



Decision Dx^{SCC}

September 2, 2020

NASDAQ:CSTL

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The Skin Cancer Diagnostics Company

**Wednesday,
September 2, 2020**

<i>Welcome and Introductions</i> 4:30pm	Frank Stokes, CFO
<i>Company Overview & Update</i> 4:35pm-4:50pm	Derek Maetzold, President & CEO
<i>Cutaneous Squamous Cell Carcinoma</i> <i>DecisionDx-SCC</i> 4:50pm-5:10 pm	Ashley Wysong, MD University of Nebraska Medical Center, Omaha NE
<i>Summary</i> 5:10pm-5:15pm	Derek Maetzold
<i>Q & A</i> 5:15pm-5:30pm	Castle Management





The Skin Cancer Diagnostics Company

Frank Stokes

CFO

Welcome and Introductions



Castle Biosciences Attendees

Name	Prior Experience
Derek Maetzold <i>Founder, Director, President and CEO</i>	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 <i>Chief Financial Officer</i>	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 <i>Chief Business Officer</i>	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 <i>Chief Commercial Officer</i>	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 <i>Chief Operations Officer</i>	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 <i>Senior Vice President, Research & Development</i>	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 <i>Vice President, Marketing</i>	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 <i>Medical Director</i>	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 <i>Executive Director, Investor Relations</i>	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.

Ashley Wysong, M.D., M.S. University of Nebraska Medical Center, Omaha NE

Dr. Ashley Wysong is the founding Chair and William W. Bruce MD Distinguished Chair of the University of Nebraska Medical Center (UNMC) Department of Dermatology. She earned her medical degree at Duke University School of Medicine, where she was valedictorian. Dr. Wysong completed her M.S. in epidemiology and residency in dermatology at Stanford University, where she also served as chief resident. Her fellowship in procedural dermatology and Mohs micrographic surgery was completed at Scripps Clinic under the direction of Dr. Hugh Greenway in Mohs surgery, Dr. Victor Ross in laser and cosmetic dermatology, and Dr. Leland Housman in veins.



The Skin Cancer Diagnostics Company

Derek Maetzold

Founder, President & CEO

Company Overview and Update



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

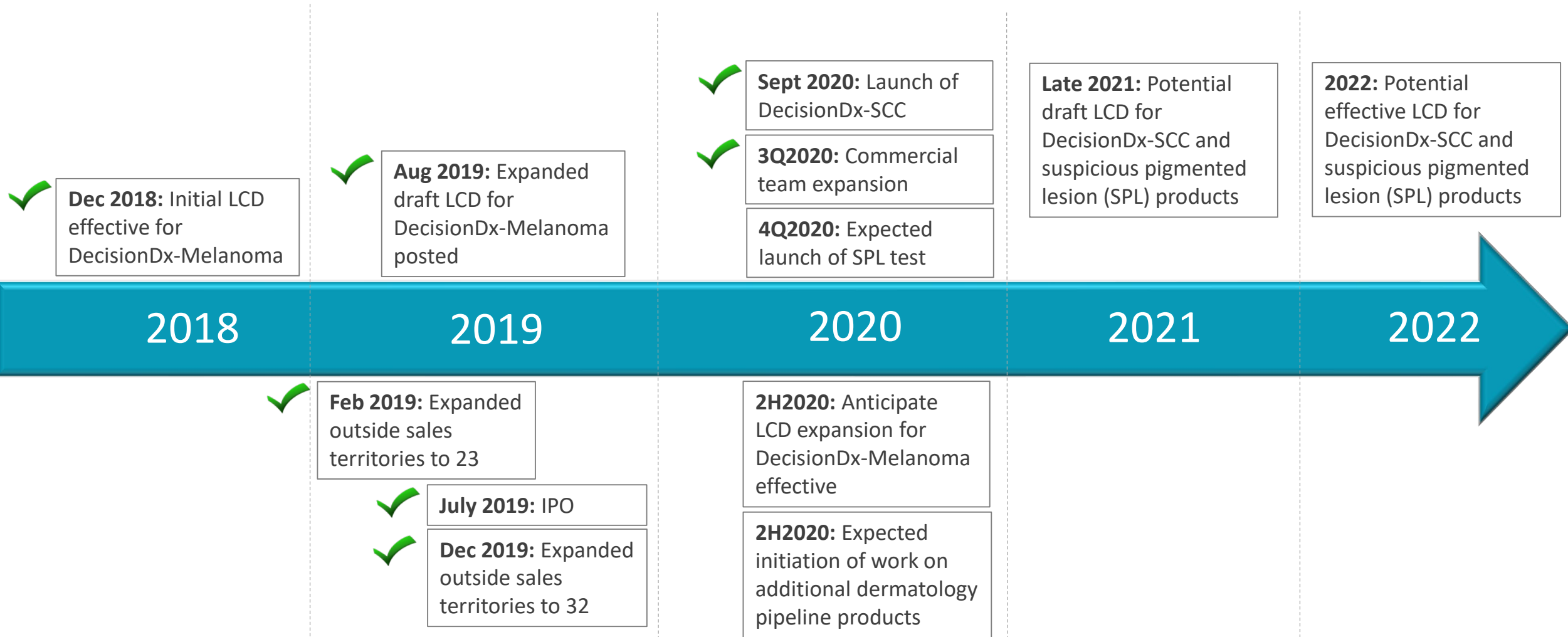
	2Q20	2Q19	Six months ended 6/30/20	Six months ended 6/30/19
Revenue	\$12.7M	\$10.7M	\$30.1	\$19.5M
DecisionDx-Melanoma reports	3,008	3,691	7,582	6,923
DecisionDx-UM reports	306	376	667	736
Operating Cash Flow	\$13.5M	\$0.5M	\$13.3M	\$1.8M
Adj. Operating Cash Flow ¹	\$3.3M	\$0.5M	\$3.0M	\$1.8M
Gross Margin	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)

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

Recent achievements and expected future milestones

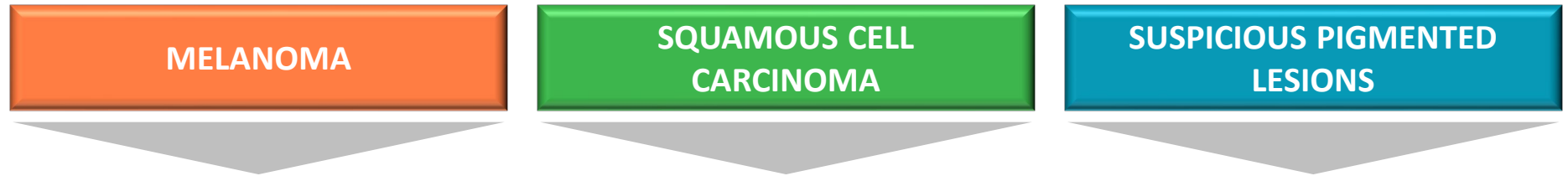
2020 milestones on track

Continued evidence development for all commercialized products



✓ = Achieved

Castle's 2020 dermatological cancer products target an estimated \$2.0B U.S. total addressable market¹



INITIAL CASTLE ADDRESSABLE MARKET²

~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:

Decision Dx
 MELANOMA

Decision Dx-SCC



Name to be announced
 (projected launch: 4Q2020)

¹U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors.

²Annual 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.

