, Greensboro, NC.
[5]Cockerell Dermatopathology, Dallas, TX.
[6]Sagis, Houston, TX.
[7]Castle Biosciences, Inc., Friendswood, TX.
[8]Baylor University Medical Center, Dallas, TX.
[9]Icahn School of Medicine, Mount Sinai, NY.
[10]Northwestern University, Chicago, IL.
[11]ProPath, Dallas, TX.

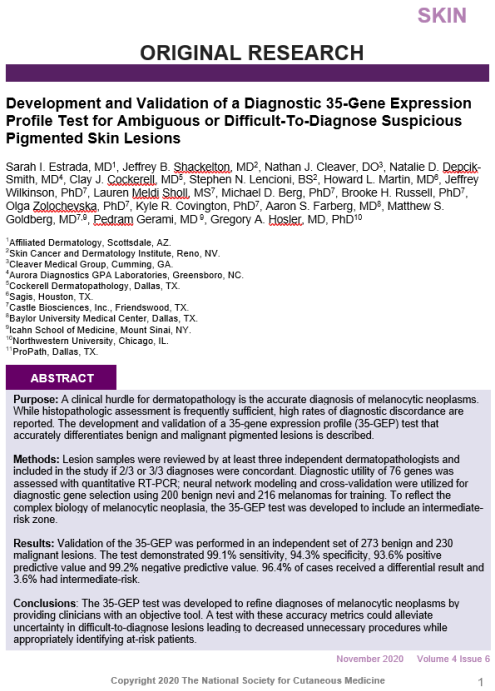
ABSTRACT

Purpose: A clinical hurdle for dermatopathology is the accurate diagnosis of melanocytic neoplasms. While histopathologic assessment is frequently sufficient, high rates of diagnostic discordance are reported. The development and validation of a 35-gene expression profile (35-GEP) test that accurately differentiates benign and malignant pigmented lesions is described.

Methods: Lesion samples were reviewed by at least three independent dermatopathologists and included in the study if 2/3 or 3/3 diagnoses were concordant. Diagnostic utility of 76 genes was assessed with quantitative RT-PCR; neural network modeling and cross-validation were utilized for diagnostic gene selection using 200 benign nevi and 216 melanomas for training. To reflect the complex biology of melanocytic neoplasia, the 35-GEP test was developed to include an intermediate-risk zone.

Results: Validation of the 35-GEP was performed in an independent set of 273 benign and 230 malignant lesions. The test demonstrated 99.1% sensitivity, 94.3% specificity, 93.6% positive predictive value and 99.2% negative predictive value. 96.4% of cases received a differential result and 3.6% had intermediate-risk.

Conclusions: The 35-GEP test was developed to refine diagnoses of melanocytic neoplasms by providing clinicians with an objective tool. A test with these accuracy metrics could alleviate uncertainty in difficult-to-diagnose lesions leading to decreased unnecessary procedures while appropriately identifying at-risk patients.



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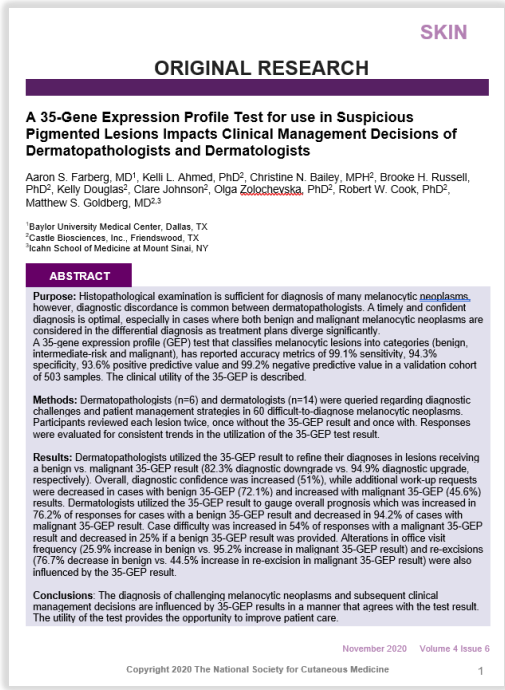


