NEWS RELEASE

New Study Shows Castle Biosciences' DecisionDx®-Melanoma Test Outperforms Staging and CP-GEP in Identifying Patients at Low Risk of Sentinel Lymph Node Positivity

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Patients identified as low risk by DecisionDx-Melanoma had a 2.8% sentinel lymph node (SLN) positivity rate, well below the National Comprehensive Cancer Network® (NCCN) guidelines' 5% threshold to forgo sentinel lymph node biopsy (SLNB) surgery

FRIENDSWOOD, Texas, April 30, 2025 (GLOBE NEWSWIRE) -- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced the publication of a new study in **Cancer Diagnosis & Prognosis** demonstrating that DecisionDx-Melanoma outperforms both American Joint Committee on Cancer (AJCC) staging and the CP-GEP test (clinicopathological and gene expression profiling model) in identifying patients at low risk of SLN positivity who may consider forgoing SLNB surgery.[1]

"When relying on genomic testing to guide critical decisions about procedures like SLNB, a test must demonstrate exceptional accuracy in identifying patients with minimal risk of metastasis," said Peter A. Prieto, M.D., MPH, lead author and triple board-certified surgical oncologist at the University of Rochester Medical Center. "Our study confirms that DecisionDx-Melanoma achieves this by providing significant risk stratification, outperforming the standard of care (i.e., AJCC staging) and the CP-GEP genomic test."

SLNB helps determine whether melanoma has spread to nearby lymph nodes. Current NCCN guidelines recommend forgoing SLNB if the risk of a positive node is below 5%, considering it at 5-10% and offering if a patient's risk exceeds 10%. The majority of newly diagnosed melanomas are T1–T2 tumors, yet more than 90% of

patients who undergo SLNB in this population receive negative results.[2,3] Further, in patients with thin tumors, the risk of procedural complications outweighs the likelihood of a positive node, underscoring the need for better tools to identify low-risk patients who can safely avoid the surgery.[4]

DecisionDx-Melanoma has been validated in multiple prospective and retrospective studies to provide significant risk stratification independent of clinicopathological features such as age and Breslow thickness.[5-8] The test provides personalized results on a patient's likelihood of sentinel lymph node positivity and risk of recurrence, helping clinicians and patients make more informed, risk-aligned melanoma management decisions.

The new study provides an analysis of the accuracy of the CP-GEP and DecisionDx-Melanoma tests in identifying patients with less than a 5% risk of SLN positivity, in T1-T2 tumors specifically, across five CP-GEP and four DecisionDx-Melanoma validation studies. Using a weighted average across all studies, patients classified as low risk by CP-GEP had an SLN positivity rate of 6.2%, exceeding the 5% NCCN threshold for ruling out SLNB. In contrast, patients identified as low risk by DecisionDx-Melanoma had a 2.8% SLN positivity rate, a significant improvement over AJCC staging. Overall, CP-GEP did not perform as well as staging alone, while DecisionDx-Melanoma outperformed staging, providing further confirmation of its ability to improve clinical decision-making and ultimately, outcomes.

"This study underscores the value of using DecisionDx-Melanoma test results to help guide improved SLNB decisions," said Matthew Goldberg, M.D., senior vice president, medical, of Castle Biosciences. "Further, it strengthens our recent prospective study findings, which show that patients with low-risk DecisionDx-Melanoma results (less than 5% likelihood of SLN positivity) who forgo SLNB surgery maintain high recurrence-free survival rates, providing clinicians and patients with greater confidence in treatment decisions guided by our test."[9]

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 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 50 peer-reviewed and published studies, providing confidence in disease management plans that incorporate the test's results. Through March 31, 2025, DecisionDx-Melanoma has been ordered more than 200,000 times for patients diagnosed with cutaneous melanoma. Learn more at **www.CastleBiosciences.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, Barrett's esophagus, mental health conditions and uveal melanoma. Additionally, the Company has active research and development programs for tests in these and other diseases with high clinical need, including its test in development for use in patients diagnosed with moderate-to-severe atopic dermatitis who are seeking systemic treatment. 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 the DecisionDx-Melanoma test to (i) provide significant risk stratification and outperform the standard of care and the CP-GEP genomic test, (ii) accurately identify patients with less than 5% risk of SLN positivity, who can safely consider forgoing the SLNB surgical procedure, and who are also unlikely to experience disease progression, (iii) enhance clinical decision-making and (iv) deliver risk-aligned patient care and provide clinicians and patients with greater confidence in treatment decisions. The words "believe," "can," "could," "potential" 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, 2024 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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