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		Available	MCR, MCRA Commercial – in process	26	Derms (including Mohs), Surgeons	
Cutaneous Squamous Cell Carcinoma / Risk of metastasis		Available	Expected draft LCD in 2021	4	Derms (including Mohs)	~4,200 current customers ¹
Suspicious Pigmented Lesions / For difficult to diagnose pigmented lesions	To be announced	Expected Q42020	Expected draft LCD in 2021	0	Dermpaths, Derms	~1,900 current dermpath customers ²

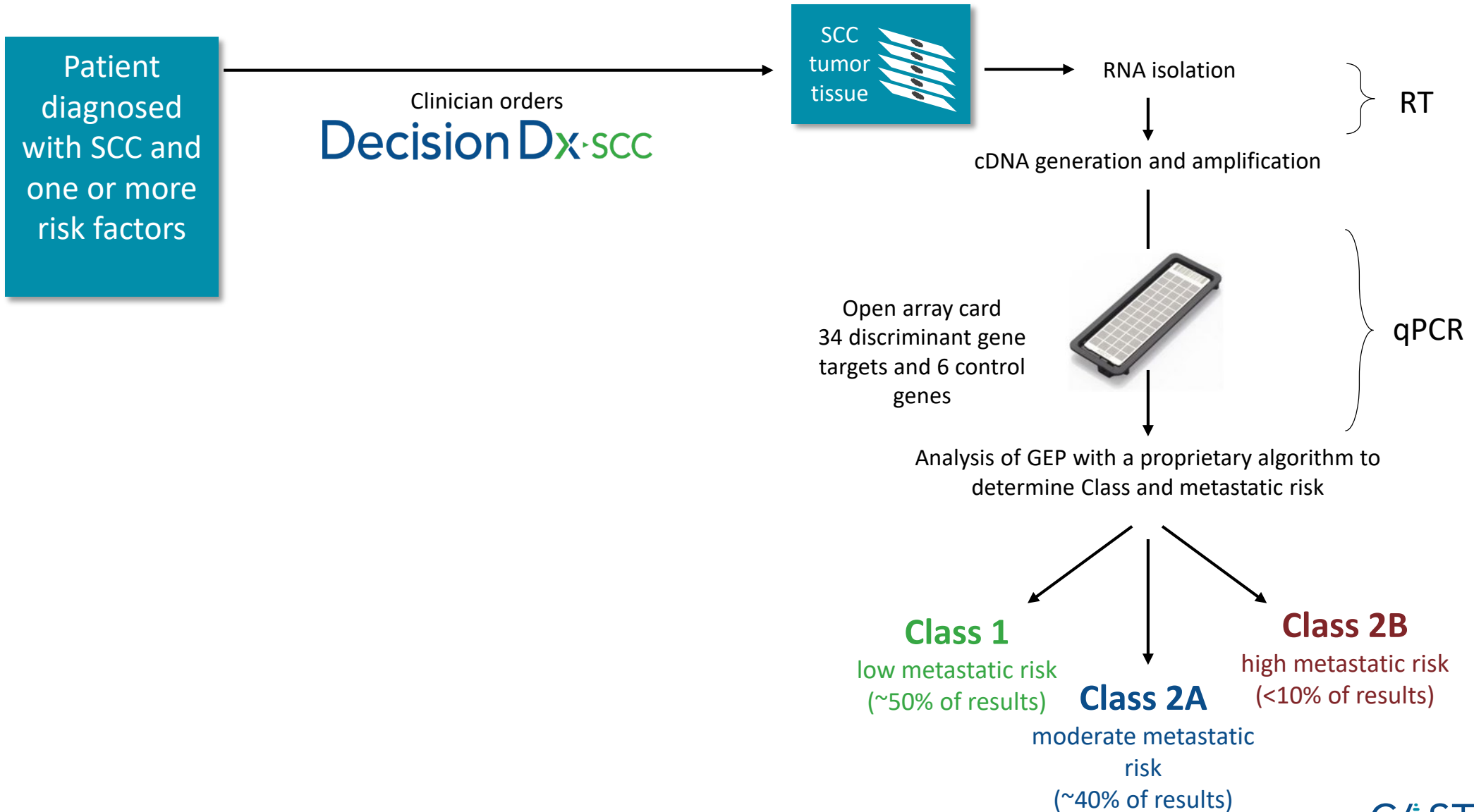
¹Clinicians who ordered DecisionDx-Melanoma in LTM (as of 6/30/2020)

²Pathologists who provided clinical specimens for DecisionDx-Melanoma in LTM (as of 6/30/2020)

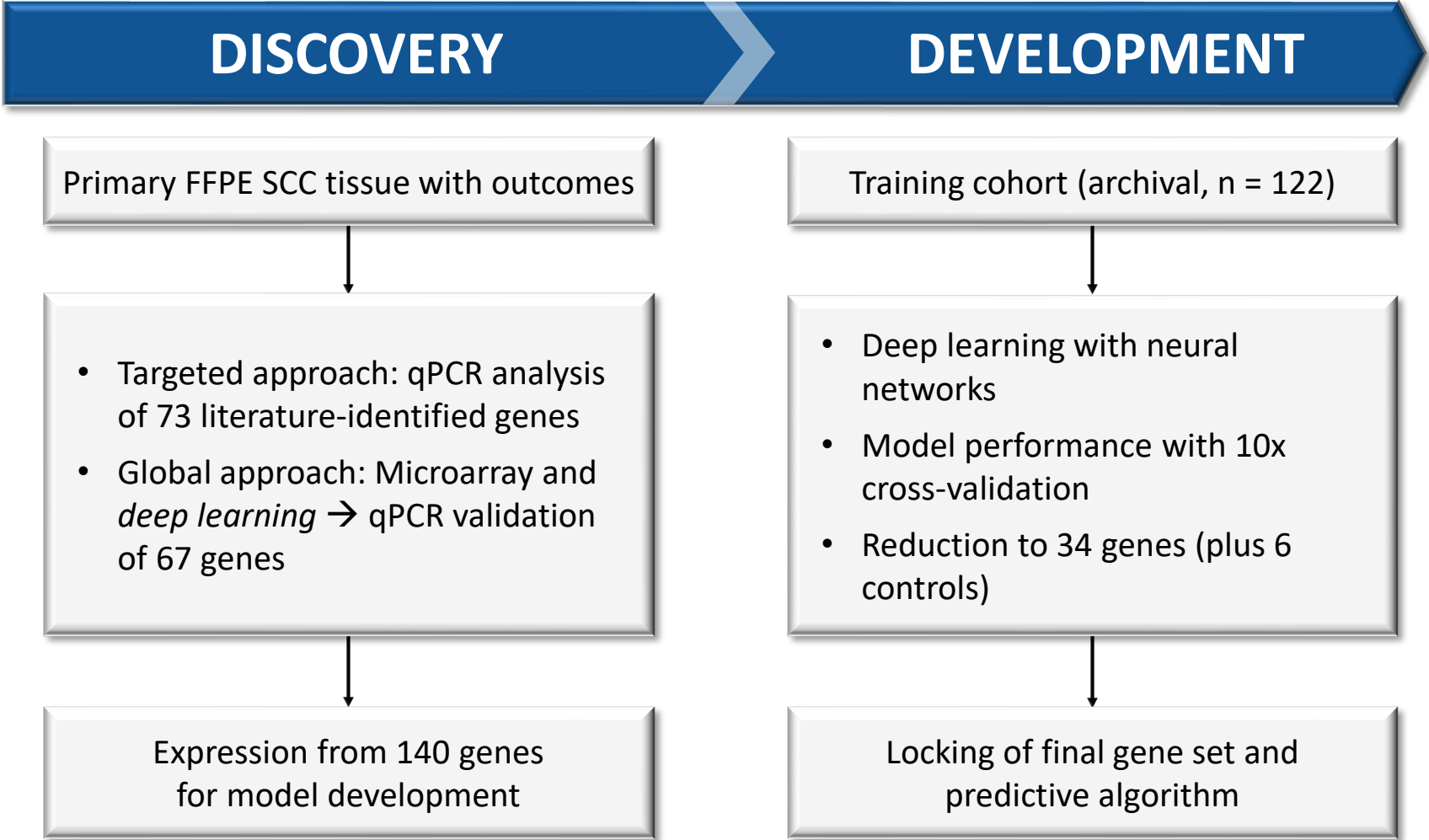
MCR = Medicare. MCRA = Medicare Advantage; current customer estimates based on LTM.