SKIN

ORIGINAL RESEARCH

A 35-Gene Expression Profile Test for use in Suspicious Pigmented Lesions Impacts Clinical Management Decisions of Dermatopathologists and Dermatologists

Aaron S. Farberg, MD[1], Kelli L. Ahmed, PhD[2], Christine N. Bailey, MPH[2], Brooke H. Russell, PhD[2], Kelly Douglas[2], Clare Johnson[2], Olga Zolochevska, PhD[2], Robert W. Cook, PhD[2], Matthew S. Goldberg, MD[2,3]

[1]Baylor University Medical Center, Dallas, TX
[2]Castle Biosciences, Inc., Friendswood, TX
[3]Icahn School of Medicine at Mount Sinai, NY

ABSTRACT

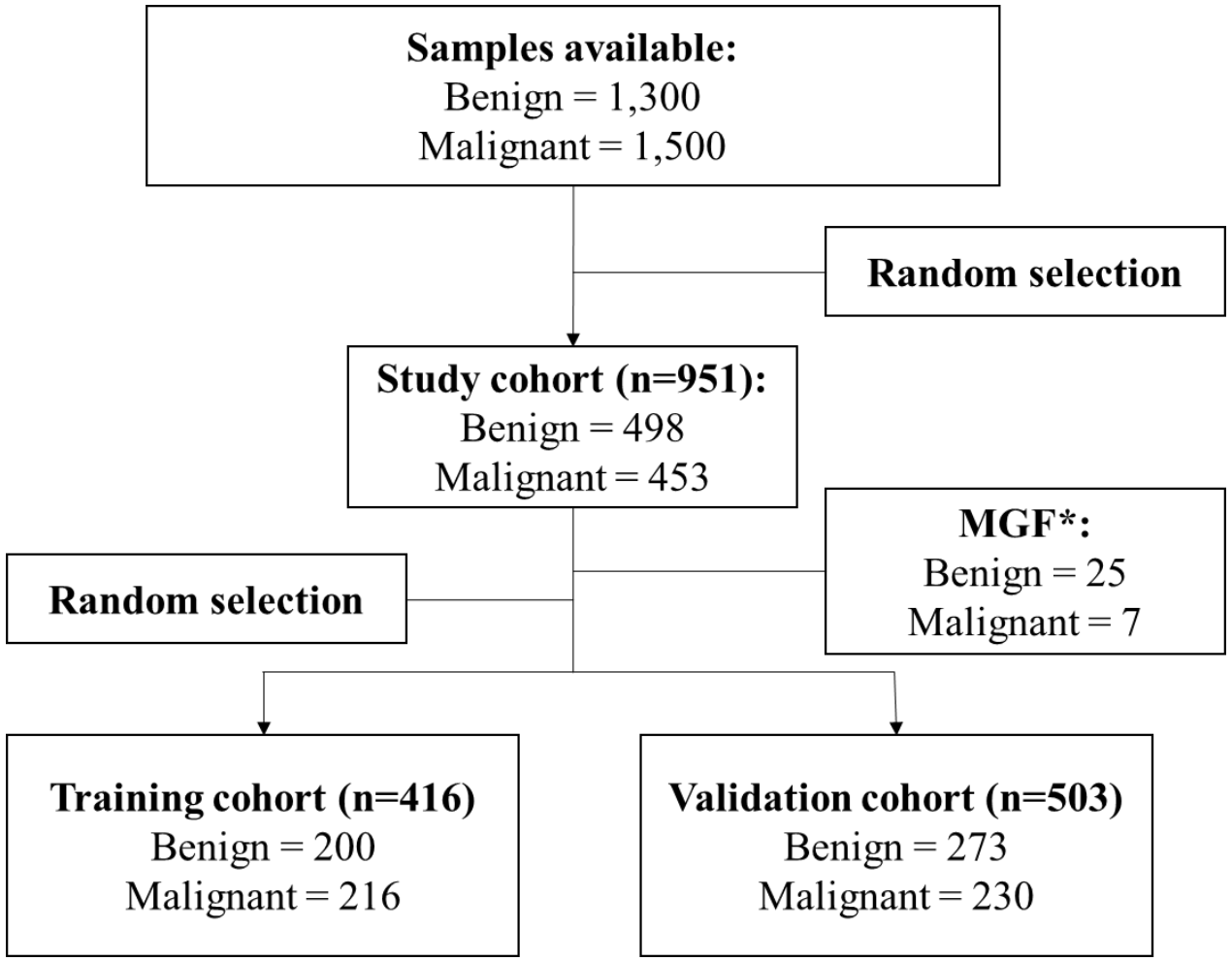
Purpose: Histopathological examination is sufficient for diagnosis of many melanocytic neoplasms, however, diagnostic discordance is common between dermatopathologists. A timely and confident diagnosis is optimal, especially in cases where both benign and malignant melanocytic neoplasms are considered in the differential diagnosis as treatment plans diverge significantly.
A 35-gene expression profile (GEP) test that classifies melanocytic lesions into categories (benign, intermediate-risk and malignant), has reported accuracy metrics of 99.1% sensitivity, 94.3% specificity, 93.6% positive predictive value and 99.2% negative predictive value in a validation cohort of 503 samples. The clinical utility of the 35-GEP is described.

