NEWS RELEASE

DecisionDx®-Melanoma Outperforms Memorial Sloan Kettering Cancer Center (MSKCC) Nomogram in Predicting Sentinel Lymph Node Positivity in Patients with Cutaneous Melanoma

10/5/2023

Study shows the DecisionDx-Melanoma test identifies more patients who can safely forego SLNB than using current guidelines alone or a clinicopathologic-only nomogram

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced a new study demonstrating DecisionDx®-Melanoma outperforms a nomogram developed at the Memorial Sloan Kettering Cancer Center (MSKCC) in predicting the risk of sentinel lymph node (SLN) positivity in patients with cutaneous melanoma (CM). The study is available online in **Anticancer Research**.

“Nearly 90% of patients receive a negative result after undergoing the sentinel lymph node biopsy (SLNB) procedure,[1-2] indicating there is a significant need for more precise methods to identify which patients can safely forego the surgery and still experience good outcomes,” said Michael Tassavor, M.D., study author, board-certified dermatologist and fellowship-trained Mohs surgeon currently practicing in New Jersey. “By providing an accurate prediction of a patient’s likelihood of having a positive SLN, DecisionDx-Melanoma test results can inform important conversations between clinicians and patients and provide added confidence in decisions to proceed without the surgery if a patient’s risk is low.”

The study evaluated the performance of two tools used to identify patients at low and high risk of SLN positivity:

1. Castle's DecisionDx-Melanoma test, which uses advanced algorithms to integrate a patient's clinical and pathologic factors with his/her tumor biology to provide a personalized prediction of the risk of SLN positivity, and melanoma recurrence and metastasis.
2. The MSKCC nomogram, which uses logistic regression and only clinical and pathologic factors to predict a patient's SLN positivity risk.

   Patients from previously published multicenter cohorts with T1-T2 tumors who had undergone the SLNB procedure (n=465) were analyzed using both DecisionDx-Melanoma and the MSKCC nomogram. Following current National Comprehensive Cancer Network (NCCN) guidelines, a risk prediction of less than 5% in the study was considered low risk for SLN positivity, where patients could safely forego the SLNB procedure. A true-to-false-negative ratio was evaluated using this 5% risk threshold. A 5% threshold represents 19 truly negative nodes for one positive SLN missed (19:1 ratio; 1/20 [5%]), meaning that for every 100 patients who avoided SLNB based on NCCN criteria, 5 would have had a missed positive SLN.

   The DecisionDx-Melanoma test resulted in a 36:1 true-to-false-negative ratio (108/3), meaning that for every 100 patients who avoided SLNB based on the test's results, only 2.7 would have had a positive SLN. This is well below the 5% low-risk threshold established by NCCN. DecisionDx-Melanoma's performance was better than that of the MSKCC nomogram, which resulted in a 9:1 true-to-false-negative ratio, suggesting that for every 100 patients avoiding SLNB using the MSKCC nomogram, 10 would have had a positive SLN. DecisionDx-Melanoma also demonstrated better accuracy in predicting SLN positivity, including higher sensitivity (95% vs. 81%) and negative predictive value (97% vs. 90%) than the MSKCC nomogram.

   Importantly, in patients with T1 tumors, for whom the decision to perform SLNB is least clear, using the DecisionDx-Melanoma test to help guide decision-making could have reduced the number of SLNBs by 43.7%, compared with standard NCCN SLNB guidance using American Joint Committee on Cancer staging, while maintaining a low false-negative rate.

DecisionDx-Melanoma has been validated to identify patients who have less than a 5% risk of a positive SLN, indicating that these patients may consider avoiding the SLNB surgical procedure.[3-4] The results of this study support these findings and demonstrate that DecisionDx-Melanoma outperforms the MSKCC nomogram in identifying patients at low risk of SLN positivity. The study provides further evidence that using DecisionDx-Melanoma to help guide decisions regarding the SLNB procedure could improve patient selection, reduce unnecessary surgical procedures and ultimately improve the care of patients with melanoma.

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 June 30, 2023, DecisionDx-Melanoma has been ordered more than 137,200 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**, **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 potential of DecisionDx-Melanoma to (i) inform important conversations between clinicians and patients and provide added confidence in decisions to proceed without the surgery if a patient's risk is low; (ii) identify patients who may consider avoiding the SLNB surgical procedure at higher rates compared to the MSKCC nomogram; and (iii) improve patient selection, reduce unnecessary surgical procedures and ultimately improve the care of patients with melanoma. The words "can," "could," "may" 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 shown in this study, including with respect to the discussion of DecisionDx-Melanoma in this press release; actual application of our DecisionDx-Melanoma test 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, 2022, our Quarterly Report on Form 10-Q for the three months ended June 30, 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.

1. Joyce KM, McInerney NM, Piggott RP, et al. Analysis of sentinel node positivity in primary cutaneous melanoma: an 8-year single institution experience. Ir J Med Sci. 2017;186(4):847-853. doi:10.1007/s11845-017-1559-2
2. Chen J, Xu Y, Wang 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(29):45671-45677. doi:10.18632/oncotarget.10140
3. Vetto JT, Hsueh EC, Gastman BR, et al. Guidance of sentinel lymph node biopsy decisions in patients with T1-T2 melanoma using gene expression profiling. Future Oncol. 2019;15(11):1207-1217. doi:10.2217/fon-2018-0912
4. Whitman ED, Koshenkov VP, Gastman BR, et al. Integrating 31-gene expression profiling with clinicopathologic features to optimize cutaneous melanoma sentinel lymph node metastasis prediction. JCO Precis Oncol. 2021;5:1466-79. doi:10.1200/PO.21.00162

Investor Contact:

Camilla Zuckero

czuckero@castlebiosciences.com

Media Contact:

Allison Marshall

amarshall@castlebiosciences.com

Source: Castle Biosciences Inc.