Workflow for DecisionDx-SCC:

Identical process to DecisionDx-Melanoma



Efficient Development: From discovery → validation



Published evidence from >1,100 patients and healthcare providers to support clinician adoption and payor adoption

Discovery and Development

202 subjects

Validation

420 subjects

Utility

564 clinicians

Wysong et al. *JAAD* 2020

Castle Biosciences Discovery Data

Wysong et al. *JAAD* 2020

Castle Biosciences Data on File

Farberg et al. *CMRO* 2020

Litchman et al. *CMRO* 2020

Teplitz et al. *JDD* 2019

Journal Pre-proof

Validation of a 40-Gene Expression Profile Test to Predict Metastatic Risk in Localized High-Risk Cutaneous Squamous Cell Carcinoma

Ashley Wysong, MD, MS, Jason G. Newman, MD, FACS, Kyle R. Covington, PhD, Sarah J. Kurley, PhD, Sherif F. Ibrahim, MD, PhD, Aaron S. Farberg, MD, Anna Bar, MD, Nathan J. Cleaver, DO, Aliy-Khan Somani, MD, PhD, David Panther, MD, David G. Brodland, MD, John Zitelli, MD, Jennifer Toyohara, MD, Ian A. Maher, MD, Yang Xia, MD, Kristin Bibee, MD, Robert Griego, MD, Darrell S. Rigel, MD, Kristen Meldi Plasseraud, PhD, Sarah Estrada, MD, Lauren Meldi Sholl, MS, Clare Johnson, RN, Robert W. Cook, PhD, Chryssyline D. Schmults, MD, MSCE, Sarah T. Aaron, MD, PhD

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CURRENT MEDICAL RESEARCH AND OPINION
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Article ID: 116283



BRIEF REPORT

Integrating gene expression profiling into NCCN high-risk cutaneous squamous cell carcinoma management recommendations: impact on patient management

Aaron S. Farberg^{1,2}, Mary A. Hall¹, Leah Douglas¹, Kyle R. Covington¹, Sarah J. Kurley¹, Robert W. Cook¹ and Scott M. Dinehart¹

¹Dermatology, Kahn School of Medicine at Mount Sinai, New York, NY, USA; ²Dermatology, Arkansas Dermatology Skin Cancer Center, Little Rock, AR, USA; ³Research and Development, Castle Biosciences, Inc, Greenwood, TX, USA; ⁴Dermatology, Baylor College of Medicine, Houston, TX, USA

OBJECTIVE: To integrate gene expression profiling into the management of high-risk cutaneous squamous cell carcinoma (cSCC) with the National Comprehensive Cancer Network (NCCN) guidelines to improve risk-aligned management recommendations.

Methods: A cohort of 300 NCCN-defined high-risk cSCC patients, along with the American Joint Committee on Cancer (AJCC) T stage, Brigham and Women's Hospital (BWH) T stage, and known patient outcomes were analyzed. Classifications using a validated 40-gene expression profile (40-GEP) test and T stage were applied to NCCN patient management guidelines. Risk-directed patient management recommendations within the NCCN guidelines framework were aligned based on risk for metastasis.

Results: Of the 300 NCCN high-risk cSCC patients, 139 (46%) were 40-GEP Class 1 and AJCC T1-T2, and 172 (57%) were Class 1 and BWH T1-T2, indicating low risk for metastasis and, thereby, suggesting low management intensity. The 40-GEP integration suggested high intensity management for only 24 (8%) patients (all Class 2B), and moderate intensity management for the remainder of the cohort.

Conclusions: The 40-GEP test can be integrated within existing NCCN guideline recommendations for managing cSCC patients to help refine risk-directed management decisions. High intensity management was deemed risk appropriate for a small subpopulation (8%). This study demonstrates that the 40-GEP test, in combination with T stage, has clinical utility to impact patient management decisions in NCCN high-risk cSCC for improving risk-aligned management within the NCCN guidelines framework.

Introduction
Cutaneous squamous cell carcinoma (cSCC) is the second most common form of skin cancer after basal cell carcinoma.¹ It occurs in approximately one million people in the U.S. and the incidence is rising, partly due to enhanced detection methods and an aging population.¹⁻⁴ Overall, approximately 6% of cSCC patients develop regional or distant metastatic lesions and survival rates are low for those who do develop metastasis.^{1,2,5-11} The number of deaths from cSCC, a large proportion of which are preceded by metastasis, has been estimated to rival that from melanoma.¹² Therefore, accurate prediction of risk is critical to potentially for optimal patient management and, ultimately, to essential for improved outcomes.

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CURRENT MEDICAL RESEARCH AND OPINION
<https://doi.org/10.1002/cmro.2020.116283>
Article ID: 116283



BRIEF REPORT

A prognostic 40-gene expression profiling test on clinical management decisions for high-risk cutaneous squamous cell carcinoma

Graham H. Litchman¹, Alison L. Fitzgerald¹, Sarah J. Kurley¹, Robert W. Cook¹ and Darrell S. Rigel²

¹National Society for Cutaneous Medicine, New York, NY, USA; ²Castle Biosciences, Inc, Greenwood, TX, USA; ³NYU Grossman School of Medicine, New York, NY, USA

OBJECTIVE: To determine how results from a prognostic 40-gene expression profiling (40-GEP) test would impact clinician management decisions and how their choices would align with a National Comprehensive Cancer Network (NCCN) compliant, risk-directed management plan for high-risk cutaneous squamous cell carcinoma (cSCC).

Methods: Clinicians attending a national dermatology conference were presented with 40-GEP test validation data. They were asked to rate clinicopathological features and molecular test results to assess their opinion of how concerning death to cSCC prognosis. When presented with vignettes describing patients with NCCN-defined high-risk features, clinicians were asked to select a treatment plan using pre-test vs 40-GEP results, then, post-test (40-GEP Class 1, 2A, or 2B result) methodology along with corresponding metastasis rates for each test group.

Results: Risk factors deemed of highest concern for metastatic outcomes were a Class 2B 40-GEP result, perineural invasion, immunosuppression, invasion beyond subcutaneous fat, and tumor diameter ≥ 1 cm on the scalp. When presented with a 40-GEP result that indicated reduced risk of metastasis (Class 1), clinicians altered their treatment management plan accordingly. Specifically, there was significant reduction in the recommendations for sentinel lymph node biopsy, adjuvant radiation or chemotherapy, follow-up time, and nodal imaging. By comparison, when a 40-GEP result indicated an increased risk of metastasis (Class 2B), significant risk-governance increases in management intensity was observed for the aforementioned clinical decisions.

Conclusions: Integration of 40-GEP results impacted management decisions in a significant and risk-appropriate manner for high-risk cSCC patient scenarios, while remaining aligned with national guidelines for patient management.

Introduction
With more than 1 million cases being diagnosed in the U.S. annually, cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer with a rapidly rising incidence rate.¹ An estimated 1.5–2% of cSCC patients die annually, and it is projected that more patients will die from cSCC than melanoma.² National Comprehensive Cancer Network (NCCN) guidelines are based in their criteria for identifying high-risk cSCC and in their approaches for management of cSCC patients considered high risk for developing recurrence and/or metastasis.³ Unfortunately, this broad definition of high-risk cSCC results in a low positive predictive value (PPV), meaning many patients deemed high risk are unlikely to develop recurrences or metastasis. Since American Joint Committee on Cancer (AJCC) and Brigham and Women's Hospital (BWH) staging systems are also limited in their accuracy for identifying high-risk patients^{4,5}, establishing risk-appropriate patient management plans remains an

unmet clinical need. Therefore, improved prognostic tools and a better-defined risk stratification system would positively enhance patient management.

A 40-gene expression profile (40-GEP) test that assesses the biology of a primary cSCC tumor was recently validated for determining metastatic potential.⁶ The 40-GEP is a prognostic test that classifies patients into three risk groups: low (Class 1), high (Class 2A), and highest (Class 2B) risk for developing regional or distant metastasis within 3 years post-diagnosis. Accurately aligning a patient's risk for metastasis with recommended treatment pathways would reduce unnecessary interventions for patients at low risk for metastasis and, conversely, would more precisely identify patients who would most benefit from more intense interventional therapies. Based on the potential utility of the 40-GEP test for guiding cSCC patient management decisions, a clinical impact study was undertaken to assess if, and to what extent, more precise risk assessment through 40-GEP testing

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²Castle Biosciences, Inc. Published by Informa UK Limited, trading as Taylor & Francis Group.
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Impact of Gene Expression Profile Testing on the Management of Squamous Cell Carcinoma by Dermatologists

Rebecca Teplitz BA,¹ Gielle Prado MD,¹ Graham H. Litchman DO MS,² Darrell S. Rigel MD MS³

¹Medical Student, New York Institute of Technology, College of Osteopathic Medicine, Old Westbury, NY; ²Clinical Research Fellow, National Society for Cutaneous Medicine, New York, NY; ³Clinical Professor, Department of Dermatology, NYU School of Medicine, New York, NY

ABSTRACT

Background: The incidence of cutaneous squamous cell carcinoma (cSCC) is increasing likely due to improved detection and a growing elderly population. Although the prognosis of cSCC is excellent with complete surgical excision, many patients who go on to develop metastasis are initially classified as low-risk. The most commonly used staging systems, American Joint Committee on Cancer (AJCC) and Brigham Women's Hospital (BWH), have low sensitivity and low positive predictive value for predicting metastasis. A gene expression profile test (cSCC-GEP) is in development to identify patients with cSCC at high risk for metastasis and death.

Objective: To determine the impact of cSCC-GEP test results on management decisions made by dermatologists for cSCC patients.

