NEWS RELEASE

Castle Biosciences Presents Data Reinforcing the Clinical Utility of Its DecisionDx® Dermatologic Portfolio

11/24/2021

Presented at American Society for Dermatologic Surgery (ASDS) 2021 Annual Meeting

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company applying innovative diagnostics to inform disease management decisions and improve patient outcomes, today announced oral presentations on its DecisionDx® gene expression profile (GEP) tests for skin cancer at the American Society for Dermatologic Surgery (ASDS) 2021 Annual Meeting, held Nov. 19-21, 2021.

“We are excited to share data further reinforcing the clinical utility of our GEP tests with leading experts and health care professionals,” said Derek Maetzold, president and chief executive officer of Castle Biosciences. “We believe our DecisionDx tests complement dermatology clinicians’ arsenal of tools and help ensure the best possible outcomes for their patients. The clinically actionable information that our tests provide can help clinicians make informed and personalized treatment decisions for each patient based on their unique biology.”

DecisionDx®-Melanoma:

DecisionDx-Melanoma is Castle’s risk-stratification GEP test that is designed to predict 5-year risk of metastasis, as well as metastasis to the sentinel lymph node (SLN), independent of traditional staging factors. The test’s Integrated Test Result (ITR) includes the traditional class designation of lowest risk (Class 1A), increased risk (Class 1B/2A) or highest risk (Class 2B), as well as a more precise risk prediction for both SLN positivity and risk of recurrence, distant metastasis and melanoma survival in patients with stage I, II or III melanoma through the i31- GEP

algorithms (i31-SLNB and i31-Risk of Recurrence (ROR)). The i31-SLNB and i31-ROR are distinct, independently validated algorithms that integrate clinicopathologic features with the DecisionDx-Melanoma score.

Nicholas Taylor, M.D., Ph.D. presented data on DecisionDx-Melanoma through an oral presentation titled "Integrated clinicopathologic data and gene expression profile predict sentinel lymph node positivity and recurrence-free and distant metastasis-free survival in cutaneous melanoma."

Study background and findings:

- The study's objective was to understand how integrating gene expression profiling with clinical and pathologic features can improve personalized medicine.
- DecisionDx-Melanoma's continuous score was integrated with clinical and pathologic factors using the proprietary i31-SLNB and i31-ROR algorithms to predict the likelihood of SLN positivity, recurrence-free survival (RFS) and distant metastasis-free survival (DMFS).
- The study results showed that patients with a negative SLN but a high-risk DecisionDx-Melanoma result for RFS had outcomes similar to patients with a positive SLN. In contrast, patients with a positive SLN but a low-risk DecisionDx-Melanoma result had outcomes similar to patients with a negative SLN.
- Overall, the study demonstrated that integrating the DecisionDx-Melanoma continuous risk score with a patient's clinicopathologic factors can identify patients at the highest and lowest risk for recurrence or metastasis, thereby informing individualized management plans for patients with melanoma.

DecisionDx®-SCC:

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 high-risk cutaneous squamous cell carcinoma (SCC) having one or more risk factors.

An oral presentation on DecisionDx-SCC titled "Incorporation of a prognostic 40-gene expression profile (40-GEP) test into risk assessment of cutaneous squamous cell carcinoma (SCC) in a Mohs micrographic surgery (MMS) treated population" was presented by Sarah T. Arron, M.D., Ph.D.

Study background and findings:

- Mohs micrographic surgery (MMS) is the current standard of care for SCC and is an effective technique for treating high-risk SCCs.
- The objective of the study was to evaluate the potential of DecisionDx-SCC to stratify metastatic risk within a high-risk SCC population treated by MMS, representing patients with the highest likelihood for complete

tumor resection.

- The study analyzed 328 patients with National Comprehensive Cancer Network (NCCN) high-risk tumors who were treated with MMS with confirmed clean margins.
- Patients receiving a DecisionDx-SCC Class 2B result had a high metastasis rate of 58.8%, suggesting that this set of patients may benefit from additional adjuvant treatment after MMS.
- Univariate and multivariate Cox regression analysis showed that DecisionDx-SCC provides independent prognostication for metastasis (hazard ratio of 15.12 and a p value of <0.001 for multivariate Class 2B results) when compared to traditional high-risk clinicopathological factors, such as presence of perineural invasion, poor differentiation and deep invasion.
- The specificity and positive predictive value (PPV) of a high-risk Class 2B DecisionDx-SCC result were higher when compared to American Joint Committee on Cancer Staging Manual Eighth Edition (AJCC8) (T3/T4 tumors) and Brigham and Women's Hospital (BWH) (T2b/T3 tumors), demonstrating that DecisionDx-SCC accurately identified the patients at highest risk for a poor outcome, while maintaining a similar negative predictive value (NPV) and sensitivity.
- Overall, the study data showed that DecisionDx-SCC demonstrated significant risk stratification for MMS-treated patients with confirmed complete margin clearance.
- Statistically significant survival analyses, adjusted for clinicopathological factors, and improved accuracy metrics compared to those of current staging systems, indicate that DecisionDx-SCC adds value to current methods of risk assessment.
- Incorporating DecisionDx-SCC into post-MMS SCC patient risk assessment could facilitate more personalized and improved patient management and disease-related outcomes.

