NEWS RELEASE

Castle Adds to Evidence Supporting Its Skin Cancer Test Portfolio through Multiple Data Presentations at the SDPA Annual Summer Dermatology Conference 2022

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New data from pooled analysis shows DecisionDx®-Melanoma can identify patients at a high risk of melanoma recurrence within a patient population deemed low risk (T1, ≤1mm) by traditional staging systems

Survey of 400 dermatologic clinicians demonstrates how DecisionDx®-SCC results can lead to risk-aligned treatment plan changes for patients with high-risk squamous cell carcinoma

Castle's laboratory workflow for MyPath® Melanoma and DecisionDx® DiffDx®-Melanoma increased the reporting of clinically actionable results to over 99% in a performance cohort of 350 archival biopsy samples

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced new data demonstrating the clinical value of the Company's tests for skin cancer in guiding more informed disease management decisions. Data on each of Castle's skin cancer tests, as outlined below, was shared during the recent Society of Dermatology Physician Assistants (SDPA) Annual Summer Dermatology Conference 2022.

DecisionDx®-Melanoma

While patients with thin cutaneous melanoma (CM) tumors (T1, ≤1mm) are typically deemed low risk by traditional staging alone, studies have shown that up to 15%[1-3] of these patients will go on to experience disease recurrence.

As such, there is an opportunity to use DecisionDx-Melanoma to identify which patients with thin CM tumors may have aggressive tumor biology and thus could benefit from increased surveillance through advanced imaging or adjuvant therapy.

“The data in this study reinforced what we find in clinical practice: some patients initially thought to be low risk by traditional, clinicopathologic staging methods can have more aggressive tumor biology, and their melanoma may come back, even after their primary tumor has been removed,” said lead study author Abel Jarell, M.D., dermatologist and dermatopathologist at Northeast Dermatology Associates in Portsmouth, New Hampshire. “DecisionDx-Melanoma can help identify these high-risk patients who may warrant a need for more intense treatment and surveillance to reduce their likelihood of recurrence and potentially improve the overall outcome of their disease.”

Patients with T1 CM (classified according to the American Joint Committee on Cancer Eighth Edition (AJCC8) staging framework) from three previously published studies were combined for analysis (N=979). The results of the analysis was shared in a poster titled, “The 31-gene expression profile test stratifies the risk of recurrence in patients with T1 cutaneous melanoma: Results of a pooled analysis of 979 patients.” The poster, which is available **here**, highlights the ability of DecisionDx-Melanoma to stratify patients with thin CM tumors according to their risk of recurrence.

Study highlights:

- In the study, patients with thin tumors who received a DecisionDx-Melanoma high-risk Class 2B result had lower 3-year recurrence-free survival than patients with a low-risk Class 1A result (75.9% vs. 97.7%) and an 8-fold higher recurrence rate (22.5% vs. 2.7%, $p<0.001$).
- Moreover, nearly one in four patients in the cohort who received a DecisionDx-Melanoma high-risk Class 2B result experienced melanoma recurrence, with a median 11-month time to recurrence.
- A high-risk Class 2B test result was a significant predictor of disease recurrence (HR=4.49, $p=0.001$), similar to a positive sentinel lymph node (SLN) (HR=4.46, $p<0.001$). As a positive SLN is evidence that a patient’s melanoma has spread, these patients are candidates for advanced imaging and potentially, adjuvant therapies. These data suggest that patients receiving a DecisionDx-Melanoma Class 2B result could benefit from similar, more intense treatment aligned to their elevated risk of recurrence.

DecisionDx®-SCC

The rise of squamous cell carcinoma (SCC) diagnoses is an emerging problem in the U.S. that is complicated by broad clinicopathological staging criteria and treatment guidelines for the disease. Castle’s DecisionDx-SCC test was designed to address this unmet medical need for patients with SCC and one or more high-risk factors. The test provides clinically actionable information about a patient’s biologic risk of metastasis, independent of

clinicopathologic factors and traditional staging systems, which can help guide more informed and risk-appropriate treatment decisions within established guidelines.

The poster, titled "Study of 400 dermatologic clinicians corroborates the clinical impact of the prognostic 40-gene expression profile (40-GEP) test in patients with high-risk cutaneous squamous cell carcinoma (SCC)," shares the impact of DecisionDx-SCC test results on clinicians' management of invasive SCC. The poster is available **here**.

"The study showed that many clinicians would consider de-escalating treatment plan decisions and potentially forgoing interventions for some patients if their DecisionDx-SCC test results indicated a low biological risk of metastasis," said Robert Cook, Ph.D., senior vice president of research and development at Castle Biosciences. "DecisionDx-SCC test results, when considered on their own and in the context of other clinicopathologic staging systems, can lead to risk-aligned treatment plan changes, either de-intensified or intensified, based on a patient's individual metastatic risk. We were pleased that the survey responses supported this."