Design, Setting, and Participants: 402 dermatologists attending a national dermatology conference completed an online survey designed to determine the impact of cSCC-GEP test results on management decisions in a variety of clinical situations. Participants answered a series of questions related to three cSCC patient vignettes, each featuring different patient and lesion characteristics.

Main Outcomes and Measures: Proportion of dermatologists who would recommend radiation, chemotherapy/immunotherapy, or sentinel lymph node biopsy (SLNB) for each patient vignette (without cSCC-GEP results, with a lower risk result, or with a higher risk result). The effect of the test results on the follow-up intervals recommended by dermatologists was also examined.

Results: In the majority of vignettes, a lower risk cSCC-GEP test result led to a statistically significant decrease in the proportion of dermatologists who would recommend radiation, chemotherapy/immunotherapy, SLNB, or quarterly follow-up. Conversely, a higher risk cSCC-GEP result significantly altered management toward increased intensity more recommendations for radiation, chemotherapy/immunotherapy, SLNB, or quarterly follow-up in all vignettes.

Conclusions and Relevance: The results of a cSCC-GEP test appear to significantly impact decisions made by dermatologists regarding subsequent management, SLNBs, and follow-up intervals for patients with cSCC.

J Drugs Dermatol. 2019;18(10):980-984.

BACKGROUND

Non-melanoma skin cancer (NMSC) is the most common malignancy in the United States. It is estimated that cutaneous squamous cell carcinoma (cSCC) represents 20% of NMSC cases with an approximate annual incidence of over 700,000, which is increasing yearly.¹ While the exact incidence of cSCC is not included in national cancer registries, a recent study showed an increase of 263% in the incidence of cSCC between 2000-2019 compared to 1976-1984.² This increasing incidence is likely due to both improved detection and the growing elderly population.³ Although the prognosis of cSCC is generally excellent with complete surgical excision, a recent study showed that roughly 4% of cases develop nodal metastases and 15% die from this disease.⁴

To more accurately identify cSCC at high risk for metastasis or death, there are two main staging systems, American Joint Committee on Cancer (AJCC) and Brigham Women's Hospital (BWH). However these staging systems have low sensitivity (22-40%) and low positive predictive value (12-13%).⁵ Many patients who develop metastasis are initially classified as low-risk, and conversely, some patients who are classified as high-risk do not go on to develop metastatic disease. Thus, accurate identification of high-risk cSCC patients is critical. Additionally, the definitive work-up and treatment indicated for high-risk cSCC remains unknown.⁶ Given the recent FDA approval of Cemiplimab[®] for the treatment of advanced cSCC and its significant side-effect profile, it is particularly important that the appropriate patients are selected for this therapy.

A gene expression profile (GEP) test is currently under development (Castle Biosciences Inc., Greenwood, TX). The goal of the 40-gene test is to improve upon current staging systems and identify patients with cSCC at high risk for metastasis and death. Previous analyses have identified 73 genes associated with cSCC recurrence and metastasis.⁷ A recent study performed microarray analysis of 80 cSCC lesions to further identify novel genes differentially expressed in high-risk cSCCs.⁸ Based on the patient's expression of these genes, machine learning can



The Skin Cancer Diagnostics Company

Ashley Wysong, MD
University of Nebraska
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Cutaneous Squamous Cell Carcinoma

Decision Dx·SCC



Cutaneous Squamous Cell Carcinoma (SCC)

Disease Incidence



- **1,000,000** new cases of SCC are estimated to be diagnosed per year in the U.S. ¹
- Current figures suggest that more than 15,000 patients die of SCC each year in the U.S. (more than twice as many from melanoma)¹

SCC incidence increases dramatically with age.

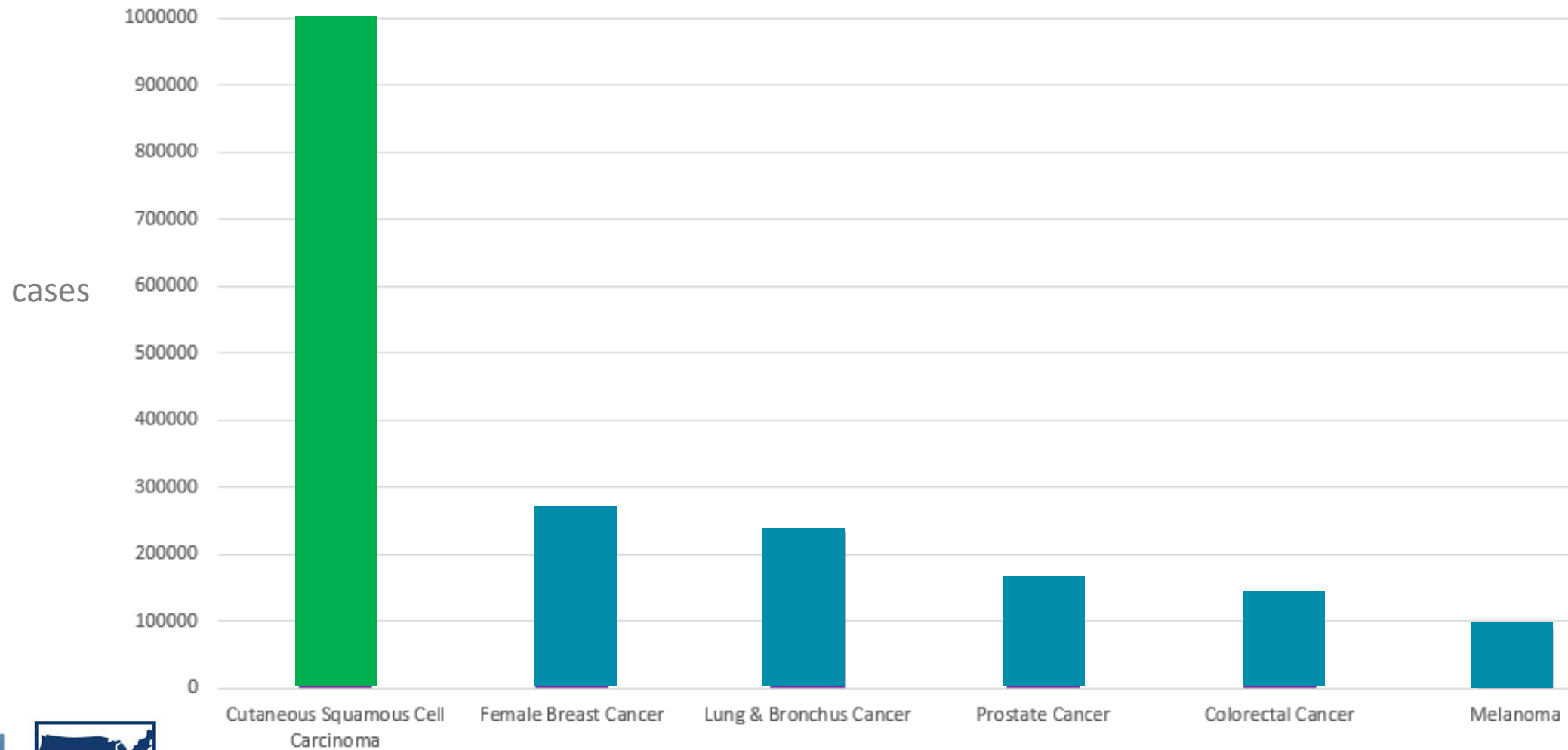
Estimates for average age at first diagnosis range from **mid-60s** to **early 70s**.²



