NEWS RELEASE

Real-World Clinical Utility Study Published in Cancer Investigation Demonstrates the Impact of DecisionDx®-SCC Test Results in Guiding Risk-Aligned Care for Patients with Cutaneous Squamous Cell Carcinoma

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Study also shows DecisionDx-SCC is being appropriately utilized by clinicians treating patients with cutaneous squamous cell carcinoma and one or more risk factors, as evidenced by first-year clinical order data

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced the publication of real-world clinical utility data in Cancer Investigation showing that clinicians are ordering DecisionDx®-SCC for the intended high-risk cutaneous squamous cell carcinoma (SCC) patient population and that use of the test's results can lead to risk-aligned changes in patient management strategies.

"The study highlighted the challenges of accurate risk assessments in the management of SCC when using clinicopathologic staging systems alone, and reinforced the need for a risk-stratification tool like DecisionDx-SCC that is designed to better identify patients with a higher likelihood of experiencing poor outcomes," said Perry B. Hooper, M.D., Department of Dermatology, Indiana University School of Medicine, Indianapolis. "The personalized information provided by the test's results can positively impact decision-making for SCC patients by helping better align treatment plans to a patient's biologic metastatic risk and reducing the likelihood of over- or undertreatment."

The paper, titled "Real-World Evidence Shows Clinicians Appropriately Use the Prognostic 40-GEP Test for High-Risk

Cutaneous Squamous Cell Carcinoma (cSCC) Patients," evaluated metrics from one year of clinical DecisionDx-SCC orders and the test's impact on real-world risk assessments and treatment decisions. The paper may be viewed from **Castle's website**.

Metrics from real-world DecisionDx-SCC orders during the first year of testing show that physicians are ordering DecisionDx-SCC for patients with one or more high-risk clinicopathologic factors:

- Of the 2,503 samples tested between Aug. 31, 2020-Aug. 31, 2021, 98.1% were successfully tested and received the following results: 68.8% received a low-risk (Class 1) result, 28.3% received a moderate-risk (Class 2A) result and 2.9% received a high-risk (Class 2B) result.
- 75% of samples had two or more high-risk clinicopathologic factors, and 98.8% of cases submitted for testing were classified as high risk or very high risk by the National Comprehensive Cancer Network (NCCN) guidelines, which closely aligns with the intended use population of the DecisionDx-SCC test.
- Despite elevated clinicopathologic metastatic risk in these real-world patients, 68.8% received a low-risk (Class 1) DecisionDx-SCC test result,reinforcing the clinical need for risk assessments that incorporate a patient's tumor biology to better align patient management plans with their biologic metastatic risk.

Real-world data involving healthcare providers who have clinical experience with DecisionDx-SCC indicates that patient management decisions can be impacted when the test's results are considered:

- Clinicians who ordered DecisionDx-SCC ten or more times during the first year of clinical orders were invited to participate in an anonymous survey study, where they were provided with six real-world high-risk SCC cases and asked what their treatment approach would be, both pre- and post-DecisionDx-SCC testing.
- The clinicians who responded (n=34) were generally well-aligned regarding the different baseline risk levels (pre-test) inherent in each of these real-world patient cases. After receiving DecisionDx-SCC test results (post-test), the clinicians aligned their overall post-test management strategy for each case and adjusted the intensity of their treatment plans significantly in a risk-aligned manner depending on the metastatic risk represented by each case's DecisionDx-SCC result. These changes were seen in specific treatment plans regarding nodal assessment via imaging, surveillance imaging, follow-up frequency, adjuvant radiation therapy and sentinel lymph node biopsy (SLNB).
- Overall, the study data support the positive impact that DecisionDx-SCC's personalized, risk-stratification results can have on patient management plans, including:
    - Helping avoid the overtreatment of patients: As an example, in Case 1 (which had the highest level of baseline overall management strategy), between 44 and 58% of clinicians who responded to the survey chose to de-escalate their overall management strategy and reduce their likelihood of performing

adjuvant radiation therapy, SLNB, imaging (nodal assessment and surveillance) after receiving a low-risk (Class 1) test result, demonstrating the potential of the test to help avoid the overtreatment of patients.
- Guiding risk-appropriate disease management decisions, alongside traditional risk factor assessments: Across all six cases, a comprehensive analysis of the clinical impact that a DecisionDx-SCC class result had on clinicians making risk-aligned changes in treatment intensity demonstrated a mean average of 47.9% for their overall management strategy approach.

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), 2A (moderate) or 2B (high) 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.

More information about Castle's tests 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**, **Twitter** 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-SCC test results to (i) lead to risk-aligned changes in patient management strategies; (ii) positively impact decision-making and patient management planning for SCC patients by helping better align treatment plans to a patient's biologic metastatic risk and reducing the likelihood of over- or undertreatment; and (iii) guide risk-appropriate disease management decisions, alongside traditional risk factor assessments. The words "can," "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 this study, including with respect to the discussion of DecisionDx-SCC 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 Quarterly Report on Form 10-Q for the three months ended June 30, 2022, 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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