Methods: Dermatopathologists (n=6) and dermatologists (n=14) were queried regarding diagnostic challenges and patient management strategies in 60 difficult-to-diagnose melanocytic neoplasms. Participants reviewed each lesion twice, once without the 35-GEP result and once with. Responses were evaluated for consistent trends in the utilization of the 35-GEP test result.

Results: Dermatopathologists utilized the 35-GEP result to refine their diagnoses in lesions receiving a benign vs. malignant 35-GEP result (82.3% diagnostic downgrade vs. 94.9% diagnostic upgrade, respectively). Overall, diagnostic confidence was increased (51%), while additional work-up requests were decreased in cases with benign 35-GEP (72.1%) and increased with malignant 35-GEP (45.6%) results. Dermatologists utilized the 35-GEP result to gauge overall prognosis which was increased in 76.2% of responses for cases with a benign 35-GEP result and decreased in 94.2% of cases with malignant 35-GEP result. Case difficulty was increased in 54% of responses with a malignant 35-GEP result and decreased in 25% if a benign 35-GEP result was provided. Alterations in office visit frequency (25.9% increase in benign vs. 95.2% increase in malignant 35-GEP result) and re-excisions (76.7% decrease in benign vs. 44.5% increase in re-excision in malignant 35-GEP result) were also influenced by the 35-GEP result.

Conclusions: The diagnosis of challenging melanocytic neoplasms and subsequent clinical management decisions are influenced by 35-GEP results in a manner that agrees with the test result. The utility of the test provides the opportunity to improve patient care.

DecisionDx DiffDx-Melanoma training and validation cohort sample selection



Estrada et al. (2020, in press) *J Cut Med SKIN*

*MGF: Multi-Gene Failure – 3.4%

DecisionDx DiffDx-Melanoma is designed and validated to improve diagnostic resolution for the benefit of patient care

	All ages N=503		Age > 65 years N=178	
	DecisionDx DiffDx-Melanoma	95% CI	DecisionDx DiffDx-Melanoma	95% CI
Sensitivity	99.1%	97.9-100	99.2%	97.6-100
Specificity	94.3%	91.5-97.1	100%	100-100
PPV	93.6%	90.5-96.7	100%	100-100
NPV	99.2%	98.1-100	98.1%	94.3-100
Intermediate-risk result	3.6%		3.4%	
Technical success rate	96%			

Samples that fall in intermediate-risk zone were excluded from the calculation.
PPV – positive predictive value; NPV – negative predictive value; CI – confidence interval.