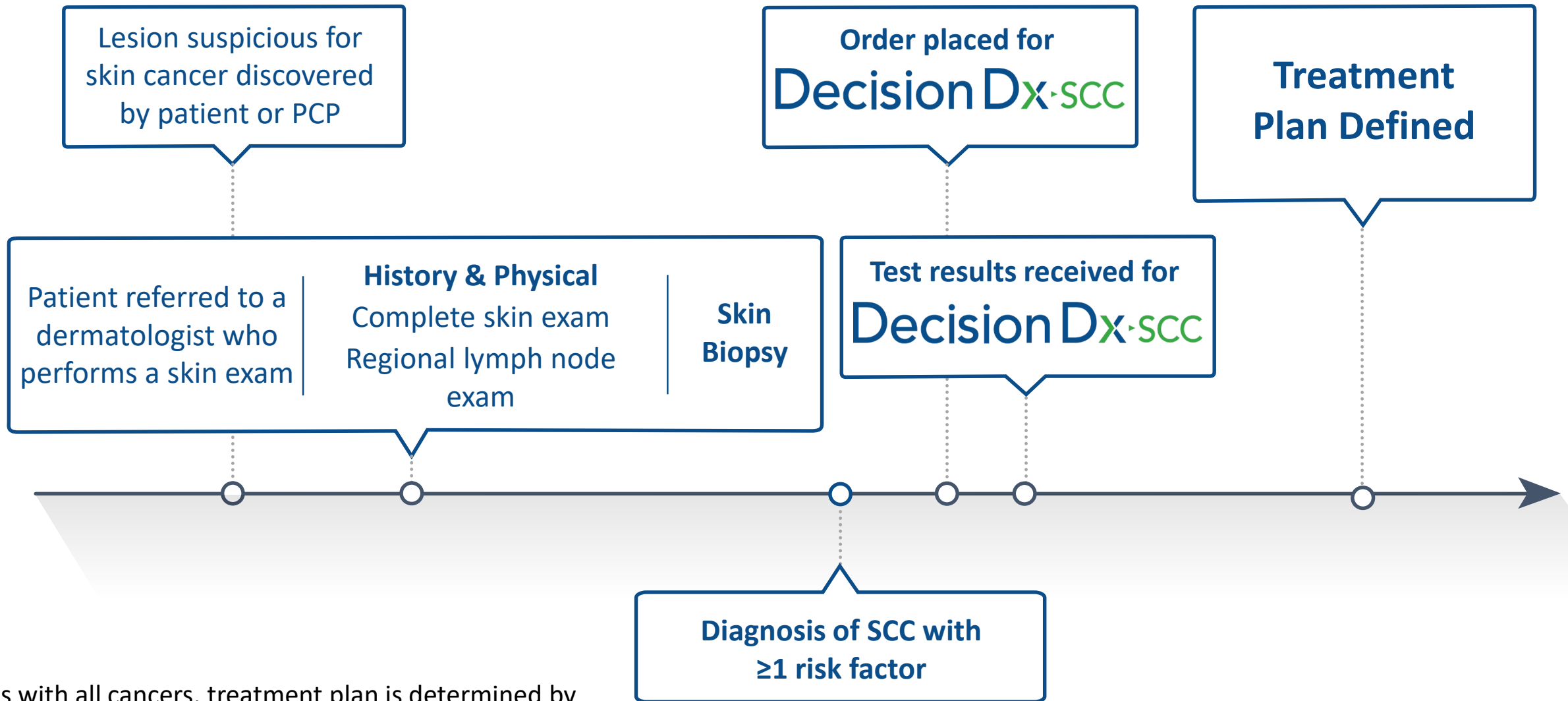
~20% of SCC cases are “high-risk”³



Annual incidence of SCC exceeds these other cancers *combined*



Patient journey for diagnosis of SCC




As with all cancers, treatment plan is determined by the risk of progression (recurrence or metastasis).^{1,2}

1. NCCN Guidelines. Squamous Cell Carcinoma. V1.2020. Accessed January 10, 2020. 2. Alam A, et al. *J Am Acad Dermatol*. 2018;78:560-78.

Staging and risk stratification of SCC:

Traditional approaches have limitations in assessing risk

Why Do We Stage Cancers?

- 
- › Physicians stage cancers in order to determine how much cancer there is and where it is located—which helps them assess the prognosis and decide on the best treatment option.^{1,2}
 - › A key part of assessing prognosis is determining the risk for recurrence for regional or distant metastasis.^{1,2}

SCC Staging Considerations

- 
- ✓ NCCN Guidelines group many patients as high risk who may be low-risk patients and may be overtreated.
 - ✓ Recurrence, metastasis, and survival are linked to T stage.
 - ✓ Traditional approaches for staging have limitations in assessing risk for metastasis.
 - ✓ Current staging systems can miss patients with aggressive disease.

The unmet need in high-risk SCC patients: Who is really at low risk or high risk for metastasis?

The Clinical Problem

Managing SCC is a significant clinical issue, as deaths from SCC are now estimated to exceed those from melanoma.

~20% of SCC patients have one or more clinical or pathological risk factors and they suffer the majority of SCC mortality. These factors alone are often not specific enough to determine risk-appropriate treatment and further management.

SCC treatment plans are guided by risk of metastasis.
Risk-appropriate SCC management is currently limited by classification systems (NCCN, BWH, AJCC) with low positive predictive value (PPV).

DecisionDx-SCC:

Designed to predict metastatic risk for *high-risk* SCC patients

Addressing the Clinical Problem

DecisionDx-SCC is validated to predict metastatic risk for individual SCC patients with one or more risk factors.

DecisionDx-SCC is a validated predictor of risk in uni- and multivariate analysis.

Incorporation of DecisionDx-SCC with traditional risk factors can improve patient classification compared to either approach alone.

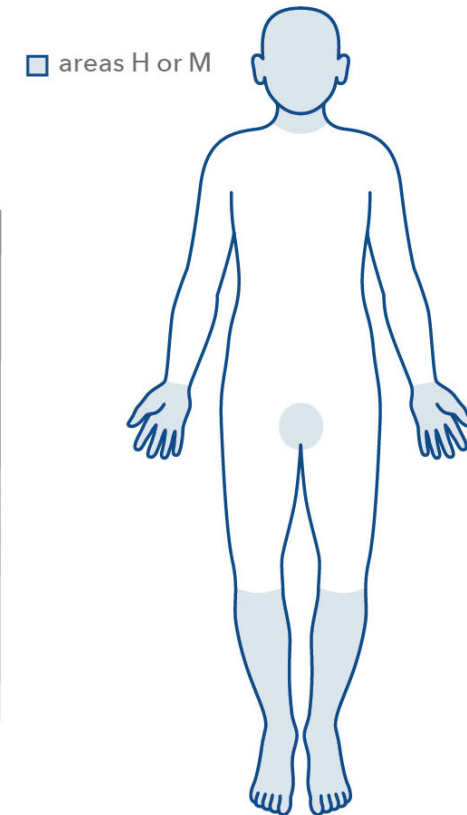
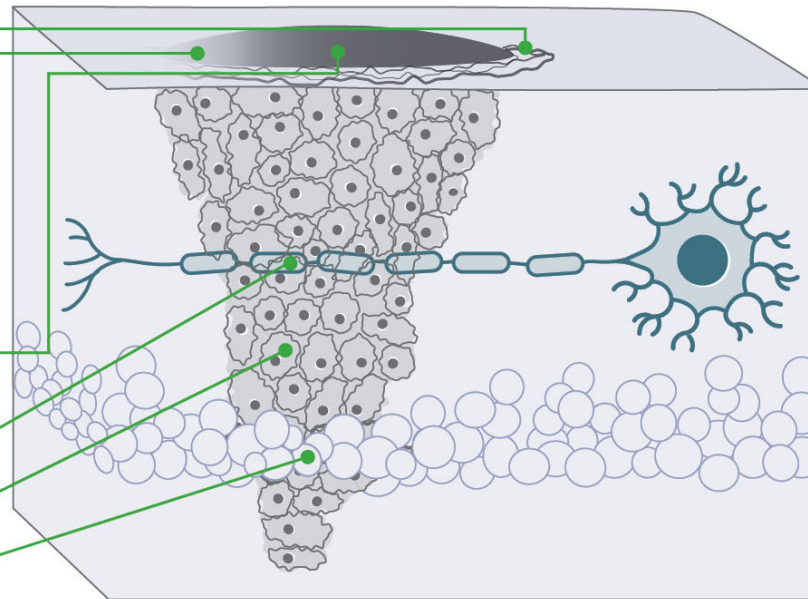
DecisionDx-SCC can inform management decisions within established guidelines.

