NEWS RELEASE

New Data to be Presented at the 2025 American Academy of Dermatology (AAD) Annual Meeting Further Strengthens Evidence Supporting the Clinical Value of Castle Biosciences' Dermatology Portfolio

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New study corroborates DecisionDx® -SCC's ability to independently predict metastatic risk in patients with high-risk cutaneous squamous cell carcinoma (SCC)

Landmark analysis of nearly 10,000 patients through Castle's collaboration with the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program Registries showed a significant association between DecisionDx® -Melanoma testing and improved survival in melanoma patients

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, will share new data on its DecisionDx-Melanoma and DecisionDx-SCC tests for patients with skin cancers at the 2025 AAD Annual Meeting, taking place March 7-11 in Orlando, Florida.

“At Castle, we are dedicated to empowering clinicians with the insights needed to make more informed decisions in the management of skin cancers,” said Rebecca Critchley-Thorne, Ph.D., vice-president, research and development, of Castle Biosciences. “We remain committed to advancing evidence development to showcase the clinical value of our tests in guiding patient care. In collaboration with leading physicians across the United States, we are excited to present new data at this year’s AAD meeting reinforcing the role of our dermatologic tests in working to improve patient outcomes.”

Details regarding Castle's posters at AAD are included below. The Company's abstract on DecisionDx-SCC was accepted as an ePoster with an oral presentation.

DecisionDx-SCC

- ePoster with Oral Presentation:60916 – An independent validation of the 40-gene expression profile (40-GEP) test for high-risk cutaneous squamous cell carcinoma (cSCC)
- Presenter and Lead Author: Emily S. Ruiz, M.D., MPH, FAAD, Brigham and Women's Hospital (BWH) and Harvard Medical School, Boston
- Date and Time: March 7 from 3:50-3:55 p.m. Eastern Time
- Location: Orange County Convention Center (West Building, Exhibit Hall B4, Poster Center 2) in the Exhibit Hall

"For patients diagnosed with high-risk cutaneous squamous cell carcinoma, understanding the risk of metastatic spread is an important part of their care journey," said Ruiz. "The study presented at AAD includes results from a novel data set showing that DecisionDx-SCC is able to independently risk assess select SCCs."

Study highlights: This study provides a validation of the ability of the DecisionDx-SCC test to predict metastatic risk in a novel, independent cohort of patients with high-risk SCC tumors (n=515). In the study, DecisionDx-SCC and BWH staging were both significant predictors of metastasis ($p < 0.05$). Overall, the study data provide further evidence that DecisionDx-SCC provides significant risk stratification ($p < 0.001$) of patients at higher risk of SCC metastasis to guide personalized, risk-aligned treatment decisions.

DecisionDx-Melanoma

- ePoster:62266 – Real-world data demonstrate the 31-GEP stratifies risk of melanoma-specific mortality and is associated with improved survival: A SEER collaboration
- Lead Author: Jason M. Rizzo, M.D., FAAD, The Woodruff Institute for Dermatology & Mohs Surgery, Naples, Florida

"Drawn from the largest real-world study of gene expression profile testing in patients with melanoma, the expanded data being presented at AAD further demonstrate how DecisionDx-Melanoma can enhance risk-aligned patient management and improve patient survival," said Rizzo. "The test's ability to more precisely predict risk, significantly and independently to traditional staging, can help clinicians better tailor their patient management plans, such as decisions about sentinel lymph node biopsies, surveillance protocols and adjuvant therapy, to the patient's individual risk of recurrence or metastasis."

Study highlights: This poster from Castle's ongoing collaboration with the National Cancer Institute's SEER Program Registries provides an updated validation of the risk-stratification performance of the DecisionDx-

Melanoma test. The study encompasses an additional year's worth of data and approximately 4,800 more patients than the initial study by **Bailey et al.** In a large, unselected real-world cohort of nearly 10,000 patients who received the DecisionDx-Melanoma test as part of their clinical care, this study demonstrates the significant independent risk stratification provided by the test, beyond American Joint Committee on Cancer Eighth Edition (AJCC8) stage, and its association with improved survival relative to matched patients who did not receive testing.

Posters will be available for viewing on monitors within the Poster Exhibits Center and via the AAD website (**https://eposters.aad.org/**) and meeting mobile app. Additionally, the abstracts will be published in an online Journal of the American Academy of Dermatology (JAAD) supplement following the meeting. For more information regarding Castle's posters and its participation at AAD, please visit booth #1661.

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 our tests to (i) empower clinicians with the insights needed to make more informed decisions in the management of skin cancers and (ii) improve patient outcomes; Castle's ability to advance evidence development to showcase the clinical value of its tests in guiding patient care; the ability of DecisionDx-SCC to help both physicians and patients make more confident, personalized treatment decisions aligned with each patient's individual predicted risk of metastasis; and the ability of DecisionDx-Melanoma to: (i) enhance risk-aligned patient management, (ii) improve patient survival and (iii) more precisely predict risk, significantly and independently to traditional staging. 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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