Estrada et al. (2020, in press) *J Cut Med SKIN*

DecisionDx®
DiffDx-Melanoma

Improving diagnostic resolution for the benefit of patient care

A definitive result from DecisionDx DiffDx-Melanoma in **≥96% of lesions** submitted for testing	Includes multiple subtypes of lesions with uncertain malignant potential	Technical success rate of 96%	5-7 day turn around time/ similar to other ancillary tests	After melanoma diagnosis, clinicians can order DecisionDx-Melanoma; uses same tissue block

Interpreted in the context of other clinical, laboratory and histopathologic information, DecisionDx DiffDx-Melanoma is designed to add diagnostic clarity and confidence for dermatopathologists, while helping dermatologists deliver more informed patient management plans.

Estrada et al. (2020, in press) *J Cut Med SKIN*

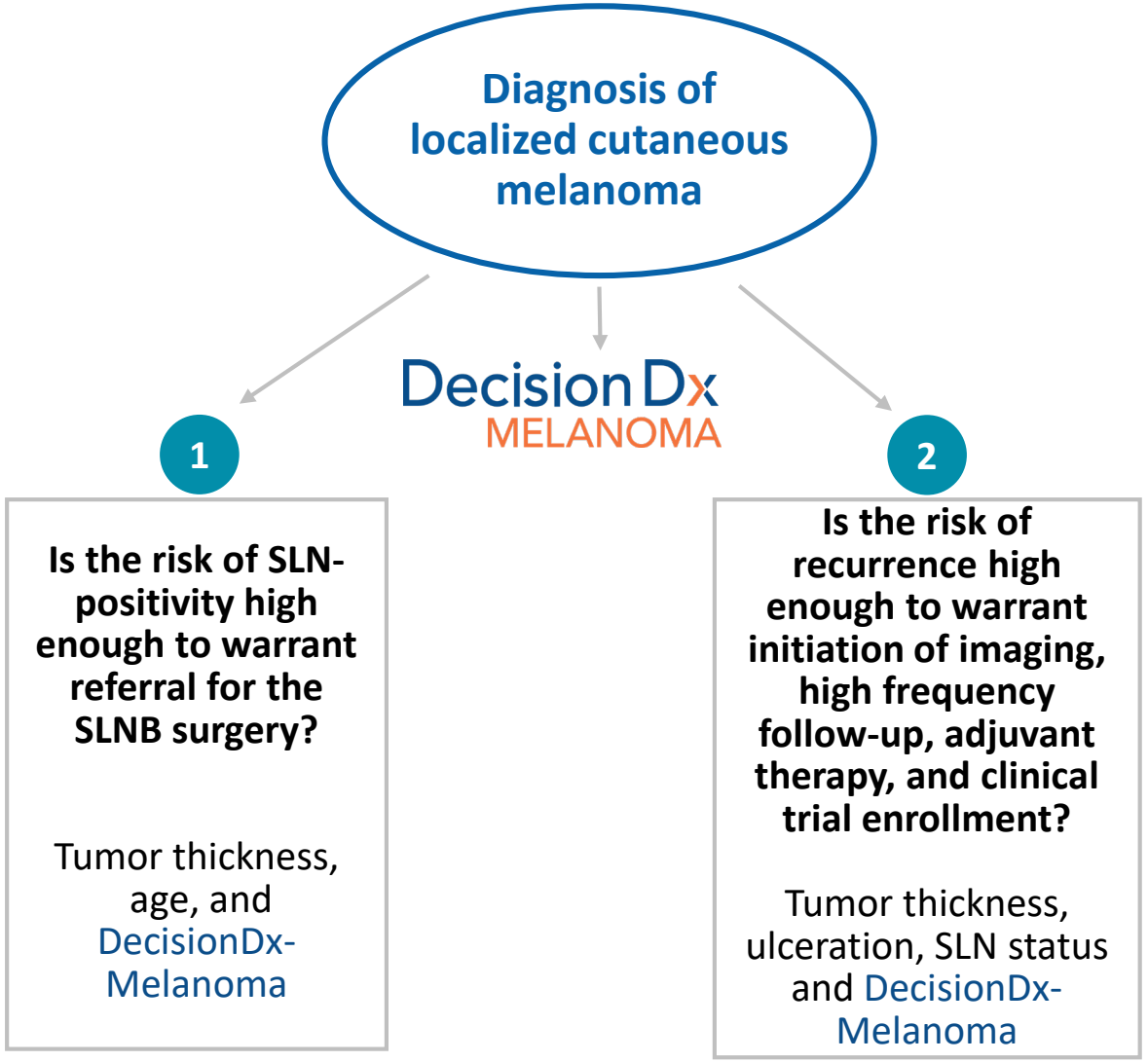
CASTLE BIOSCIENCES

Derek Maetzold
Founder, President & CEO

Summary

CASTLE BIOSCIENCES
The Skin Cancer Diagnostics Company

Once a patient is diagnosed with melanoma, clinicians can utilize Castle's DecisionDx-Melanoma test to aid with two important clinical questions