Decision Dx-SCC

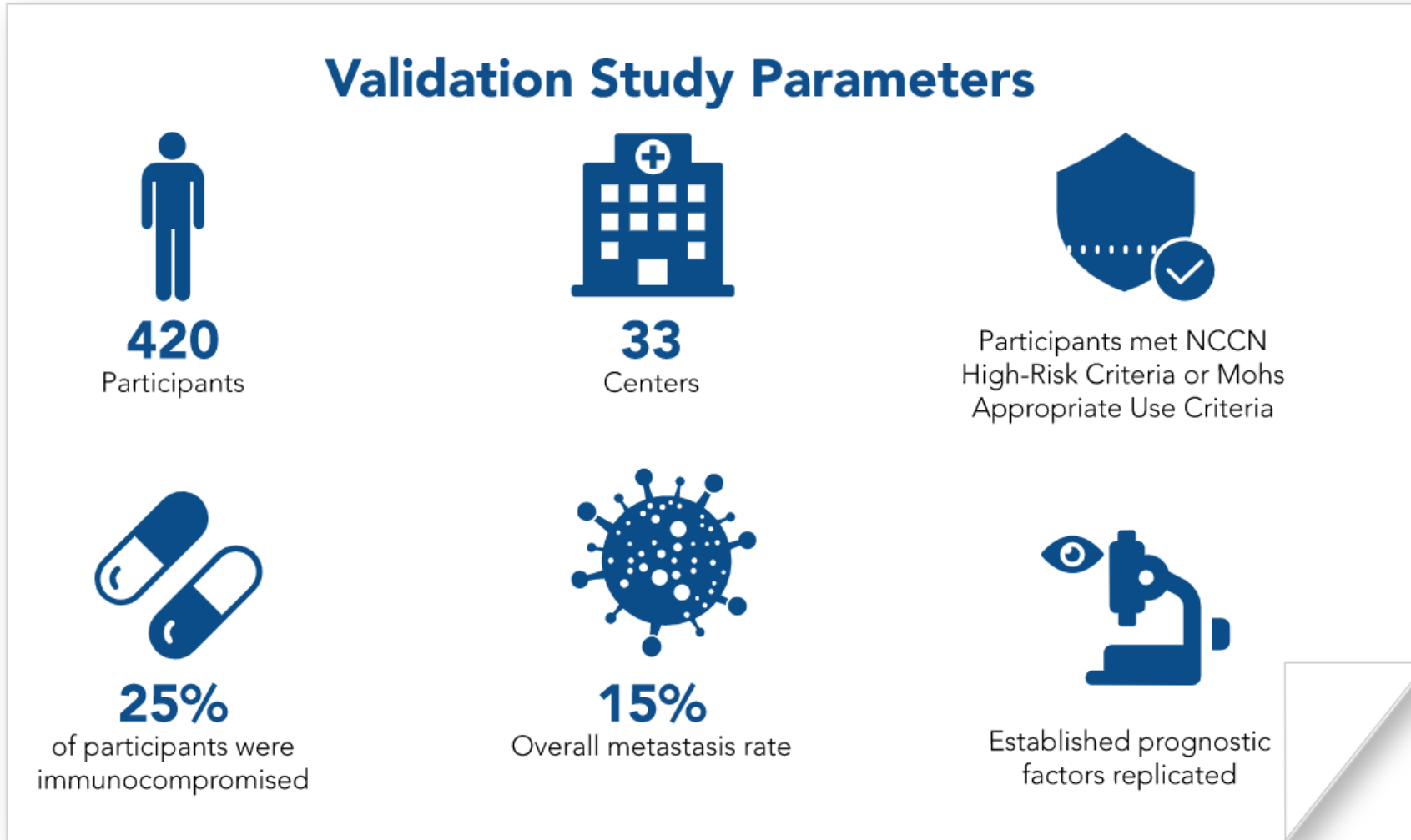
Intended Use: DecisionDx-SCC is indicated for patients *diagnosed* with cutaneous squamous cell carcinoma *and* one or more risk factors. **DecisionDx-SCC is designed to predict individual metastatic risk to inform risk-appropriate management.**

For SCC patients with one or more of the following risk factors:

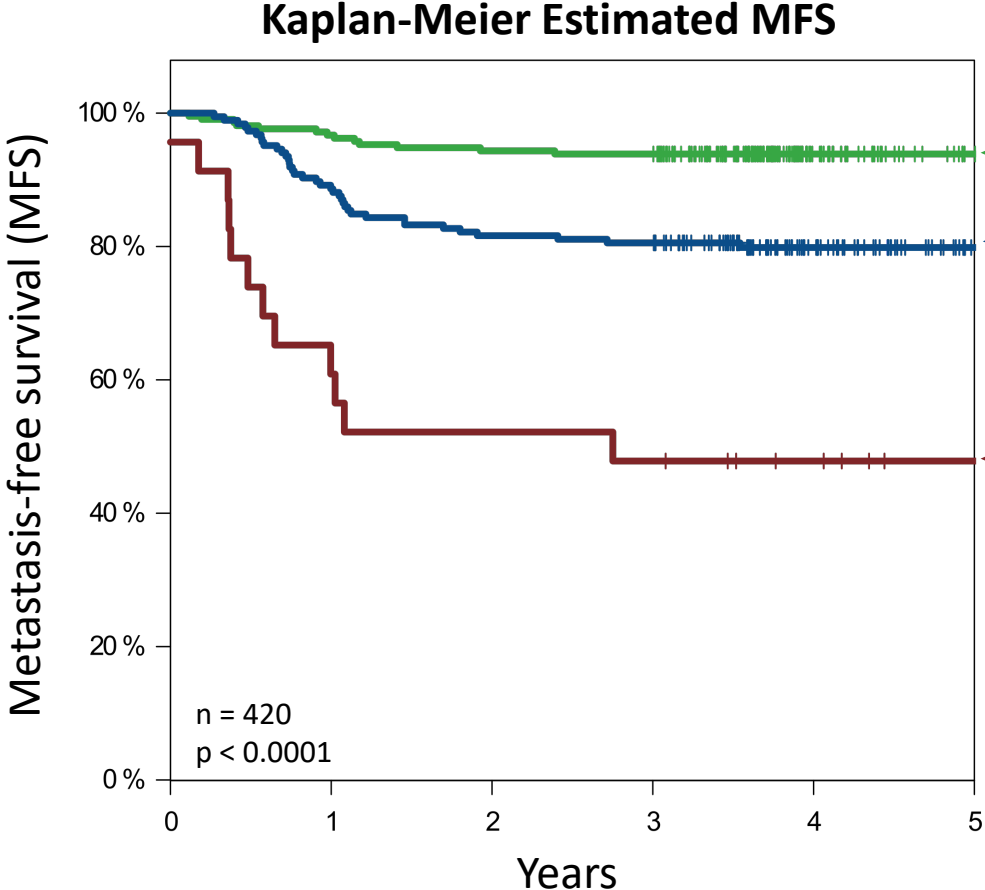
- Tumor size ≥ 2 cm anywhere on the body
- Tumor location on the head, neck, hands, genitals, feet or pretibial surface (areas H or M)
- Immunosuppression
- Rapidly growing tumor
- Tumor with poorly defined borders
- Tumor at a site of prior radiation or chronic inflammation
- Perineural invasion (PNI)
- Poorly differentiated tumor grade
- Deep tumor (has invaded beyond subcutaneous fat)



DecisionDx-SCC independent validation study



DecisionDx-SCC is validated to predict metastatic risk for individual SCC patients with one or more risk factors



