NEWS RELEASE

Castle Biosciences Presents Data Supporting the Utility of Its Tests in the Clinical Care of Patients with Skin Cancers at the 2024 Winter Clinical Dermatology Conference - Hawaii®

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FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, will present new data across its dermatologic portfolio of commercially available and pipeline gene expression profile (GEP) tests at the 2024 Winter Clinical Dermatology Conference - Hawaii, being held Jan. 12-17 in Honolulu, Hawaii.

“We are committed to challenging current disease management paradigms and building the evidence supporting our portfolio of clinically actionable molecular tests and their use to improve decision-making for patients with skin cancers and inflammatory skin diseases,” said Robert Cook, Ph.D., senior vice president of research and development at Castle Biosciences. “As such, we are proud to share our latest data at Winter Clinical – Hawaii in collaboration with leading physicians who we believe share our vision of transforming the management of these potentially serious diseases.”

Highlights from Castle’s posters at Winter Clinical – Hawaii are included below. Posters will be displayed for viewing in the Coral Ballroom 2 through Jan. 16 at 1 p.m. Hawaii Standard Time.

DecisionDx-Melanoma

- Real-world evidence confirms risk stratification of the 31-GEP and i31-GEP in prospectively tested patients with stage I-III cutaneous melanoma
- Summary: To further advance personalized patient care, Castle's DecisionDx-Melanoma test result, based on a patient's tumor biology, was integrated with clinical and pathological factors using a validated proprietary algorithm (i31-GEP for risk of recurrence, or ROR). The i31-GEP ROR provides a more personalized, precise risk of tumor recurrence to guide clinical management of CM. This study aimed to validate the DecisionDx-Melanoma test and i31-GEP ROR algorithm in a real-world cohort of patients with stage I-III CM (n=1,831) who received the DecisionDx-Melanoma test as part of their routine clinical care. The study confirmed the independent and significant risk-stratification provided by DecisionDx-Melanoma and its integrated i31-GEP ROR algorithm, identifying patients at high risk of melanoma recurrence to guide important, risk-appropriate interventions, such as imaging surveillance and immunotherapy, that can potentially improve patient outcomes.
- View poster **here**.

DecisionDx-SCC

- The 40-gene expression profile (40-GEP) test identifies cutaneous squamous cell carcinoma (cSCC) patients at high risk of metastasis within lower-staged tumors to better guide treatment decisions
- Summary: This study evaluated the ability of DecisionDx-SCC to independently improve the identification of lower-staged tumors at increased risk of metastasis. Improved risk assessment in these lower-staged subsets is important as up to one-third of all metastatic events have been reported for patients originally staged with T1 tumors. Within a cohort of SCC patients considered lower risk by current staging alone, DecisionDx-SCC identified those at a substantially higher risk of metastasis. These results represent a clinically significant improvement in risk assessment for SCC patients with observed rates of metastasis over 10% and 20%, respectively, which are clinically actionable for nodal staging or post-operative adjuvant radiation. Combining traditional risk classification systems with a patient's individual biologic risk, as provided by the DecisionDx-SCC test, can improve the accuracy of risk assessment to inform important patient treatment decisions.
- View poster **here**.

MyPath Melanoma

- Diagnostic discordance among histopathological reviewers for difficult-to-diagnose melanocytic lesions
- Summary: Diagnostic discordance in cutaneous melanocytic lesions is well documented and prevalent among difficult-to-diagnose cases, for which histopathology may be insufficient for a definitive diagnosis. MyPath Melanoma testing is available for ambiguous melanocytic neoplasms to add clarity to these diagnoses. This study showed that in a large cohort of patients with suspicious lesions (n=3,317), approximately 24% were difficult to diagnose, supporting the need for an objective diagnostic tool like MyPath Melanoma to aid in

providing an accurate diagnosis to help ensure appropriate patient management.

- View poster **here**.