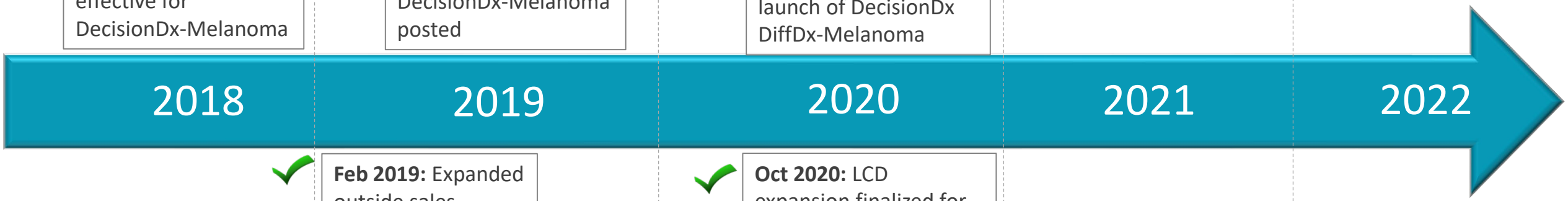
SLN = sentinel lymph node; SLNB = sentinel lymph node biopsy. MCR=Medicare Cost Report.

Source: AJCC v7 *J Clin Oncol* 2009; SEER data release 2017; Morton et al. *N Engl J Med* 2014; Whiteman et al. *J Invest Dermatol* 2015; Shaikh et al. *J Natl Cancer Inst* 2016; Poklepovic and Carvajal. *Oncology* 2018; Sondak and Zager. *Ann Surg Oncol* 2010. Moody et al. *Euro Jrnl Surg Onc* 2017.

Recent achievements and expected future milestones

2020 milestones on track

Continued evidence development for all commercialized products



Dec 2018: Initial LCD effective for DecisionDx-Melanoma

Aug 2019: Expanded draft LCD for DecisionDx-Melanoma posted

Feb 2019: Expanded outside sales territories to 23

July 2019: IPO

Dec 2019: Expanded outside sales territories to 32

Sept 2020: Launch of DecisionDx-SCC

3Q2020: Commercial team expansion

4Q2020: Expected launch of DecisionDx DiffDx-Melanoma

Oct 2020: LCD expansion finalized for DecisionDx-Melanoma, effective date 11/22/20