Comprehensive Diagnostic Offering:

Castle's Comprehensive Diagnostic Offering (CDO) leverages the strengths of both myPath® Melanoma and DecisionDx® DiffDx™-Melanoma, two GEP tests designed to provide a highly accurate, objective result to aid dermatopathologists and dermatologists in characterizing difficult-to-diagnose melanocytic lesions.

"A comprehensive diagnostic offering (CDO) increases rates of actionable results of the 23- and 35-gene expression profile test for use as ancillary diagnostics for difficult-to-diagnose melanocytic lesions" was presented as part of an industry-sponsored session by Matthew Goldberg, M.D., medical director of Castle Biosciences.

Background and conclusions:

- Diagnostic ambiguity of melanocytic lesions can lead to clinical management uncertainty and complex conversations with patients regarding treatment and follow-up care.
- Castle's Comprehensive Diagnostic Offering (CDO) is designed to leverage the strengths of both myPath

Melanoma and DecisionDx DiffDx-Melanoma to report actionable results of benign gene expression profile or malignant gene expression profile for the greatest number of lesions submitted for testing.

- Castle's CDO workflow significantly improved the reporting of clinically actionable results (benign or malignant) from ~77% with myPath alone, to more than 98% when run as part of the diagnostic workflow with DecisionDx DiffDx-Melanoma.

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 sentinel lymph node positivity, independent of traditional staging factors, and has been studied in more than 5,700 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 Sept. 30, 2021, DecisionDx-Melanoma has been ordered 84,195 times for use in patients with cutaneous melanoma.

More information about the test and disease can be found at **www.CastleTestInfo.com**.

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 test and disease can be found at **www.CastleTestInfo.com**.

About Castle Biosciences' Comprehensive Diagnostic Offering for Difficult-to-Diagnose

Melanocytic Lesions

Castle Biosciences' comprehensive diagnostic offering leverages the strengths of myPath® Melanoma and DecisionDx® DiffDx™-Melanoma. These gene expression profile tests are designed to provide a highly accurate, objective result to aid dermatopathologists and dermatologists in characterizing difficult-to-diagnose melanocytic lesions. Of the approximately 2 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 highly 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 DecisionDx DiffDx-Melanoma are designed to reduce uncertainty and provide confidence for dermatopathologists and help dermatologists deliver more informed patient management plans.

More information about the test and disease can be found at **www.CastleTestInfo.com**.

About Castle Biosciences

Castle Biosciences (Nasdaq: CSTL) is a commercial-stage diagnostics company focused on providing physicians and their patients with personalized, clinically actionable genomic information to make more accurate treatment decisions. The Company currently offers tests for patients with cutaneous melanoma (DecisionDx®-Melanoma, DecisionDx®-CMSeq), cutaneous squamous cell carcinoma (DecisionDx®-SCC), suspicious pigmented lesions (myPath® Melanoma and DecisionDx® DiffDx™-Melanoma) and uveal melanoma (DecisionDx®-UM, DecisionDx®-PRAME and DecisionDx®-UMSeq). For more information about Castle's gene expression profile tests, visit **www.CastleTestInfo.com**.

Castle also has active research and development programs for tests in other dermatologic 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. Castle Biosciences is based in Friendswood, Texas (Houston), and has laboratory operations in Phoenix.

For more information, visit **www.CastleBiosciences.com**.

Forward-Looking Statements

The information in this press release contains forward-looking statements and information within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. These forward-looking statements include, but are not limited to, statements concerning the clinical utility of our GEP tests with leading experts and health care professionals, including their ability to help clinicians make informed and patient-specific treatment decisions, and ensure the best possible outcomes for their patients, DecisionDx-Melanoma's ability to identify patients at the highest and lowest risk for recurrence or metastasis and inform individualized management plans for patients with melanoma, and DecisionDx-SCC's ability to stratify risk for MMS-treated patients with confirmed complete margin clearance, add value to current methods of risk assessment and facilitate more personalized and improved patient management and disease-related outcomes. 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 that contradict earlier study results and findings, our GEP tests' actual utility in practice may not yield the aforementioned benefits to patients demonstrated in study results, and the risks set forth in our Quarterly Report on Form 10-Q for the quarter ended Sept. 30, 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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