NEWS RELEASE

Data Presentations at 2023 Winter Clinical Dermatology Conference - Hawaii® Support Clinical Value of Castle Biosciences' Skin Cancer Test Portfolio

1/17/2023

Real-world data from Castle's collaboration with the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program registries confirm ability of DecisionDx®-Melanoma to identify patients with high-risk tumor biology in a cohort of patients with a negative lymph node

New clinician-developed real-world algorithm provides a framework to incorporate DecisionDx®-SCC test results into clinical practice within established guidelines

Survey of dermatologists shows that diagnostic GEP test results from MyPath ® Melanoma and DiffDx ® - Melanoma can aid in making personalized and appropriate patient management decisions

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced that new data supporting the clinical value of the Company's skin cancer test portfolio is being shared in poster presentations at the 2023 Winter Clinical Dermatology Conference - Hawaii®, being held Jan. 13-18 in Kohala Coast, Hawaii.

"At Castle, we are committed to challenging the status quo to improve disease management through deep scientific expertise, unique value insight and strong data development," said Derek Maetzold, president and chief executive officer of Castle Biosciences. "The data that we are presenting at the 2023 Winter Clinical Dermatology Conference – Hawaii demonstrates the ability of our tests to help guide personalized and risk-aligned patient management decisions with a goal of enabling better patient outcomes."

The posters below will be displayed for viewing in the Grande Ballroom Salon III for the duration of the conference.

DecisionDx®-Melanoma

Poster title: Improved prognostic guidance by the 31-gene expression profile test for clinical decisions after a negative lymph node for patients with cutaneous melanoma

This study evaluated the ability of the DecisionDx-Melanoma test to identify patients with high-risk tumor biology in an unselected, clinically tested cohort of patients in the SEER registries with negative lymph nodes (LN) (n=3,271). Patients with low-risk (Class 1A) test results had higher three-year melanoma-specific survival (MSS) than patients with a high-risk (Class 2B) result (Class 1A: 99.7% vs. Class 2B: 91.8%, $p<0.001$), demonstrating the ability of the test to stratify patients according to their risk of dying from their disease. Additionally, DecisionDx-Melanoma was a significant and independent predictor of MSS compared to traditional staging factors, with higher hazard ratios (HR) in multivariable analysis than American Joint Committee on Cancer (AJCC) staging (Class 2B HR: 10.50 vs. AJCC stage IIC HR: 4.58). Overall, the results showed that in patients with a negative LN, DecisionDx-Melanoma could identify those who are more or less likely to die within three years from their melanoma to guide risk-aligned management and surveillance to improve patient outcomes (i.e., directing patients with high-risk tumor biology to higher intensity treatments, such as adjuvant therapy and clinical trials, and patients with low-risk tumor biology to lower intensity management).

The poster may be viewed **here**.

DecisionDx®-SCC

Poster title: Integration of the 40-gene expression profile (40-GEP) for management and treatment of high-risk cutaneous squamous cell carcinoma (cSCC): a real-world algorithm

Three private-practice Mohs surgeons who have used DecisionDx-SCC to risk-stratify their high-risk cSCC patients merged their management approaches into a singular algorithm that provides guidance on how to incorporate the test's results into practice within National Comprehensive Cancer Network (NCCN) guidelines. The guidance includes common management decisions within NCCN guidelines involved in the treatment of high-risk cSCC patients, including surveillance imaging, sentinel lymph node biopsy (SNLB), adjuvant radiation therapy (ART) and clinical follow-up based on the patient's DecisionDx-SCC results. The algorithm developed in the study provides a framework to implement NCCN guideline recommendations through the use of DecisionDx-SCC testing that can enable personalized management of patients based on their risk of poor outcomes.

The poster may be viewed **here**.

MyPath® Melanoma and DiffDx®-Melanoma

Poster title: A clinical impact study of dermatologists' use of the 23- or 35-gene expression profile tests to guide surgical excision and enhance management plan confidence

In this study, thirty-two board-certified dermatologists who had prior experience with diagnostic GEP tests were asked to evaluate six real-world scenarios involving patients with ambiguous melanocytic lesions. Based on the patient's pathology report and diagnostic GEP results (if available), the dermatologists were asked three questions regarding their management plan, recommended follow-up schedule and their overall confidence in their plan. The vast majority of excision decisions and follow-up changes were aligned with GEP results across the uncertain scenarios. Additionally, there was an increase in overall management plan confidence when a GEP result was available. Overall, the study demonstrates how diagnostic GEP test results can aid clinicians in making personalized and more confident patient management decisions.

