NEWS RELEASE

Prospective, Multicenter Study Demonstrates That DecisionDx®-Melanoma Test Results Can Significantly Reduce the Number of Sentinel Lymph Node Biopsy (SLNB) Procedures Performed When Used Within the Context of Current Guidelines

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FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced the publication of data from a prospective, multicenter study, called DECIDE.[1,2] In the study, DecisionDx®-Melanoma test results influenced 85% of clinicians' decisions regarding the sentinel lymph node biopsy (SLNB) surgical procedure. Additionally, use of the tests' results within current guideline recommendations led to a significant reduction in SLNB procedures performed, demonstrating the potential clinical value of the test to guide risk-aligned patient care.

"DecisionDx-Melanoma is the best-studied molecular test for use in cutaneous melanoma to date, with studies involving more than 10,000 research subjects. DecisionDx-Melanoma provides personalized information about a patient's risk of sentinel lymph node (SLN) positivity to inform decisions about whether to safely forego or pursue an SLNB," said Maki Yamamoto, M.D., board-certified surgical oncologist and associate professor of surgery at the University of California-Irvine School of Medicine in Orange, California. "The data from this prospective, multicenter study showed that clinicians who used the test performed fewer SLNBs overall, which can alleviate complication rates and high costs associated with the procedure, and focus surgical procedures on patients who have a greater likelihood of being SLN positive."

"We believe DecisionDx-Melanoma has the ability to influence management decisions based on ample evidence

provided in more than 40 peer-reviewed studies and the experience of clinical use in more than 120,000 patients," said Robert Cook, Ph.D., senior vice president of research and development at Castle Biosciences. "We also believe that the use of molecular tests to guide clinical decisions adds value that is independent from the clinicopathologic risk factors traditionally used in melanoma risk assessment. We are pleased the DECIDE study results showed that using our DecisionDx-Melanoma test in combination with clinicopathologic features demonstrated superiority over the use of clinicopathologic factors alone to guide appropriate decisions about SLNB use."[3]

Study highlights:

- SLNB surgery is an invasive surgical procedure that is used for risk-stratification purposes; according to recent studies, the procedure returns a surgical result that is negative for metastatic spread in up to 88% of patients and has a reported complication rate of 11%.[4,5]
- This prospective, multicenter study included patients with invasive cutaneous melanoma who were being considered for an SLNB procedure and had a T-stage of:
    - T1a (and at least one adverse, high-risk feature),
    - T1b or
    - T2.
- Clinicians received DecisionDx-Melanoma test results prior to making final SLNB decisions and were asked which features influenced their decision on whether to perform the procedure. Potential influencing factors included DecisionDx-Melanoma test results, patient preference and clinical and pathological features.
- The data showed that DecisionDx-Melanoma test results influenced 85% of SLNB decisions, the highest percentage reported in the study, followed by patient preference.
    - When DecisionDx-Melanoma test results influenced for SLNB, the procedure was performed in 92% of the cases in the study; similarly, when the test result influenced against SLNB, the decision was made to forego SLNB in 70% of cases. These data show that use of the test's results can guide risk-aligned, clinical decision-making regarding the SLNB surgical procedure, within current guidelines. Of the remaining 30% of cases where the clinician's decision was influenced by DecisionDx-Melanoma test results to forego SLNB but the biopsy was performed, 83% were influenced by patient preference.
- Patients receiving a high-risk (Class 2B) DecisionDx-Melanoma test result had a 22% SLN positivity rate, more than double the historical positivity rate in this patient population.
- The use of DecisionDx-Melanoma test results within current guidelines resulted in a significant reduction in SLNB procedures performed, compared to SLNB decisions based on a patient's clinicopathologic risk factors alone ($p<0.01$).

The publication can be found **here**.

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 more than 40 peer-reviewed and published studies, providing confidence in disease management plans that incorporate the test's results. Through Dec. 31, 2022, DecisionDx-Melanoma has been ordered 120,287 times for patients diagnosed with cutaneous melanoma. More information about the test and disease 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**.

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 of DecisionDx-Melanoma test results to (i) when used within the context of current guidelines, significantly reduce the number of SLNB procedures performed; (ii) provide clinical value and guide risk-aligned patient care and clinical decision-making regarding the SLNB surgical procedure; (iii) alleviate complication rates and high costs associated with the SLNB procedure, and focus surgical procedures on patients

who have a greater likelihood of being SLN positive; and (iv) demonstrate the test's added value that is independent from important clinicopathologic risk factors traditionally used in melanoma risk assessments. The words "believe," "can," "potential," "will" 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 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 three months ended September 30, 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. DECIDE: DecisionDx-Melanoma Impact on Sentinel Lymph Node Biopsy Decisions and Clinical Outcomes
2. Yamamoto M, Sickle-Santanello B, Beard T, et al. The 31-gene expression profile test informs sentinel lymph node biopsy decisions in patients with cutaneous melanoma: results of a prospective, multicenter study [published online ahead of print, 2023 Jan 16]. Curr Med Res Opin. 2023;1-7. doi:10.1080/03007995.2023.2165813
3. Glazer AM, Tassavor M, Portela D, et al. The Integrated 31-Gene Expression Profile Test (i31-GEP) for Cutaneous Melanoma Outperforms the CP-GEP at Identifying Patients who can Forego Sentinel Lymph Node Biopsy when Applying NCCN Guidelines. SKIN J Cutan Med 2022; 6(6):474–481. doi: https://doi.org/10.25251/skin.6.6.4
4. Chen J, Xu Y, Zhou Y, et al. Prognostic role of sentinel lymph node biopsy for patients with cutaneous melanoma: a retrospective study of surveillance, epidemiology, and end-result population-based data. Oncotarget. 2016;7:45671–45677.
5. Moody JA, Ali RF, Carbone AC, et al. Complications of sentinel lymph node biopsy for melanoma – a systematic review of the literature. Eur J Surg Oncol. 2017;43(2):270–277.

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