NEWS RELEASE

Largest Prospective Study to Date Further Supports Performance of DecisionDx®-UM for Metastatic Risk Stratification in Uveal Melanoma and Utility of PRAME Biomarker for Refining Risk When Considered with DecisionDx-UM Class Result

5/8/2024

Oral presentation at ARVO shares ground-breaking findings from the ongoing Collaborative Ocular Oncology Group (COOG) study 2 (COOG2) of patients with uveal melanoma (UM)

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced new data from a study further confirming the performance of its DecisionDx-UM test as a robust independent predictor of metastasis-free survival (MFS) in patients diagnosed with UM. Further, the study provides prospective validation data supporting Preferentially Expressed Antigen in Melanoma (PRAME) as a risk refinement tool when considered in the context of a Class 1 or Class 2 DecisionDx-UM test result. The data was presented at the Association for Research in Vision and Ophthalmology (ARVO) 2024 Annual Meeting in Seattle.

Uveal melanoma is an aggressive cancer of the eye, and despite high primary tumor cure rates, metastatic disease spread eventually impacts about half of all patients.[1] The DecisionDx-UM test is considered the standard of care in the management of newly diagnosed UM to assist in determining risk of metastasis, which is critical for informing appropriate treatment plans.

“The latest findings from the COOG2 study not only further support DecisionDx-UM’s ability to predict metastatic

risk, but also highlight the utility of PRAME as a valuable adjunct biomarker for further risk refinement when considered in conjunction with a DecisionDx-UM result," said lead study author and COOG investigator Zelia Correa, M.D., Ph.D., professor of ophthalmology and director of ocular oncology at the Bascom Palmer Eye Institute and Sylvester Comprehensive Cancer Center of the University of Miami Miller School of Medicine. "The study data provides support for combining the reported expression status of the PRAME gene with the DecisionDx-UM class result to enhance metastatic risk prediction. Specifically, distinguishing between PRAME-negative (-) and PRAME-positive (+) subgroups within DecisionDx-UM Class 1 and Class 2 tumors provides additional biological insights into an individual patient's likelihood of metastasis. This information can be utilized to optimize surveillance and guide more nuanced and risk-aligned treatment decisions."

Details regarding the presentation at ARVO are included below:

- Oral Presentation Title: Collaborative Ocular Oncology Group study 2 (COOG2): Prospective multi-center validation of the 15-gene expression profile (GEP)/PRAME molecular prognostic tool for uveal melanoma in 1586 patients
- Session Type: Paper Session (Wednesday, May 8)
- Presentation Number: 4273
- Summary: This prospective, multi-center study included 1,586 patients with posterior UM tumors enrolled across 26 ocular oncology centers in the United States and Canada. In the study, a DecisionDx-UM Class 2 result was the most robust independent predictor of MFS (HR 6.03; 95% CI, 4.49-8.09); P<0.001), followed by PRAME status (HR 1.77; 95% CI, 1.39-2.27; P<0.001). Patients with Class 2 tumors had considerably worse outcomes than those with Class 1 tumors, regardless of PRAME status; however, PRAME+ tumors fared worse within each GEP class (versus PRAME-). When considered together, five-year MFS rates were 95.6% (95% CI, 93.9-97.4) for Class 1/PRAME-, 80.6% (73.9-87.9) for Class 1/PRAME+, 57.6% (50.6-65.7) for Class 2/PRAME- and 44.8% (38.0-52.8) for Class 2/PRAME+. Overall, the study confirms the prognostic accuracy of the DecisionDx-UM test and provides the first prospective validation of PRAME status as a risk refinement tool when considered in the context of a Class 1 or Class 2 DecisionDx-UM result. These two tests together can guide more precise and risk-aligned decision-making for patients with UM, including referrals, intensity of imaging surveillance and eligibility for ongoing clinical trials.

J. William Harbour, M.D., ophthalmologist, ocular oncologist, and professor and chair of the department of ophthalmology at UT Southwestern Medical Center, is a leading innovator in the treatment and study of UM and an executive committee member of the COOG. As the original developer of the DecisionDx-UM test, which was licensed to Castle in 2009, Harbour continues to drive important advancements in the treatment of UM and co-authored this study with Correa.

The presented abstract described above can be viewed online in the **ARVO Meeting Planner**.

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 (UM). DecisionDx-UM is the standard of care in the management of newly diagnosed UM 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 UM 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 currently the only prognostic test for UM 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 UM 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 **here**.

About DecisionDx®-PRAME

Castle Biosciences offers testing with DecisionDx-PRAME as an optional add-on to the DecisionDx-UM test. PRAME (preferentially expressed antigen in melanoma) is an antigen gene that is not expressed at appreciable levels in normal adult tissues, but its expression can become aberrantly increased in some types of cancer, including melanoma. Once expressed, the PRAME protein can be processed and presented on the surface of cells, thereby serving as a potential target for therapeutic intervention. PRAME-directed therapies are being explored in multiple cancer types, including uveal melanoma. More information about DecisionDx-PRAME can be found **here**.

About the Collaborative Ocular Oncology Group

The Collaborative Ocular Oncology Group (COOG) is the largest collaborative working group in North America comprised of ocular and medical oncologists specialized in the treatment of patients with intraocular cancers, currently focusing on UM. The group is dedicated to a collaborative, evidence-based approach to advancing the care of patients with UM and other eye cancers through precision diagnostic, prognostic and therapeutic breakthroughs. Comprised of more than 25 leading academic and private ocular oncology centers of excellence, the COOG has been continually funded by the National Cancer Institute for over a decade. The COOG has conducted two large multi-center prospective studies of prognostic biomarkers in UM, the first and only such studies ever conducted in this cancer to date, and is planning a major expansion into adjuvant and metastatic clinic trials in patients with UM. More information about the COOG can be found **here**.

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: (i) the ability of the DecisionDx-UM test to assist in determining risk of metastasis to inform appropriate treatment plans; (ii) the utility of PRAME as a valuable biomarker when considered in conjunction with a DecisionDx-UM test result; and (iii) the ability of the DecisionDx-UM test and PRAME to guide more nuanced and risk-aligned treatment decisions for patients with UM, including referrals, intensity of imaging surveillance and eligibility for ongoing clinical trials. 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, 2023, our Quarterly Report on Form 10-Q for the quarter ended March 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.

1. Kujala E, Mäkitie T, Kivelä T. Very long-term prognosis of patients with malignant uveal melanoma. Invest Ophthalmol Vis Sci. 2003 Nov 1;44(11):4651.

Investor Contact:

Camilla Zuckero

czuckero@castlebiosciences.com

Media Contact:

Allison Marshall

amarshall@castlebiosciences.com

Source: Castle Biosciences Inc.