NEWS RELEASE

Castle Biosciences Collaborates with the National Cancer Institute to Link DecisionDx®-Melanoma Testing Data with SEER Registries' Cutaneous Melanoma Cases

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Analysis of the first subset of linked SEER patient data demonstrates DecisionDx®-Melanoma testing was associated with improved overall survival rates compared to untested patients

DecisionDx-Melanoma stratifies patient risk of death in an unselected, prospectively tested population of patients 65 years and older, consistent with prior study cohorts

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a leader in transforming disease management and improving patient outcomes through innovative diagnostics, today announced a 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.

CM cases in the SEER registries that were diagnosed between 2013-2018 were linked with DecisionDx-Melanoma results and additional clinicopathologic information from patients tested between 2013-2018. The Company expects to continue collaborating with the NCI to link the SEER registries' CM cases diagnosed post-2018 with DecisionDx-Melanoma test results. The initial linked dataset is expected to be broadly available to interested researchers through the standard data request process for SEER Specialized Datasets in 2022.

Data analysis from the first subset of patients was shared in a poster presentation at the 2022 Winter Clinical Dermatology Conference, held Jan. 14-19 in Koloa, Hawaii.

“We are excited to collaborate with the NCI to link DecisionDx-Melanoma test results with the SEER registries’ data,” said Derek Maetzold, president and chief executive officer of Castle Biosciences. “Castle is committed to providing clinically actionable tests to improve patient outcomes. Analysis from the first subset of patients (65 years or older at time of diagnosis and diagnosed in 2016 or later) provides real-world evidence of the capability of our test to do just that. Specifically, when controlling for demographic and clinicopathological variables, patients tested with DecisionDx-Melanoma had better overall survival rates over 2.5 years than patients not tested.”

The poster, titled “31-gene expression profile testing survival benefit in a population-based analysis of cutaneous melanoma patients ≥65 years of age,” highlighted the first analysis of Castle’s DecisionDx-Melanoma testing data in the NCI’s SEER Program registry. The poster can be viewed **here**.

Study methods and findings:

- DecisionDx-Melanoma is Castle’s gene expression profile test that uses an individual patient’s tumor biology to predict the risk of cutaneous melanoma metastasis or recurrence, as well as the risk of sentinel lymph node (SLN) positivity, independent of traditional staging factors. Among other outputs of the test, DecisionDx-Melanoma classifies a patient’s tumor as lowest risk of recurrence/metastasis (Class 1A), increased risk of recurrence/metastasis (Class 1B/2A) or highest risk of recurrence/metastasis (Class 2B).
- All incident CM cases diagnosed between 2013-2018 in the NCI’s SEER Program registry were included in the study. The SEER registries linked CM cases in the registry to DecisionDx-Melanoma testing data provided by Castle Biosciences.
- While all CM diagnoses between 2013-2018 were included in the linkage, this analysis was limited to a subset of 2,048 patients with Stage I-III melanoma who were ≥65 years or older at the time of diagnosis and were diagnosed between 2016-2018 to account for access to adjuvant therapy.
- Patients tested with DecisionDx-Melanoma were successfully matched to those not tested with DecisionDx-Melanoma based on clinical, pathological and demographic data.
- After matching, patients tested with DecisionDx-Melanoma had better overall survival rates than patients who had not been tested, demonstrating a direct effect of DecisionDx-Melanoma testing on patient survival (hazard ratio=0.66 compared to untested patients, p=0.002).
- The results also confirmed DecisionDx-Melanoma’s ability to stratify patient risk in an unselected, prospectively tested population of CM patients into low (Class 1A) and high-risk (Class 2B) mortality groups.
- Patients who received a DecisionDx-Melanoma high-risk result had a ten-fold increase in death rate compared to patients who received a low-risk result (12.3% death rate for a Class 2B result compared to 1.5% for a Class 1A result), demonstrating the independent prognostic value of the test.
- In sum, the study data provide direct evidence that CM patients tested with DecisionDx-Melanoma have

better survival rates than untested patients, suggesting that the test can aid in risk-aligned treatment plans for improved patient outcomes and survival rates.

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 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 the SEER Program

The Surveillance, Epidemiology and End Results (SEER) Program (**https://seer.cancer.gov/**) is an authoritative source for cancer statistics in the United States. The SEER Program provides information on cancer statistics in an effort to reduce the cancer burden among the U.S. population and is supported by the **Surveillance Research Program (SRP)** in the NCI's **Division of Cancer Control and Population Sciences (DCCPS)**. The SEER Program registries collect data on cancer cases diagnosed in their catchment area from various locations and sources throughout the United States. Data collection began in 1973 with a limited number of registries and continues to expand to include even more areas and demographics today covering 48% of US population. The SEER Program registries link to data provided by a variety of federal and commercial partners to support the research community in conducting cancer surveillance and epidemiological research. The data are available to qualified researchers.

About Castle Biosciences

Castle Biosciences (Nasdaq: CSTL) is a leading diagnostics company that provides personalized, clinically actionable information to clinicians and patients to inform treatment decisions and improve health outcomes. The Company is focused on transforming the disease management paradigm in skin cancer and other diseases with high clinical

need by leveraging advanced technologies for its portfolio of innovative diagnostic tests.

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 timing and availability of linked data in the SEER database; DecisionDx-Melanoma's contribution to increased survival rates for patients with CM; and DecisionDx-Melanoma's ability to aid in risk-aligned treatment plans for improved patient outcomes and survival rates. 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 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 quarter ended September 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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