Class 1 – Low Biological Risk

Less than half the general study population risk

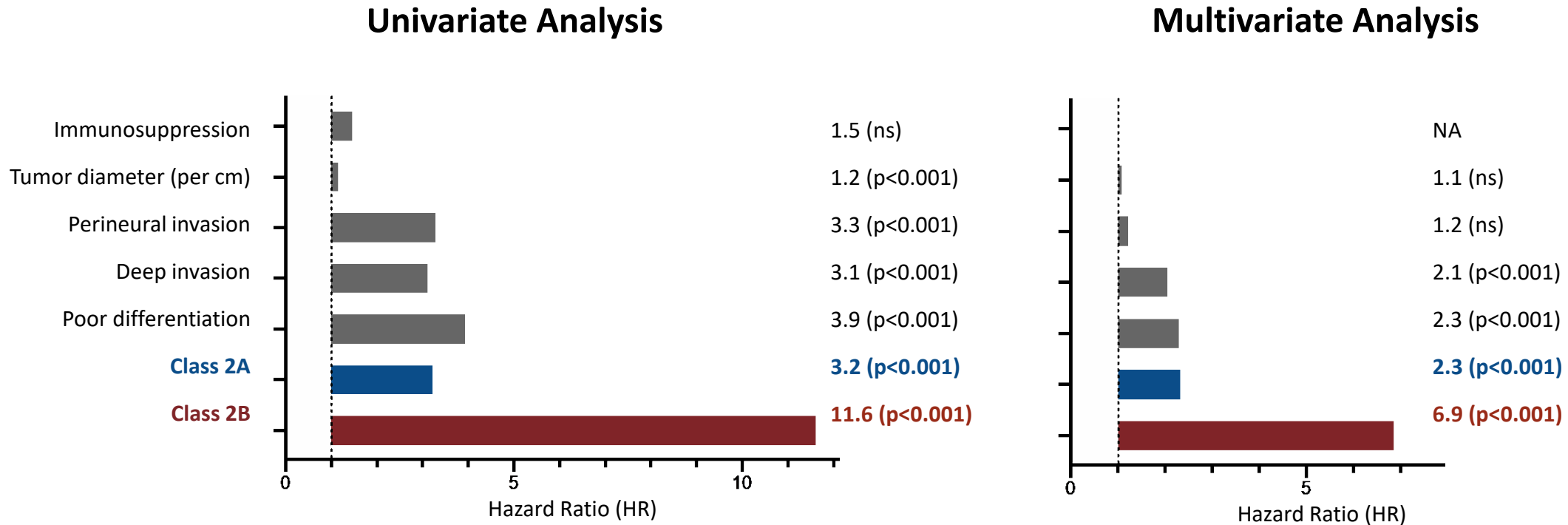
Class 2A – Moderate Biological Risk

Similar to the strongest traditional factors

Class 2B – High Biological Risk

≥50% risk of metastasis

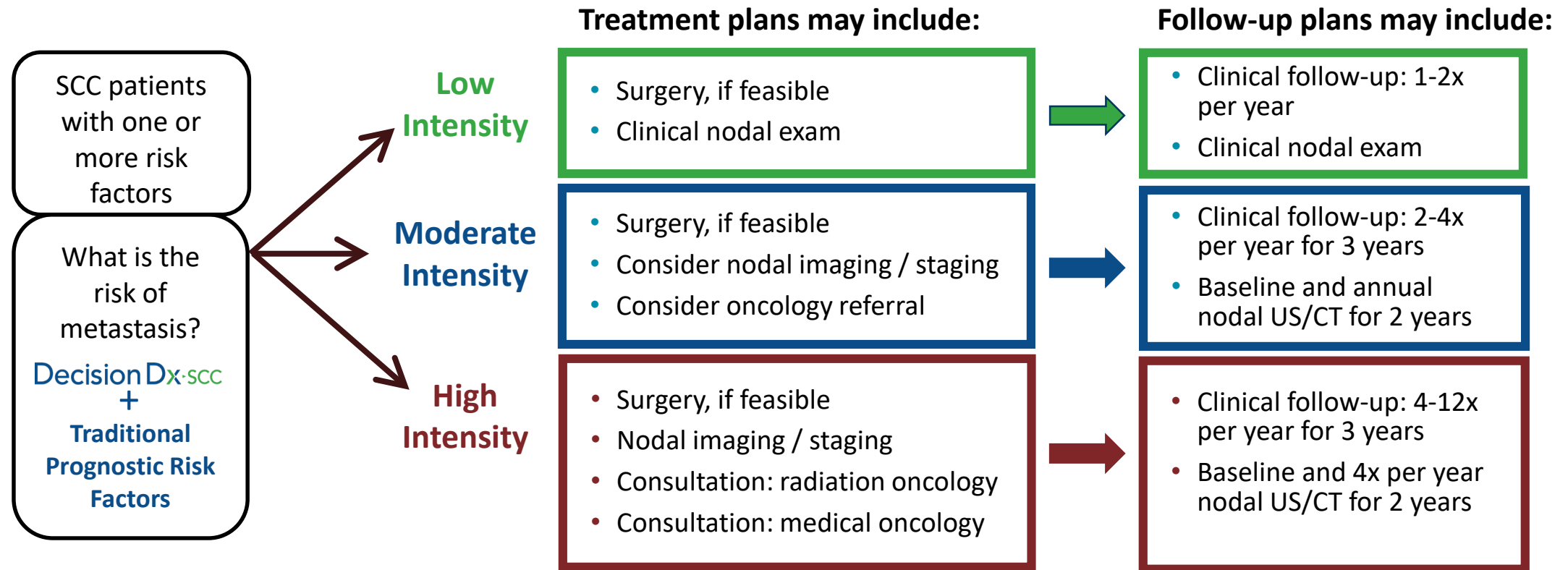
Class 2A and Class 2B are independent predictors of metastasis



What is the impact of DecisionDx-SCC?

- An SCC with deep invasion is 2.1x more likely to metastasize than without.
- Adding a Class 2A results shifts that to 4.8x more likely to metastasize.
- Adding a Class 2B result shifts that to 14.5x more likely to metastasize.

DecisionDx-SCC is designed to predict metastatic risk for high-risk SCC patients



DecisionDx-SCC results can inform management decisions within established guidelines

Integrating DecisionDx-SCC into clinical care of patients

Patient
Characteristics



Clinical and
Pathologic Tumor
Characteristics



Tumor Biology



Decision Dx^{SCC}



The Skin Cancer Diagnostics Company

Derek Maetzold

Founder, President & CEO

Summary



Launch objectives are being achieved

- Accelerated disease state training during peak of COVID
- Conducted virtual National Sales Meeting for final training
- Successfully completed virtual speaker training
- August 31, 2020: commercially available

DecisionDx-SCC
Cutaneous Squamous Cell Carcinoma (SCC)

Accurately identify the risk of metastasis with **DecisionDx-SCC**

DecisionDx-SCC complements factors used in clinical assessments, providing a more accurate prediction to better inform treatment and follow-up.

DecisionDx-SCC is the strongest independent predictor of SCC metastasis.

CLASS 1: LOW BIOLOGICAL RISK
Metastatic risk was lower than that of the independent validation cohort.

CLASS 2A: MODERATE BIOLOGICAL RISK
Confirmatory of the validated established factors (Deep Invasion, poor differentiation, BSM1/2/3/7).

CLASS 2B: HIGH BIOLOGICAL RISK
100% risk of metastasis.

Incorporation of risk factors into classification compared to clinical factors

DecisionDx-SCC complements factors used in clinical assessments, providing a more accurate prediction to better inform treatment and follow-up.

DecisionDx-SCC results can inform management decisions for patients.

Established management options have early detection of metastasis, improved therapy and improved survival.¹ DecisionDx-SCC test results are reported independently and in combination with clinical factors.

Cutaneous squamous cell carcinoma (SCC) is an emerging problem in the U.S.

Although most patients with SCC have an excellent prognosis, there is a subset of patients at risk of metastasis. Metastatic SCC is deadly. Patients with one or more risk factors suffer the majority of SCC mortality, however these factors alone are often not specific enough to determine their risk-appropriate treatment and further management.

DecisionDx-SCC is a gene expression profile (GEP) test that is validated to predict metastatic risk for individual SCC patients with one or more risk factors.

It is independently validated in a 420-patient cohort of high-risk SCC patients with 3-year outcomes. DecisionDx-SCC is the strongest independent predictor of metastasis in univariate (figure) and multivariate analyses (shown).

COHORT CLASS RESULTS DISTRIBUTION

Class 1: 100% Low Risk (100%)
Class 2A: 100% Moderate Risk (100%)
Class 2B: 100% High Risk (100%)

UNIVARIATE ANALYSIS¹

Risk Factor	Hazard Ratio (95% CI)
Immunosuppression	1.8 (p<0.001)
Tumor Diameter	1.2 (ns)
Perineural Invasion	3.3 (p<0.001)
Deep Invasion	3.3 (p<0.001)
Poor Differentiation	3.3 (p<0.001)
Class 2B	11.8 (p<0.001)

RISK IDENTIFIED
CastleTestInfo.com

DECISIONDX-SCC STRATIFICATION IN COMBINATION WITH RISK FACTORS

The table below presents overall rate of metastasis for patients with primary SCC compared to the subgroup that has 1 high-risk factor as well as 2 high-risk factors from the 420 patient clinical validation cohort. A Class 1 result reduced the metastatic rate from 8.2% to 4.0% in patients with 1 high-risk factor. A Class 2B result more than doubled the metastatic rate to 50.0% in both groups.¹

*10/63 overall metastases (16 occurred within 3 years). The remaining 3 occurred greater than 3 years following diagnosis.