The poster may be viewed **here**.

About DecisionDx®-Melanoma

DecisionDx-Melanoma is a risk stratification gene expression profile test. It is designed to inform two clinical questions in the management of cutaneous melanoma: a patient's individual risk of sentinel lymph node (SLN) positivity and a patient's personal risk of melanoma recurrence and/or metastasis. By integrating tumor biology with clinical and pathologic factors using a validated proprietary algorithm, DecisionDx-Melanoma is designed to provide a comprehensive and clinically actionable result to guide risk-aligned patient care. DecisionDx-Melanoma has been shown to be associated with improved patient survival and has been studied in more than 9,000 patient samples. DecisionDx-Melanoma's clinical value is supported by more than 35 peer-reviewed and published studies, providing confidence in disease management plans that incorporate the test's results. Through Sept. 30, 2022, DecisionDx-Melanoma has been ordered 112,821 times for patients diagnosed with cutaneous melanoma.

About DecisionDx®-SCC

DecisionDx-SCC is a 40-gene expression profile test that uses an individual patient's tumor biology to predict individual risk of cutaneous squamous cell carcinoma metastasis for patients with one or more risk factors. The test result, in which patients are stratified into a Class 1 (low), 2A (moderate) or 2B (high) risk category, predicts individual metastatic risk to inform risk-appropriate management.

Peer-reviewed publications have demonstrated that DecisionDx-SCC is an independent predictor of metastatic risk

and that integrating DecisionDx-SCC with current prognostic methods can add positive predictive value to clinician decisions regarding staging and management.

About MyPath® Melanoma and DiffDx®-Melanoma

MyPath Melanoma and DiffDx-Melanoma are Castle's two gene expression profile tests designed to provide an accurate, objective result to aid dermatopathologists and dermatologists in characterizing difficult-to-diagnose melanocytic lesions. Of the approximately two million suspicious pigmented lesions biopsied annually in the U.S., Castle estimates that approximately 300,000 of those cannot be confidently classified as either benign or malignant through traditional histopathology methods. For these cases, the treatment plan can also be uncertain. Obtaining accurate, objective ancillary testing can mean the difference between a path of overtreatment or the risk of undertreatment. Interpreted in the context of other clinical, laboratory and histopathologic information, MyPath Melanoma and DiffDx-Melanoma are designed to reduce uncertainty and provide confidence for dermatopathologists and help dermatologists deliver more informed patient management plans.

More information about Castle's tests and these diseases can be found at **www.CastleTestInfo.com**.

About Castle Biosciences

Castle Biosciences (Nasdaq: CSTL) is a leading diagnostics company improving health through innovative tests that guide patient care. The Company aims to transform disease management by keeping people first: patients, clinicians, employees and investors.

Castle's current portfolio consists of tests for skin cancers, uveal melanoma, Barrett's esophagus and mental health conditions. Additionally, the Company has active research and development programs for tests in other diseases with high clinical need, including its test in development to predict systemic therapy response in patients with moderate-to-severe psoriasis, atopic dermatitis and related conditions. To learn more, please visit **www.CastleBiosciences.com** and connect with us on **LinkedIn**, **Facebook**, **Twitter** and **Instagram**.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. These forward-looking statements include, but are not limited to,

statements concerning: the potential of (i) MyPath® Melanoma and DiffDx®-Melanoma to aid in making personalized and appropriate patient management decisions; (ii) DecisionDx-Melanoma to identify patients with a negative SLN who are more or less likely to die within three years from their melanoma to guide risk-aligned management and surveillance to improve patient outcomes; (iii) DecisionDx-SCC testing to enable personalized management of patients based on their risk of poor outcomes; and (iv) diagnostic GEP test results to aid clinicians in making personalized and more confident patient management decisions. The words “can,” “could” 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: subsequent study or trial results and findings may contradict earlier study or trial results and findings or may not support the results obtained in these studies, including with respect to the discussion of our skin cancer test portfolio in this press release; actual application of our tests may not provide the aforementioned benefits to patients; and the risks set forth under the heading “Risk Factors” in our Quarterly Report on Form 10-Q for the three months ended September 30, 2022, and in our other filings with the SEC. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements, except as may be required by law.

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Source: Castle Biosciences, Inc.