NEWS RELEASE

Data to be Presented at the 2022 American Academy of Dermatology (AAD) Annual Meeting Demonstrate Ability of DecisionDx®-Melanoma and DecisionDx®-SCC to Inform Clinical Decision Making

3/25/2022

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced upcoming presentations on two of its skin cancer gene expression profile (GEP) tests at the 2022 American Academy of Dermatology (AAD) Annual Meeting, being held in Boston, March 25-29, 2022.

“We are pleased to once again have the opportunity to share data supporting the value of our tests in the management of patients with skin cancer,” said Derek Maetzold, president and chief executive officer of Castle Biosciences. “Our data presentations at AAD highlight two of our proprietary GEP tests, DecisionDx®-Melanoma and DecisionDx®-SCC, and their ability to independently risk-stratify patients with melanoma or high-risk squamous cell carcinoma, respectively, to potentially guide better informed and more risk-aligned patient care.”

DecisionDx-Melanoma

Title: “The 31-gene expression profile stratifies recurrence and metastasis risk in patients with cutaneous melanoma”
Poster number: 32344
Presenter: Abel Jarell, M.D., Northeast Dermatology Associates, P.C., Portsmouth, N.H.
Date: Saturday, March 26, 2022
Location: Poster Presentation Center 2 in the Exhibit Hall

Time: 3:30-3:35 p.m. Eastern time

DecisionDx®-Melanoma is Castle's 31-GEP test designed to use a patient's tumor biology to predict individual risk of cutaneous melanoma metastasis or recurrence, as well as risk of sentinel lymph node positivity, independent of traditional staging factors. The test classifies a patient's tumor as low risk of recurrence/metastasis (Class 1A), increased risk (Class 1B/2A) or high risk (Class 2B).

Consistent with previous studies, the poster reports that DecisionDx-Melanoma significantly stratified patients according to their metastatic risk (RFS, DMFS and MSS $p<0.001$). Further, the poster data demonstrates DecisionDx-Melanoma's potential to guide patient care as a significant, independent predictor of metastatic recurrence compared to staging using the American Joint Committee on Cancer Staging Manual Eighth Edition (AJCC8) framework (high-risk Class 2B result: hazard ratio 5.38, $p=0.014$). Moreover, a high-risk Class 2B DecisionDx-Melanoma test result in Stage I and II patients (classified according to AJCC8 staging) was associated with lower patient survival (DMFS and MSS) than that of Stage III patients, showing that the DecisionDx-Melanoma test result provides additional risk information as a complement to existing melanoma management plans.

Additionally, combining a patient's DecisionDx-Melanoma test result (specifically, a low-risk Class 1A test result) with sentinel lymph node (SLN) status, a commonly used prognostic indicator, was associated with improved recurrence outcomes compared to relying on a negative or positive SLN status alone (recurrence free was 98.0% for Class 1A/SLN negative vs. 93.8% for SLN negative alone, and 100% for Class 1A/SLN positive vs. 80.4% for SLN positive alone). Similar improvements in recurrence accuracy were observed in the high-risk Class 2B DecisionDx-Melanoma test result (recurrence free was 84.6% for Class 2B/SLN negative vs. 93.8% for SLN negative alone and 73.3% for Class 2B/SLN positive vs 80.4% for SLN positive alone). The results of the study provide further support for the ability of DecisionDx-Melanoma to provide independent risk-stratification to determine the likelihood that a patient's cancer will spread or recur, as well as complement other risk assessment methods, to guide more precise and personalized patient care.

DecisionDx-SCC

Title: "Clinical usage data demonstrates appropriate utilization of the prognostic 40-gene expression profile (40-GEP) test for cutaneous squamous cell carcinoma with one or more risk factors"
Poster number: 35334
Presenter: Aaron S. Farberg, M.D., Baylor Scott & White Health System, Dallas
Date: Sunday, March 27, 2022
Location: Poster Presentation Center 1 in the Exhibit Hall
Time: 9:30-9:35 a.m. Eastern time

DecisionDx-SCC is Castle's prognostic 40-GEP test designed to use a patient's tumor biology to predict individual risk of metastasis for patients diagnosed with cutaneous squamous cell carcinoma (SCC) who have one or more high-risk factors. The test stratifies patients into one of three classes based on their biologic risk of metastasis: Class 1 (low risk), Class 2A (moderate risk) or Class 2B (high risk).

Clinical validity and utility of the DecisionDx-SCC test has been reported. Results of those studies indicate that the information provided by the test can improve stratification of high-risk SCC patients and, if incorporated into clinical assessments with any number of traditional clinicopathologic risk factors, could assist physicians in guiding more risk-appropriate surveillance and treatment decisions.

DecisionDx-SCC is validated for use in patients with high-risk SCC, defined as the presence of one or more clinicopathologic risk factors, and clinical data has demonstrated its ability to accurately and independently stratify patients according to their biologic risk of metastasis. Analysis of one year of real-world clinical data (2,503 DecisionDx-SCC test orders received between Aug. 31, 2020-Aug. 31, 2021) showed that the intended use population (high-risk SCC patients) aligns with the cases submitted for testing, indicating that physicians understand the appropriate use criteria for the test. Of note, within this high-risk population, nearly 70% of patients received a DecisionDx-SCC Class 1 test result, signifying that they have a biologically lower risk for metastasis. Overall, the current study data, combined with the presented previous validation data, indicates that the testing population aligns with a high-risk population.

About DecisionDx®-Melanoma

DecisionDx-Melanoma is a gene expression profile test that uses an individual patient's tumor biology to predict individual risk of cutaneous melanoma metastasis or recurrence, as well as risk of sentinel lymph node positivity, independent of traditional staging factors, and has been studied in more than 6,000 patient samples. Using tissue from the primary melanoma, the test measures the expression of 31 genes. The test has been validated in four archival risk of recurrence studies of 901 patients and six prospective risk of recurrence studies including more than 1,600 patients. Impact on patient management plans for one of every two patients tested has been demonstrated in four multicenter and single-center studies including more than 560 patients. The consistent performance and accuracy demonstrated in these studies provides confidence in disease management plans that incorporate DecisionDx-Melanoma test results. To predict risk of recurrence and likelihood of sentinel lymph node positivity, the Company utilizes its proprietary algorithms, i31-ROR and i31-SLNB, to produce an Integrated Test Result. Through Dec. 31, 2021, DecisionDx-Melanoma has been ordered 90,154 times for use with patients 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.

More information about the Castle tests 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 and Barrett's esophagus. 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 capability of DecisionDx-Melanoma and DecisionDx-SCC to independently and significantly risk-stratify patients according to their metastatic risk to guide better informed and more risk-aligned patient care; DecisionDx-Melanoma's ability to provide additional risk information as a complement to existing melanoma management plans and guide more precise and personalized patient care; and DecisionDx-SCC's ability to assist physicians in guiding more risk-appropriate surveillance and treatment decisions. 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, subsequent study results and findings may contradict earlier study results and findings, including with respect to the discussion of DecisionDx-Melanoma and DecisionDx-SCC 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 Annual Report on Form 10-K for the fiscal year ended Dec. 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.

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Source: Castle Biosciences, Inc.