NEWS RELEASE

Castle Biosciences' DecisionDx®-SCC Data Earns Top Five Abstract at NCCN 2025, Shows Significantly Enhanced Risk Stratification Beyond Current Staging Within NCCN Risk Groups

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New, combined validation cohort of 1,412 patients with high-risk squamous cell carcinoma (SCC) demonstrates that the addition of DecisionDx-SCC to Brigham & Women's Hospital (BWH) staging significantly refines metastatic risk prediction in patients classified as High-Risk and Very High-Risk by National Comprehensive Cancer Network (NCCN) guidelines to support improved, risk-aligned treatment pathway decisions

Castle will also present new data showing DecisionDx®-Melanoma as a significant predictor of mortality in a real-world cohort of nearly 7,000 patients with early-stage cutaneous melanoma (CM), reinforcing its value in identifying patients who may benefit from treatment plan strategies to improve outcomes

FRIENDSWOOD, Texas, March 28, 2025 (GLOBE NEWSWIRE) -- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, will share new data on its risk-stratification tests for patients with skin cancers, DecisionDx-SCC and DecisionDx-Melanoma, via two poster presentations at the NCCN 2025 Annual Conference, being held March 28-30 in Orlando, Florida. As a top five, blue-ribbon abstract at the conference, Castle’s poster on DecisionDx-SCC will also be shared in a special oral presentation with the other top-scoring submissions.

"Our latest data at NCCN highlight the significant prognostic capabilities of DecisionDx-SCC and DecisionDx-Melanoma, demonstrating their ability to enhance risk stratification beyond traditional staging,” said Rebecca Critchley-Thorne, Ph.D., vice-president, research and development, of Castle Biosciences. “By providing critical

insights into predicted metastatic risk and survival likelihood, these tests equip clinicians with actionable results to enable more precise, personalized treatment decisions that may help optimize patient management and care."

Castle's posters will be available for viewing during the general poster sessions on March 28. As a top-scoring submission, Castle's DecisionDx-SCC abstract will also be published in the print version of the JNCCN—Journal of the National Comprehensive Cancer Network. Additional details are included below:

DecisionDx-SCC

- Poster 5: Metastasis-free Survival Prediction with the 40-gene Expression Profile Test in Patients with Cutaneous Squamous Cell Carcinoma Risk Stratified According to the National Comprehensive Cancer Network Guidelines®
- Oral Poster Presentation: Friday, March 28, 3:45-5 p.m. Eastern Time
- Session: Oral Presentations from Top Poster Presenters and NCCN Foundation Young Investigator Awardees
- Presenter and Study Author: Shlomo A. Koyfman, M.D., director of the precision oncology program and director of head and neck radiotherapy at the Taussig Cancer Institute, Cleveland Clinic, Cleveland

Study highlights: This study assessed how integrating the DecisionDx-SCC test with BWH staging within NCCN guidelines can improve prognostic accuracy. An analysis of a new, combined multi-center cohort of 1,412 high-risk SCC patients, with one or more NCCN High-Risk or Very-High-Risk factors, showed that DecisionDx-SCC significantly enhanced metastatic risk stratification in NCCN High- and Very-High-Risk patient populations ($p < 0.001$). The test significantly improved BWH staging's risk prediction accuracy ($p < 0.001$). Compared to the broader NCCN risk stratification, when DecisionDx-SCC was combined with BWH staging, Class 1 (low risk) test results showed a nearly two-fold decrease in metastatic risk and Class 2B (highest risk) results showed more than a five-fold increase in risk in lower-stage (BWH T1/T2a) NCCN High-Risk patients. These findings show that DecisionDx-SCC can significantly refine risk assessment when used with established staging methods, enabling more accurate, personalized treatment decisions based on a patient's predicted metastatic risk.

DecisionDx-Melanoma

- Poster 31: The 31-GEP stratifies risk of death in patients with stage I-IIA cutaneous melanoma: A SEER real-world evidence study
- Lead Author: Harrison Nguyen, M.D., MBA, MPH, Houston Skin, Houston

Study highlights: This poster, part of Castle's ongoing collaboration with the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program Registries, presents new validation of the DecisionDx-Melanoma test's risk-stratification performance in patients with thin/early-stage CM tumors (stage I-IIA). In a large, unselected real-world cohort of 6,892 patients classified as low risk by the American Joint Committee on Cancer Eighth Edition

(AJCC8) staging system, the test identified individuals at higher risk of death. In multivariable analysis that included key AJCC8 staging criteria such as tumor thickness and ulceration as well as age and mitotic rate, the data demonstrated that the DecisionDx-Melanoma test is a significant predictor of both melanoma-specific and overall mortality. These findings highlight the test's significant, independent risk-stratification capabilities, helping to identify patients at greater risk than indicated by AJCC8 staging alone who may benefit from enhanced surveillance and management to improve outcomes.

All abstracts at the conference will be published online at **JNCCN.org**.

About DecisionDx-SCC

DecisionDx-SCC is a 40-gene expression profile test that uses an individual patient's tumor biology to predict individual risk of cutaneous squamous cell carcinoma metastasis for patients with one or more risk factors. The test result, in which patients are stratified into a Class 1 (low), Class 2A (higher) or Class 2B (highest) risk category, predicts individual metastatic risk to inform risk-appropriate management. Peer-reviewed publications have demonstrated that DecisionDx-SCC is an independent predictor of metastatic risk and that integrating DecisionDx-SCC with current prognostic methods can add positive predictive value to clinician decisions regarding staging and management. Learn more at **www.CastleBiosciences.com**.

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 50 peer-reviewed and published studies, providing confidence in disease management plans that incorporate the test's results. Through Dec. 31, 2024, DecisionDx-Melanoma has been ordered more than 191,000 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 to help guide systemic therapy selection for patients with moderate-to-severe atopic dermatitis seeking biologic 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 DecisionDx-SCC to support improved, risk-aligned treatment pathway decisions; DecisionDx-Melanoma's value in identifying CM patients who may benefit from enhanced surveillance and management strategies to improve outcomes; and the significant prognostic capabilities of DecisionDx-SCC and DecisionDx-Melanoma and their ability to (i) enhance risk stratification beyond traditional staging and (ii) equip clinicians with actionable results to enable more precise, personalized treatment decisions and optimize patient management and care. 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, 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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Source: Castle Biosciences, Inc.

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