Study highlights:

- The majority of clinicians (approximately 80%) indicated they would recommend ordering DecisionDx-SCC for patients with SCC lesions on high-risk locations when also considering the size of the lesion.
- Previous studies[4,5] have found that DecisionDx-SCC test results (low, moderate or high biological risk results) led to risk-aligned decreases or increases in clinician-directed treatment plans.
- The survey results supported this, with the majority of clinicians who recommend the use of interventions for patients with high-risk SCC indicating they would consider forgoing certain treatments (64% for radiologic nodal imaging, 68% for SLN biopsy and 66% for adjuvant radiation therapy) for at least some patients who received a DecisionDx-SCC Class 1 test result (low biologic risk of metastasis).
- Intention to further reduce recommendations for radiologic nodal imaging or SLN biopsy with a Class 1 test result was seen in those clinicians who were already using DecisionDx-SCC in their clinical practice (72% and 75%, respectively), accentuating the impact of the test among users.

MyPath® Melanoma and DecisionDx® DiffDx®-Melanoma

MyPath Melanoma and DecisionDx DiffDx-Melanoma are Castle's diagnostic tests designed to provide objective, highly accurate results to aid in the diagnosis of suspicious melanocytic lesions with ambiguous histopathology. The tests can provide clinically actionable information to help guide and potentially increase confidence in a diagnosis, if any uncertainty or discordance exists, to help clinicians deliver more informed patient management plans and provide their patients with more appropriate and individualized care.

The poster, titled "The current 23- and 35-gene expression profile (GEP) ancillary diagnostic testing workflow for

difficult-to-diagnose melanocytic lesions increases the rate of actionable results to 99%," highlights how the current laboratory workflow for Castle's two diagnostic tests can leverage the strengths of both individual tests to report accurate and clinically actionable results. The poster can be viewed **here**.

Study highlights:

- In the current laboratory workflow, clinical samples are processed first through MyPath Melanoma, and if a technical failure or intermediate result is received, processed next through DecisionDx DiffDx-Melanoma.
- In the study, the test workflow demonstrated a high rate of accuracy in the performance cohort, with 96.0% sensitivity and 87.8% specificity.
- Based on the analysis of Castle test results reported over a six-month period (June 3-Dec. 3, 2021), the current workflow substantially improved the reporting of clinically actionable results from a historic rate of ~77% with MyPath Melanoma alone to over 99% when both tests were run in a combined workflow.

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 (CM) metastasis or recurrence, as well as the risk of sentinel lymph node positivity, independent of traditional staging factors, and has been studied in more than 6,300 patient samples. Using tissue from the primary melanoma, the test measures the expression of 31 genes. Additionally, Castle has an ongoing collaboration with the National Cancer Institute (NCI) to link DecisionDx-Melanoma testing data with data from the Surveillance, Epidemiology and End Results (SEER) Program's registries on CM cases. This collaboration has resulted in Castle's analysis of 5,226 samples (clinically tested through December 31, 2018) in a study to evaluate melanoma-specific survival and overall survival; in this study, patients tested with DecisionDx-Melanoma had better survival rates than untested patients, and the data suggested that DecisionDx-Melanoma can accurately risk-stratify for disease progression to aid in risk-aligned treatment plans for improved patient outcomes and survival. 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. Additionally, impact on patient management plans for one of every two patients tested has been shown in five multi-center/single-center studies including more than 800 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 March 31, 2022, DecisionDx-Melanoma has been ordered 97,288 times for 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.

About MyPath® Melanoma and DecisionDx® DiffDx®-Melanoma

MyPath Melanoma and DecisionDx DiffDx-Melanoma are two gene expression profile tests designed to provide a highly 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 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 Castle's 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, 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**.

Biosciences, Inc.

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 opportunity to use DecisionDx®-Melanoma to identify which patients with thin CM tumors may have aggressive tumor biology; the ability of DecisionDx-Melanoma to identify patients who could benefit from increased surveillance through advanced imaging or adjuvant therapy to reduce their likelihood of recurrence and improve the overall outcome of their disease; our belief that patients receiving a DecisionDx-Melanoma Class 2B result could benefit from more intense treatment aligned to their elevated risk of recurrence, similar to patients receiving a positive SLN; our belief that some traditionally low risk CM patients can have more aggressive tumor biology and experience recurrence, even after their primary tumor has been removed; the ability of our DecisionDx-SCC test to lead to risk-aligned treatment plan changes for patients with high-risk SCC and help guide more informed and risk-appropriate treatment management decisions within established guidelines, including forgoing unnecessary, invasive interventions in a risk-appropriate manner, consistent with the reduced biologically determined risk of metastasis; and the ability of our MyPath Melanoma and DecisionDx DiffDx-Melanoma diagnostic tests to provide clinically actionable information to help guide and potentially increase confidence in a diagnosis, and the potential of the current laboratory workflow for our two diagnostic tests to leverage the strengths of both individual tests to report accurate and clinically actionable results. The words "potential," "may," "could" and "can" 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 this study, including with respect to the discussion of our skin cancer test portfolio in this press release; actual application of our skin cancer 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 March 31, 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.

[1]Whiteman DC, et al. Journal Inv Derm. 2015;135(4):1190-1193.

[2]Gershenwald JE, et al. Ann Surg Oncol. 2018;25(8):2105-2110.

[3]Kalady MF, et al. Annals of surgery. 2003;238(4):528-535.

[4]Farberg, et al. SKIN 2022, 6(2)

[5]Arron, et al. J Drugs Dermatol 2021 Jun 1;20(6)

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