NEWS RELEASE

Castle Biosciences Publishes DecisionDx®-Melanoma Study on the Validation of the i31-GEP SLNB Artificial Intelligence Algorithm

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Study demonstrated improved prediction for sentinel lymph node (SLN) status compared to clinicopathologic features alone

Study also demonstrated that DecisionDx®-Melanoma's i31-GEP SLNB algorithm provides high correlation between prediction of SLN positivity rates and observed rates

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company applying innovative diagnostics to inform disease management and improve patient outcomes, today announced the publication of a study validating performance of a novel algorithm designed to integrate the DecisionDx®-Melanoma gene expression profile (GEP) test with clinicopathologic features (i31-GEP SLNB) to determine sentinel lymph node biopsy (SLNB) positivity risk in patients with cutaneous melanoma.

DecisionDx-Melanoma is Castle's risk-stratification GEP test that is designed to predict 5-year risk of metastasis as well as metastasis to the SLN. The test's Integrated Test Result (ITR) includes the traditional class designation of lowest risk (Class 1A), increased risk (Class 1B/2A) or highest risk (Class 2B), as well as a more precise risk prediction for both SLNB positivity and risk of recurrence, distant metastasis and melanoma survival in patients with stage I, II or III melanoma through the i31- GEP algorithms (SLNB and Risk of Recurrence). The i31-GEP SLNB and ROR are distinct independently validated algorithms that integrate clinicopathologic features with the DecisionDx-Melanoma score.

“The majority of patients who undergo the SLNB surgical procedure receive a negative result,” said Robert Cook, Ph.D., senior vice president of research and development of Castle Biosciences and study author. “The i31-GEP SLNB clinical validation data showed that integrating clinicopathologic risk factors with the DecisionDx-Melanoma test provided very high correlation between the predicted and the actual, or observed, rates and a high sensitivity in identifying patients at low risk for SLN metastasis who may be able to safely avoid the SLNB procedure. Importantly, the study demonstrated that the DecisionDx-Melanoma test result was the most important variable in predicting SLN positivity.”

The article, titled “Integrating 31-Gene Expression Profiling with Clinicopathologic Features to Optimize Cutaneous Melanoma Sentinel Lymph Node Metastasis Prediction,” was published in the peer-reviewed journal JCO® Precision Oncology and can be accessed **here**. The study highlights the development and validation of the i31-GEP SLNB algorithm.

Study background:

- National guidelines recommend that an SLNB be offered to patients with >10% likelihood of SLN positivity (typically thought to encompass T2-T4 tumors), but do not recommend SLNB for patients who are thought to have <5% likelihood of a positive SLN (typically thought to encompass T1a tumors without high-risk features).
- The decision to perform SLNB is less certain for patients with higher-risk T1 melanomas (T1a tumors with high-risk features or T1b tumors) in which a positive node is expected 5%-10% of the time.
- The integrated DecisionDx-Melanoma test result for SLNB (i31-GEP SLNB) was designed to combine DecisionDx-Melanoma’s output, a risk assignment based on GEP analysis, with clinicopathologic risk factors.
- The study describes the development and validation of the i31-GEP SLNB, which utilizes a neural network algorithm to integrate the continuous DecisionDx-Melanoma result with patient histologic and clinical features.
- The i31-GEP SLNB algorithm was developed in a cohort of 1,398 patients and independently validated on a cohort of 1,674 patients.

Study findings:

- In comparison to all clinicopathologic features considered, the DecisionDx-Melanoma continuous score was the most important variable for prediction of a positive SLN, with a P value of less than 0.001.
- The i31-GEP SLNB algorithm demonstrated a very high correlation comparing predicted versus observed SLN positivity rates of 0.999 (1.0 is complete correlation).
- The i31-GEP SLNB algorithm demonstrated a highly sensitive prediction of SLN positivity rates (95.1%) compared to observed rates.
- In patients with T1-T4 tumors, the i31-GEP SLNB increased the percentage of patients predicted to have <5%

SLN positivity risk from 8.5%, using current staging guidelines, to 27.7%.

- Specifically, for patients predicted to have 5%-10% risk by current guidelines, the i31-GEP SLNB restratified 63% of cases to an SLN positivity risk of <5% or >10%.
- The i31-GEP SLNB identified patients with <5% SLN positivity risk, who might forego SLNB, or those with >10% SLN positivity risk, who might be offered SLNB, according to current guidelines.
- These data demonstrated that the i31-GEP SLNB could provide personalized risk estimates for SLN positivity, potentially reducing the number of SLNBs and provide additional information to appropriately identify patients at the highest risk of having a positive SLN.
- This personalized information may help clinicians and their patients make more informed decisions about the SLNB surgical procedure.

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 sentinel lymph node positivity, independent of traditional staging factors, and has been studied in more than 5,700 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 DecisionDx-Melanoma test result. Through June 30, 2021, DecisionDx-Melanoma has been ordered 78,277 times for use in patients 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 commercial-stage diagnostics company focused on providing physicians and their patients with personalized, clinically actionable genomic information to make more accurate treatment decisions. The Company currently offers tests for patients with cutaneous melanoma (DecisionDx®-Melanoma, DecisionDx® -CMSeq), cutaneous squamous cell carcinoma (DecisionDx®-SCC), suspicious pigmented lesions (myPath® Melanoma, DecisionDx® DiffDx™-Melanoma) and uveal melanoma (DecisionDx®-UM, DecisionDx®-PRAME and DecisionDx®-UMSeq). For more information about Castle's gene expression profile tests, visit **www.CastleTestInfo.com**.

Castle also has active research and development programs for tests in other dermatologic 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. Castle Biosciences is based in Friendswood, Texas (Houston), and has laboratory operations in Phoenix.

For more information, visit **www.CastleBiosciences.com**.

Forward-Looking Statements

The information in this press release contains forward-looking statements and information 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 DecisionDx-Melanoma's ability to predict 5-year risk of metastasis as well as metastasis to the SLN, provide personalized risk estimates for SLN positivity, reduce the number of SLNBs, provide additional information to appropriately identify patients at the highest risk of having a positive SLN, and help clinicians and their patients make more informed decisions about the SLNB surgical procedure. 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 that contradict earlier study results and findings, DecisionDx-Melanoma's ability to provide the aforementioned benefits to patients, and the risks set forth in our Quarterly Report on Form 10-Q for the quarter ended June 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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