Inflammatory Skin Disease Pipeline Program

- Gene expression differences identified in skin samples of mycosis fungoides, atopic dermatitis and psoriasis
- Summary: The goal of Castle's innovative pipeline initiative is to develop a genomic test aimed at guiding systemic therapy selection for patients with moderate-to-severe atopic dermatitis (AD), PSO and related conditions. The test in development would help personalize therapy selection for patients based on their molecular profile and help determine which therapy may best help to manage their symptoms. At the recent 2023 Fall Clinical Dermatology Conference®, Castle **presented data** showing the ability of its pipeline test in development to identify distinct gene expression profiles of super-responders to an AD therapy and also distinguish between AD, PSO and mycosis fungoides (MF) skin lesions. Castle's poster at Winter Clinical – Hawaii builds on this data by showing the ability of the pipeline test in development to determine the gene expression profile of super-responders to a PSO therapy.
- View poster **here**.

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 40 peer-reviewed and published studies, providing confidence in disease management plans that incorporate the test's results. Through Sept. 30, 2023, DecisionDx-Melanoma has been ordered more than 146,000 times for patients diagnosed with cutaneous melanoma.

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.

About MyPath® Melanoma

MyPath Melanoma is Castle's gene expression profile test designed to provide an accurate, objective result to aid dermatopathologists and dermatologists in characterizing difficult-to-diagnose melanocytic lesions. Of the approximately two million suspicious pigmented lesions biopsied annually in the U.S., Castle estimates that approximately 300,000 of those cannot be confidently classified as either benign or malignant through traditional histopathology methods. For these cases, the treatment plan can also be uncertain. Obtaining accurate, objective ancillary testing can mean the difference between a path of overtreatment or the risk of undertreatment. Interpreted in the context of other clinical, laboratory and histopathologic information, MyPath Melanoma is designed to reduce uncertainty and provide confidence for dermatopathologists and help dermatologists deliver more informed patient management plans.

About Castle's Inflammatory Skin Disease Pipeline Program

Inflammatory skin disease accounts for a significant number of patient visits to both primary care and dermatology clinics across the United States every year. Psoriasis (PSO) and atopic dermatitis (AD) are among the most common inflammatory skin conditions, and patient quality of life is severely impacted by these chronic diseases. Fortunately, systemic medications developed over the past 15 years have demonstrated a significant improvement in patients' lives. In the United States alone, there are about 18 million patients diagnosed with PSO and AD, and approximately 450,000 patients annually are eligible for these systemic therapies. While there are now many effective treatment options available for those with moderate-to-severe inflammatory skin diseases, current clinical practice relies on a trial-and-error approach for therapy selection.

To answer this unmet clinical need, in 2021, Castle initiated a prospective, multi-center clinical study (IDENTITY) to develop and validate a gene expression profile (GEP) test to help guide systemic therapy selection for patients with moderate-to-severe AD, PSO and other related diseases. In 2022, the Company initiated a second, prospective study (SIGNAL-MF) to investigate the possibility of the pipeline test including an ancillary component to help identify lesions that may be mycosis fungoides (MF), a rare and serious type of skin cancer, often referred to as cutaneous T-cell lymphoma, that is easily mistaken for AD and PSO. MF requires a rigorous histologic and molecular workup to diagnose, and patients with MF being treated for presumed AD or PSO can further delay this critical diagnosis.

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 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, psoriasis and related conditions. 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: our ability to continue building the evidence supporting our portfolio of clinically actionable molecular tests and their use to improve decision-making for patients with skin cancers; the ability of DecisionDx-Melanoma and its integrated i31-GEP ROR algorithm, to identify patients at high risk of melanoma recurrence in order to guide important, risk-appropriate interventions, such as imaging surveillance and immunotherapy and improve patient outcomes; the ability of combining traditional risk classification systems with a patient's individual biologic risk, as provided by the DecisionDx-SCC test, to improve the accuracy of risk assessment to inform important patient treatment decisions; the ability of MyPath Melanoma to aid in providing an accurate diagnosis to help ensure appropriate patient management; and the ability of its innovative pipeline initiative to identify distinct gene expression profiles of super-responders to an AD therapy and also distinguish between AD, PSO and MF skin lesions. The words "can," "may" 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, including with respect to the discussion of DecisionDx-Melanoma, DecisionDx-SCC, MyPath Melanoma and Castle's inflammatory skin disease pipeline test 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, 2022, our Quarterly Report on Form

10-Q for the three months ended September 30, 2023, 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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