2H2020: Expected initiation of work on additional dermatology pipeline products

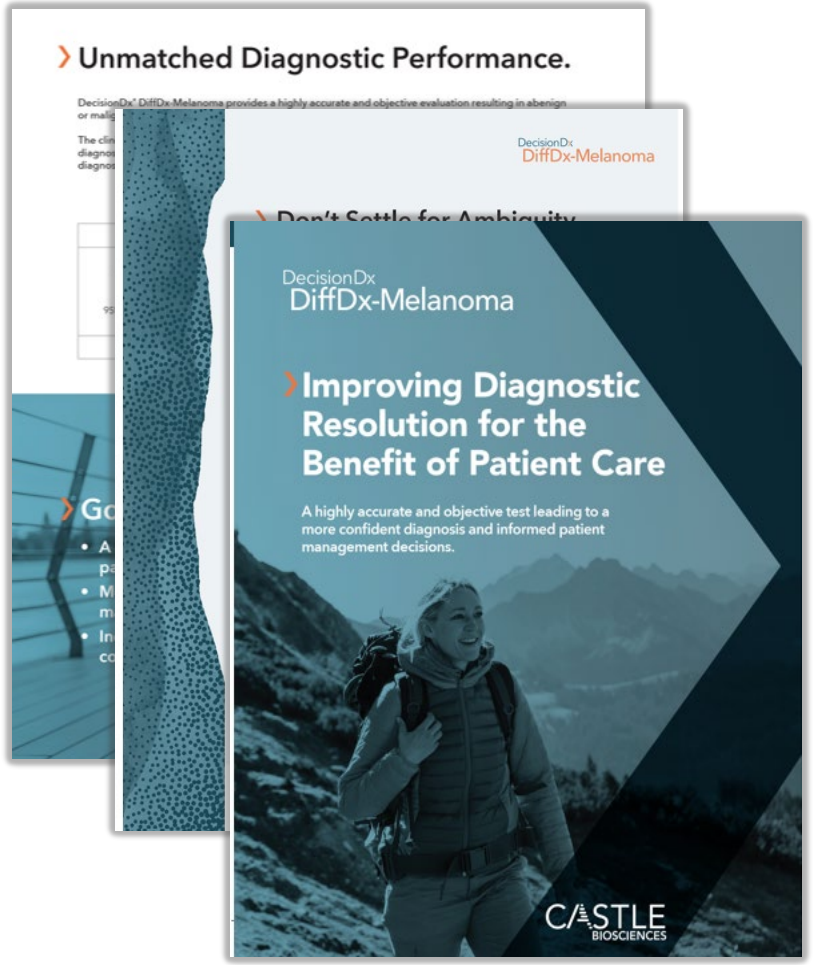
Late 2021: Potential draft LCD for DecisionDx-SCC and DecisionDx DiffDx-Melanoma

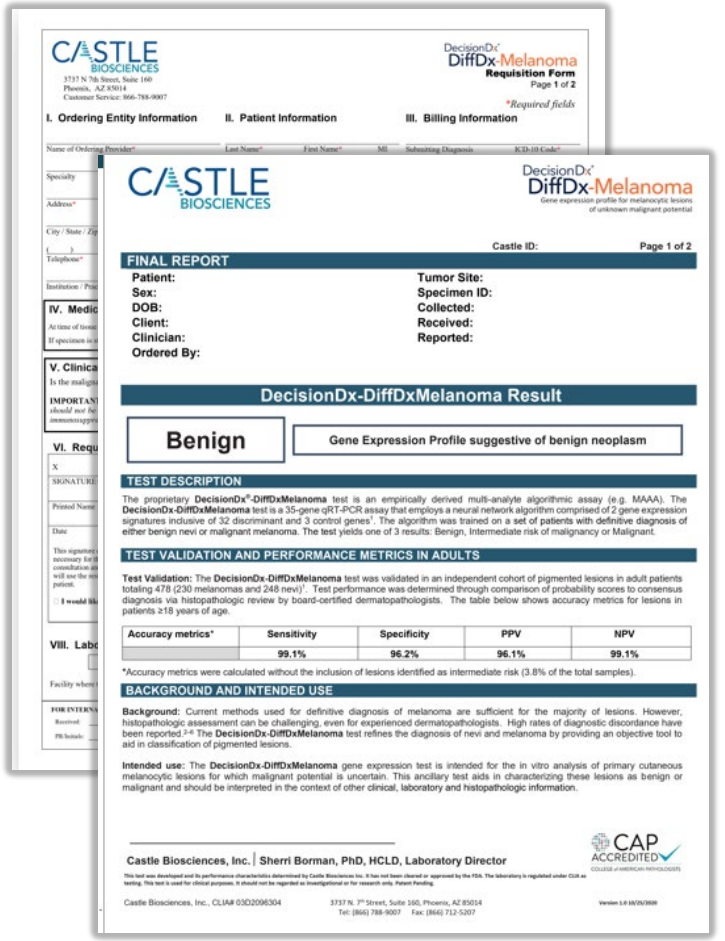
2022: Potential effective LCD for DecisionDx-SCC and DecisionDx DiffDx-Melanoma

