NEWS RELEASE

Recent Publications Affirm the Value of Gene Expression Profile Testing in Guiding a Definitive Diagnosis and Clinical Decision-Making in Melanocytic Lesions of Uncertain Malignant Potential

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Two studies published in the Journal of Cutaneous Pathology and Melanoma Management demonstrate the significant disagreement that exists in the diagnosis of melanocytic lesions using pathology alone, the variability of surgical management of lesions among treating dermatologists, and the risk-aligned changes and confidence in these decisions that can result from GEP testing [1,2]

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 two recent studies that provide further support for the clinical need of its MyPath® Melanoma gene expression profile (GEP) test, designed to aid in providing an accurate diagnosis for ambiguous melanocytic lesions of uncertain malignant potential.

“For many concerning pigmented lesions, a definitive histopathologic diagnosis is clear: a malignant melanoma or a benign nevus,” said Matthew Goldberg, M.D., board-certified dermatologist and dermatopathologist, and senior vice president, medical, of Castle Biosciences. “For a substantial subset of lesions, however, a final diagnosis can vary widely depending on which dermatopathologist reviews a biopsy sample, as our study further illustrated.”

A recent study published in the **Journal of Cutaneous Pathology** found that in a large cohort of patients with suspicious lesions (n=3,317), approximately 24% had differing diagnoses by the nine board-certified dermatopathologists who reviewed samples in the study, indicating that these lesions had ambiguous features and were difficult to diagnose. [1] “These findings support the need for an objective diagnostic tool like MyPath Melanoma

to aid in providing an accurate diagnosis for ambiguous melanocytic lesions in the context of other clinical and histopathological findings," added Goldberg.

Alexander Witkowski, M.D., Ph.D., dermatologist and assistant professor of dermatology at the Oregon Health & Science University in Portland, Oregon, a leading institution in the study and research of melanoma, provided additional evidence supporting the clinical need for GEP testing in another recent study published in **Melanoma Management** , in which management changes in response to GEP test results were analyzed for patients with ambiguous melanocytic lesions. [2] In the study, 32 board-certified dermatologists reviewed 24 randomized patient scenarios in which benign or malignant GEP test results were either provided or blinded from respondents. The dermatologists were then asked a set of standardized questions inquiring about how they would treat the patient (e.g., no further treatment needed, surgical excision with small margins, wide-local excision, etc.), which follow-up schedule they would recommend and their confidence in that management plan.

Without GEP guidance, variation in the surgical management of each lesion was demonstrated, further supporting the need for GEP testing in lesions with ambiguous diagnoses. The study data showed that benign GEP results prompted 84.2% of clinicians to decrease the recommended surgical margins for lesions, while malignant GEP results prompted all the clinicians (100%) to increase their surgical excision recommendations. Further, most clinicians (72.2%) reduced and nearly all (98.9%) increased their follow-up frequency for benign or malignant GEP results, respectively. There was also an overall increase in patient management plan confidence with GEP results (67.4% with benign results and 54.9% with malignant results).

"GEP testing with MyPath Melanoma increases confidence and helps to guide the management decisions dermatologists and other healthcare providers make when choosing what to do with a suspicious mole, particularly when the results of a pathology report are unclear," added Witkowski. "GEP testing provides significant value for clinicians and patients, and that's exactly what we saw in our study. This molecular test provides an objective data point that can help improve definitive melanoma diagnosis and earlier treatment."

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 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; and the ability of MyPath Melanoma to aid in providing an accurate diagnosis, including where pathological diagnosis is uncertain, to help ensure appropriate patient management. 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 MyPath Melanoma 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, 2023, our Quarterly Report on Form 10-Q for the three months ended June 30, 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.

1. Hosler GA, Goldberg MS, Estrada SI, et al. Diagnostic discordance among histopathological reviewers of melanocytic lesions. J Cutan Pathol . 2024; 51(8): 624-633. doi:10.1111/cup.14635
2. Witkowski A, Jarell AD, Ahmed KL, et al. A clinical impact study of dermatologists' use of diagnostic gene expression profile testing to guide patient management. Melanoma Manag. 2024; 11(1). doi: 10.2217/mmt-2023-0002

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