NEWS RELEASE

Long-term Outcomes Data Shared at SSO 2024 Show That Patients with a Low-Risk DecisionDx®-Melanoma Test Result Were Recurrence Free at Three Years, Including Those Who Utilized the Test to Help Guide the Decision to Avoid an SLNB

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Castle's second presentation at SSO 2024 shows that in a study of 979 patients, DecisionDx-Melanoma demonstrated clinical use value in patients with TI cutaneous melanoma (CM), identifying high-risk patients who could consider a more intensive treatment pathway, such as a sentinel lymph node biopsy (SLNB) and imaging surveillance

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced that new data highlighting the performance of its DecisionDx-Melanoma test in predicting risk of sentinel lymph node (SLN) positivity in patients with CM is being presented at the Society of Surgical Oncology 2024 (SSO 2024) Annual Meeting, being held March 20-23 in Atlanta.

"We have previously demonstrated that our DecisionDx-Melanoma test identifies patients who are eligible for an SLNB but have less than a 5% likelihood of being SLN positive, and could therefore consider avoiding the procedure," said Derek Maetzold, president and chief executive officer of Castle Biosciences. "We have also demonstrated that our test is a strong and independent predictor of metastasis. The study that was orally presented at SSO 2024 demonstrates that patients who did avoid an SLNB procedure had excellent outcomes to date. This demonstration is highly important as it showed that our test can help patients avoid an unnecessary procedure."

DecisionDx-Melanoma is supported by 50 peer-reviewed publications involving more than 10,000 patient samples, demonstrating its robust value in guiding risk-aligned patient care. The test has been designed and validated to inform two clinical questions in the management of melanoma: a patient's risk of melanoma recurrence and metastasis, and their individual risk of SLN positivity, as highlighted in Castle's SSO 2024 abstracts outlined below.

DecisionDx®-Melanoma

- Oral Presentation Number and Title: 62: Prospective validation of the i31-gene expression profile test for cutaneous melanoma to select patients who may consider foregoing sentinel lymph node biopsy
- Session: Melanoma Parallel Session
- Presenter and Lead Author: J. Michael Guenther, M.D., St. Elizabeth Physicians, Edgewood, Kentucky

Summary: This study shares three-year outcomes data from Castle's prospective, multicenter study of patients with CM who were being considered for an SLNB (n=322). SLNB is an invasive surgical procedure used to determine whether a patient's cancer has spread to nearby lymph nodes; the procedure returns a surgical result that is negative for metastasis in approximately 88% of patients. Current National Comprehensive Cancer Network® guidelines use a 5% likelihood of SLN positivity as the threshold to avoid versus consider/recommend an SLNB due to an increased risk of metastasis. DecisionDx-Melanoma has been validated to provide a patient's individualized risk of SLN positivity (i31-GEP for SLNB) by integrating clinical and pathologic risk factors with the patient's tumor biology. In the study, no patients with a DecisionDx-Melanoma predicted risk of SLN positivity less than 5% had a positive SLN (among all tumor stages studied). If DecisionDx-Melanoma was used to inform management decisions, the test's results could have further reduced the number of patients with T1-T2 tumors who could have avoided SLNB by 25%. Additionally, at three years, all patients with a low-risk DecisionDx-Melanoma test result were recurrence free (recurrence free survival of 100%). These data demonstrate that use of DecisionDx-Melanoma test results can guide accurate, risk-aligned clinical decision-making regarding the SLNB surgical procedure, within current guidelines. Further, the test can identify low-risk patients who can safely consider foregoing SLNB, thereby reducing unnecessary SLNB procedures (by approximately 25% in this study alone) and the associated costs and risks of complications that accompany them.

ePoster Number and Title: E309: Utility of 31-gene expression profile test in identifying patients with T1 cutaneous melanoma at high risk of SLN positivity and recurrence

Session: Melanoma Parallel Session

Summary: In a pooled cohort of 979 patients with thin (T1) tumors, a DecisionDx-Melanoma Class 2B result was the strongest predictor of a positive SLN, among other risk factors that included patient age, tumor location, Breslow thickness, tumor ulceration and more. While the study outlined above demonstrates the ability of the test

to identify patients at low risk of SLN positivity who can safely forgo SLNB, this study shows that it can also identify patients at high risk who should consider it. By identifying patients who have a higher risk of SLNB positivity and recurrence, DecisionDx-Melanoma can help determine which patients should be considered for more intensive management, such as SLNB, increased follow-up frequency and imaging surveillance, to improve patient outcomes.

ePosters are available for conference attendees in the ePoster Online Gallery.

About DecisionDx®-Melanoma

DecisionDx-Melanoma is a gene expression profile risk stratification test. It is designed to inform two clinical questions in the management of cutaneous melanoma: a patient's individual risk of sentinel lymph node (SLN) positivity and a patient's personal risk of melanoma recurrence and/or metastasis. By integrating tumor biology with clinical and pathologic factors using a validated proprietary algorithm, DecisionDx-Melanoma is designed to provide a comprehensive and clinically actionable result to guide risk-aligned patient care. DecisionDx-Melanoma has been shown to be associated with improved patient survival and has been studied in more than 10,000 patient samples. DecisionDx-Melanoma's clinical value is supported by 50 peer-reviewed and published studies, providing confidence in disease management plans that incorporate the test's results. Through Dec. 31, 2023, DecisionDx-Melanoma has been ordered more than 150,000 times for patients diagnosed 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, Barrett's esophagus, mental health conditions and uveal melanoma. Additionally, the Company has active research and development programs for tests in other diseases with high clinical need, including its test in development to help guide systemic therapy selection for patients with moderate-to-severe atopic dermatitis, psoriasis and related conditions. To learn more, please visit **www.CastleBiosciences.com** and connect with us on **LinkedIn**, **Facebook**, **X** 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 ability of DecisionDx-Melanoma test to (i) identify high risk patients who could consider a more intensive treatment pathway, (ii) further reduce the number of patients with T1-T2 tumors who could have avoided SLNB by 25% and (iii) guide accurate, risk-aligned clinical decision-making regarding the SLNB surgical procedure, within current guidelines. The words "believe," "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 these studies, including with respect to the discussion of our tests 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 year ended December 31, 2023, 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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