✓ = Achieved

DecisionDx DiffDx-Melanoma launch objectives are on track

- Accelerated disease state training
- National Sales Meeting for final training of new commercial team
- Fourth quarter 2020: commercially available





DecisionDx®
DiffDx-Melanoma

Improving diagnostic resolution for the benefit of patient care

To aid dermatopathologists in characterizing **suspicious pigmented lesions**	**~300,000** suspicious pigmented lesions annually; $**600M** U.S TAM[1]	Technical success rate of 96%	2 **peer-reviewed publications**[2] to date	Utilizing **existing relationships within** the dermatologic community (dermpaths, derms)

Interpreted in the context of other clinical, laboratory and histopathologic information, DecisionDx DiffDx-Melanoma is designed to add diagnostic clarity and confidence for dermatopathologists, while helping dermatologists better understand the clinical implications for more informed patient care

[1] based on Castle estimates, [2] accepted manuscripts

CASTLE BIOSCIENCES

Castle's 2020 dermatological cancer products target an estimated $2.0B U.S. total addressable market[1]

	MELANOMA	SQUAMOUS CELL CARCINOMA	SUSPICIOUS PIGMENTED LESIONS
INITIAL CASTLE ADDRESSABLE MARKET[2]	**~130,000 patients** classified as Stage I, II or III **~$540M Estimated U.S. TAM**	**~200,000 patients** present with high-risk features **~$820M Estimated U.S. TAM**	**~300,000 patients** with an indeterminant biopsy **~$600M Estimated U.S. TAM**
CSTL's PROPRIETARY GENE EXPRESSION PROFILE TEST:	DecisionDx MELANOMA	DecisionDx-SCC	DecisionDx® DiffDx-Melanoma

[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.

THANK YOU

CASTLE BIOSCIENCES
The Skin Cancer Diagnostics Company

Use of Non-GAAP Financial Measures (UNAUDITED)

- In this presentation, we use the metric of Adjusted Operating Cash Flow, which is a non-GAAP financial measure and is not calculated in accordance with generally accepted accounting principles in the United States (GAAP). This non-GAAP financial measure reflects adjustments to net cash provided by operating activities to remove the effects of two payments we received associated with government aid to healthcare providers due to COVID-19, which we believe are not indicative of our ongoing operations.

- We use Adjusted Operating Cash Flow internally because we believe this metric provides useful supplemental information in assessing our cash flow performance from our core ongoing business activities by removing the effects of these items on our operating cash flows. We believe this metric is also useful to investors as a supplement to GAAP measures in analyzing the performance of our business. However, this non-GAAP financial measure 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. This non-GAAP financial measure is not meant to be a substitute for net cash 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 this non-GAAP financial measure to the most directly comparable GAAP financial measure are presented on the next slide.

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 June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
(in thousands)				
Adjusted operating cash flow				
Adjusted operating cash flow (Non-GAAP)	$ 3,269	$ 482	$ 3,018	$ 1,770
Receipt of Medicare advance payment[1]	8,350	—	8,350	—
Receipt of HHS provider relief funds[2]	1,882	—	1,882	—
Net cash provided by operating activities (GAAP)	$ 13,501	$ 482	$ 13,250	$ 1,770

1 In April 2020, we received an advance payment of $8.3 million from the Centers for Medicare & Medicaid Service (CMS), which will be applied against future Medicare claims that we submit for reimbursement later in 2020. 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 future claims are submitted for reimbursement and applied against this balance, we will 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).