NEWS RELEASE

Castle Announces Early Exploratory Study Data for Potential Development of a Complementary Test to Accompany DecisionDx®-UM That Could Aid in the Early Detection of Uveal Melanomas

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Renowned eye cancer expert and study investigator, Amy Schefler, M.D., will share early data from a study to explore the potential for developing a complementary test that would be tailored for individuals presenting with small, suspicious lesions of uncertain malignant potential

Data will be presented at the 2023 American Academy of Ophthalmology (AAO) Annual Meeting in San Francisco

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced new discovery data from an ongoing study exploring the potential for developing a complementary, minimally invasive test to evaluate small, suspicious lesions of uncertain malignant potential in patients' eyes.

"We are excited about the possibility of developing a new minimally invasive test that would complement our current test offerings for patients with uveal melanoma, including DecisionDx®-UM, and reinforce our dedication to this important patient population," said Robert Cook, Ph.D., senior vice president of research and development at Castle Biosciences. "This test would potentially identify aggressive uveal melanomas when they are small and more likely to be cured by prompt therapeutic interventions."

Bill Harbour, M.D., ophthalmologist, ocular oncologist, and professor and chair of the department of ophthalmology at UT Southwestern Medical Center, is also collaborating with Castle on the study. Harbour is a leading innovator in

the treatment and study of uveal melanoma and the original developer of the DecisionDx-UM test, which he licensed to Castle in 2009.

“For small ocular tumors suspected of being an early melanoma, the current standard of care is a ‘watch and wait’ approach using certain clinical characteristics to estimate the risk of malignancy,” said Harbour. “Unfortunately, this approach is highly subjective and can lead to both under- and over-treatment of patients. Through this study, we are looking for aqueous biomarkers that can easily and safely be obtained from the front part of the eye during a quick office procedure that would signal a small tumor may be malignant, which could prompt a definitive tumor biopsy and appropriate intervention.”

Study data is being shared by Amy Schefler, M.D., board-certified ocular oncologist and vitreoretinal surgeon at Retina Consultants of Texas, in an educational presentation this morning at AAO. The presentation details are as follows:

Presentation title: Uveal Melanoma Liquid Biopsies: Are We Going Anywhere?

Section I: Loch Ness Monster’s Deep-Diving into Liquid … Biopsies
Session: PTH02
Date & Time: Friday, Nov. 3, 8:05-9:05 a.m. Pacific Time
Location: WEST 2002

Castle expects to share additional updates in 2024 on the ongoing exploratory study and potential development of a complementary test. An excerpt from Schefler’s presentation regarding the study can be viewed **here**.

About the Ongoing Exploratory Study

Each year, up to 12,000 individuals present with a small suspicious uveal melanocytic lesion of uncertain malignant potential in one of their eyes; however, only about 2,000 of these patients will be diagnosed with uveal melanoma and undergo definitive tumor treatment and molecular prognostic biopsy. The current clinical standard of care to determine which patients to treat involves a “watch and wait” approach that consists of monitoring lesions for growth or appearance of high-risk features that would indicate transformation into a malignant melanoma. Castle’s ongoing exploratory study is investigating the potential for developing a test that would complement DecisionDx-UM and provide a minimally invasive solution to identify lesions with aggressive biology earlier, enabling more timely treatment with the goal of improving uveal melanoma patient outcomes.

About DecisionDx®-UM

DecisionDx-UM is Castle Biosciences’ 15-gene expression profile (GEP) test that uses an individual patient’s tumor biology to predict individual risk of metastasis in patients with uveal melanoma. DecisionDx-UM is the standard of care in the management of newly diagnosed uveal melanoma in the majority of ocular oncology practices in the

United States. Since 2009, the American Joint Committee on Cancer (AJCC; v7 and v8) Staging Manual for UM has specifically identified the GEP test as a prognostic factor that is recommended for collection as a part of clinical care. Further, the National Comprehensive Cancer Network (NCCN) guidelines for uveal melanoma include the DecisionDx-UM test result as a prognostic method for determining risk of metastasis and recommended differential surveillance regimens based on a Class 1A, 1B and 2 result. DecisionDx-UM is the only prognostic test for uveal melanoma that has been validated in prospective, multi-center studies, and it has been shown to be a superior predictor of metastasis compared to other prognostic factors, such as chromosome 3 status, mutational status, AJCC stage and cell type.

It is estimated that nearly 8 in 10 patients diagnosed with uveal melanoma in the United States receive the DecisionDx-UM test as part of their diagnostic workup.

More information about the test and disease 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 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: (i) the potential for developing a complementary, minimally invasive test to evaluate small, suspicious lesions of uncertain malignant potential in patients' eyes; (ii) the ability of such test to identify aggressive uveal melanomas when they are small and more likely to be cured by prompt therapeutic interventions; (iii) the timing of additional test and study updates and (iv) the ability of DecisionDx-UM to be a superior predictor of

metastasis compared to other prognostic factors, such as chromosome 3 status, mutational status, AJCC stage and cell type. The words “can,” “would” 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 shown in this study, including with respect to the discussion of DecisionDx-UM in this press release; actual application of our DecisionDx-UM test 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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