NEWS RELEASE

Expanded SEER Registries Dataset Shows Improved Survival for DecisionDx®-Melanoma Tested Patients Compared to Untested Patients

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In a recent study, patients diagnosed with melanoma and tested with DecisionDx-Melanoma had improved survival (27% improvement in melanoma-specific survival) compared to untested patients

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced new data from a recent study in which patients tested with DecisionDx®-Melanoma in addition to traditional clinicopathologic factors had improved survival compared to patients with only traditional clinicopathologic factors available to determine their treatment and follow-up plan. The study is part of the Company's 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 cutaneous melanoma (CM) cases. The data will be shared in a poster presentation at the 18th European Association of Dermato Oncology (EADO) Congress, being held virtually and in Seville, Spain, April 21-23, 2022.

"Once again, the real-world data analyzed as part of our collaboration with NCI has shown the potential for a strong survival benefit in patients whose melanoma management plans included personalized test results provided by DecisionDx-Melanoma," said Derek Maetzold, president and chief executive officer of Castle Biosciences. "We are committed to improving health through innovative tests that guide patient care. This study data demonstrated the ability of our test to help patients and clinicians in informing disease management and treatment plans that have the potential to improve patient survival."

The poster, titled “Incorporating the 31-gene expression profile test stratifies survival outcomes and leads to improved survival compared to clinicopathologic factors alone: A Surveillance, Epidemiology, and End Results (SEER) Program collaboration,” discusses the full cohort of data obtained thus far through the collaboration. The poster examines the impact of testing with DecisionDx-Melanoma on a patient’s survival and the ability of DecisionDx-Melanoma to accurately risk-stratify a group of real-world, unselected, prospectively tested patients with CM. The poster can be viewed **here**.

As part of Castle’s collaboration with NCI, patient data, including melanoma-specific survival (MSS), overall survival (OS) and additional clinicopathologic information provided by the SEER registries, was linked to data for patients with Stage I-III CM who had been tested with DecisionDx-Melanoma.

To assess if patients tested with DecisionDx-Melanoma had higher survival rates than patients who were not tested with DecisionDx-Melanoma, a group of tested patients (n=3,261) was matched to a group of patients who did not receive DecisionDx-Melanoma test results as part of their clinical care (n=10,863); the matching was based on 11 clinicopathologic and socioeconomic variables using a 1:3 ratio. The untested patients and their clinicians had only the traditional clinicopathologic features upon which to develop a melanoma treatment plan. Matching cases were limited to diagnoses in 2016 and forward to account for potential access to adjuvant therapy. In the study, patients tested with DecisionDx-Melanoma had improved survival compared to untested patients, with a 27% (hazard ratio (HR)=0.73, p=0.028) and 21% (HR=0.79, p=0.006) MSS and OS survival benefit, respectively. This suggests that DecisionDx-Melanoma test results can aid in providing more risk-aligned treatment plans for improved patient outcomes.

Additionally, similar to previously published retrospective and prospective studies, DecisionDx-Melanoma was able to accurately and independently risk-stratify patients for MSS and OS. Moreover, the data indicated that a DecisionDx-Melanoma Class 2B result was a significant and independent predictor of MSS (HR= 8.51, p<0.001) and OS (HR= 2.48, p<0.001), and conferred the highest risk of all clinicopathologic factors included in multivariable analyses that included age, ulceration status, Breslow thickness and sentinel lymph node status.

Overall, the study data showed that the precise, personalized test results provided by DecisionDx-Melanoma have the potential to improve patient survival when used as part of a melanoma management plan. In the study, patients tested with DecisionDx-Melanoma, whose clinicians also had the benefit of the patient’s clinicopathologic factors traditionally used to assess metastatic risk, had improved survival compared to patients with only traditional clinicopathologic factors available to determine their treatment and follow-up plan.

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 clinically tested samples thus far (as of April 21, 2022) in a study to evaluate risk of recurrence; 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 Dec. 31, 2021, DecisionDx-Melanoma has been ordered 90,154 times for patients with cutaneous melanoma.

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 potential for a strong survival benefit or improved patient survival in patients whose melanoma management plans include personalized test results provided by DecisionDx-Melanoma; the ability of DecisionDx-Melanoma to help patients and clinicians in informing disease management and treatment plans that have the potential to improve patient survival; and the ability of DecisionDx-Melanoma to aid in providing more risk-aligned treatment plans for improved patient outcomes. The words "potential," "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, 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 DecisionDx-Melanoma test discussed 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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