Result	n	Metastasis Rate	n	Metastasis Rate	n	Metastasis Rate
Overall Cohort	420	19.0%	171	8.2%	249	19.7%
Class 1	212	6.6%	101	4.0%	111	9.0%
Class 2A	185	20.0%	65	10.8%	120	25.0%
Class 2B	23	52.2%	5	68.0%	18	50.0%

COMPARISON WITH CLINICAL FACTORS

Risk Factor	Class 1	Class 2A	Class 2B
DecisionDx-SCC	Class 1	Class 2A	Class 2B
Poor differentiation			
Perineural invasion			
Deep invasion**			
Tumor diameter (per cm)			
Immunosuppression			

**Deep invasion: beyond subcutaneous fat.

ADDITIONAL INFORMATION

The proprietary DecisionDx-SCC GEP is derived from a panel of 40 differentially expressed genes: AC105111, LOC100281996, LOC100281997, LOC100281998, LOC100281999, LOC100282000, LOC100282001, LOC100282002, LOC100282003, LOC100282004, LOC100282005, LOC100282006, LOC100282007, LOC100282008, LOC100282009, LOC100282010, LOC100282011, LOC100282012, LOC100282013, LOC100282014, LOC100282015, LOC100282016, LOC100282017, LOC100282018, LOC100282019, LOC100282020, LOC100282021, LOC100282022, LOC100282023, LOC100282024, LOC100282025, LOC100282026, LOC100282027, LOC100282028, LOC100282029, LOC100282030, LOC100282031, LOC100282032, LOC100282033, LOC100282034, LOC100282035, LOC100282036, LOC100282037, LOC100282038, LOC100282039, LOC100282040.

All data shown in this report were collected prospectively in a primary clinical trial. The test was independently validated in a secondary clinical trial.

REFERENCE LIST

- Wynne A, Heenan JJ, Congdon KP, et al. (2019) *Journal of the American Academy of Dermatology*.
- Castle Biosciences. Data on File.
- National Comprehensive Cancer Network (NCCN). *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cutaneous Squamous Cell Carcinoma*, Version 1.2020.
- Alam M, Kempson A, Karam C, et al. (2019) *Journal of the American Academy of Dermatology*.
- Farberg AL, Hall MA, Douglas L, et al. (2019) *Journal of the American Academy of Dermatology*.

CLINICAL VALIDITY AND RISK OF METASTASIS

Molecular Signature Result	3-year Metastasis Free Survival
Class 1	83.5%
Class 2A	80.5%
Class 2B	47.8%

The DecisionDx-SCC test was validated to predict a patient's individual risk of metastasis (regional or distant) in a multi-center (33), 420-patient study in patients diagnosed with localized cutaneous squamous cell carcinoma (SCC) and one or more risk factors.¹

3-year Metastasis Free Survival (MFS) for the entire population was 65.5%. Patients without a metastatic event had a minimum of 3 years follow-up. Median time to metastasis was 0.51 years.¹

INTENDED USE

Background: Risk-appropriate SCC management is limited by classification systems (NCCN, AJCC, BWH) with low positive predictive value. Guidelines provide a range of management options based on risk, for patients with localized, surgically resectable SCC.¹

Intended use: DecisionDx-SCC is indicated for patients with cutaneous squamous cell carcinoma (SCC) and one or more high-risk factors (see Test Requirement Form). DecisionDx-SCC predicts individual metastatic risk to inform risk appropriate management.¹

DecisionDx-SCC has not been evaluated for testing in tissue from locally recurrent tumors.

TEST DESCRIPTION

The DecisionDx-SCC test is a qRT-PCR assay of 6 control and 34 discriminant genes (40 in total) that uses a neural network algorithm comprised of two gene expression signatures to classify patients into risk categories. The algorithm was trained on a set of patients with known outcomes (n=22). The algorithmic score from both signatures is converted to results reflecting risk classification: Class 1 for low risk, Class 2A for moderate risk, and Class 2B for highest risk of metastasis. This test has not been validated in patients with clinical features different from those described in the Intended Use section above.

Castle Biosciences, Inc. | Sherri Borman, PhD, HCLD, Lab Director

Castle Biosciences, Inc. CLM# 030209054 1310 W. 17th Street, Suite 100, Phoenix, AZ 85014 Tel: 866-786-0927 Fax: 866-324-2224 www.castlebio.com

CAP ACCREDITED

Decision Dx-SCC

Designed to predict individual metastatic risk to inform risk-appropriate management

For **high-risk** SCC patients with one or more risk factors

200,000 high-risk patients annually;
\$820M U.S TAM¹

Validated in **420-patient cohort** of high-risk SCC from **33 U.S. centers**

4 peer-reviewed publications to date;
Over **1,400 patients** enrolled in studies to date from **92 centers**

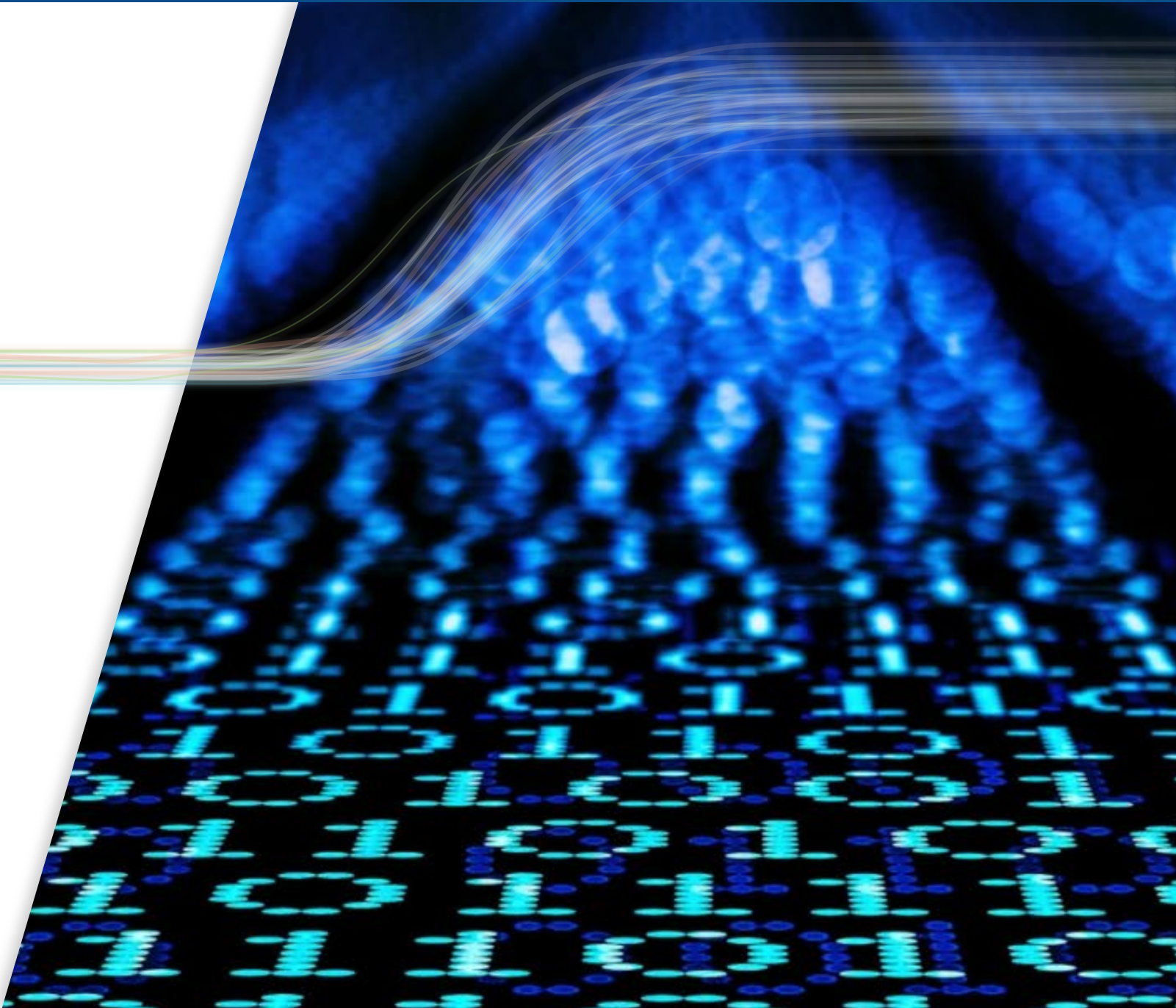
Utilizing **existing sales channels**: dermatologists (including Mohs surgeons)

Incorporation of DecisionDx-SCC with traditional risk factors can improve patient classification compared to traditional risk factors alone

¹ based on Castle estimates



THANK YOU



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
<i>(in thousands)</i>				
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)	<u>\$ 13,501</u>	<u>\$ 482</u>	<u>\$ 13,250</u>	<u>\$ 1,770</u>

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).