NEWS RELEASE

New Data at AACR Annual Meeting Highlights Use of DecisionDx®-Melanoma to Identify Early-Stage Melanoma Patients at High Risk of Distant Metastasis

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FRIENDSWOOD, Texas, April 25, 2025 (GLOBE NEWSWIRE) -- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, will share new research intended to improve the care of patients with cutaneous and uveal melanoma (CM and UM, respectively) via poster presentations at the American Association for Cancer Research® (AACR) Annual Meeting 2025, being held April 25-30 in Chicago.

"At Castle Biosciences, our commitment to advancing care for melanoma patients helps drive our continuous innovation," said Rebecca Critchley-Thorne, Ph.D., vice president, research and development, of Castle Biosciences. "The new data being presented at AACR underscores this commitment and further advances our mission to improve health through innovative tests that can help guide personalized treatment strategies designed to enhance patient outcomes."

Castle will present the following posters at AACR (all times Central Time). The corresponding abstracts are available on AACR's website using the inline links below.

DecisionDx-Melanoma

- **Abstract 3344**: The 31-gene expression profile identifies patients at risk of developing early distant metastases and can guide risk-appropriate surveillance strategies
- Lead Author and Presenter: Merve Hasanov, M.D., oncologist and director of the division of medical oncology at The Ohio State University Comprehensive Cancer Center, Columbus, Ohio

- Session Category: Clinical Research
- Session Title: Prognostic Biomarkers 2
- Location: Poster Section 32
- Poster Board Number: 14
- Date & Time: April 28, 2-5 p.m.
- Summary: Building on findings presented at **ASCO 2024**, this study demonstrates that DecisionDx-Melanoma can identify early-stage CM patients (American Joint Committee on Cancer (AJCC) stage I-II, n=1,661) at higher risk of distant metastasis (DM) not only to the central nervous system (CNS), but also to the lung, liver and bone. Patients with Class 2B (highest risk) results showed significantly higher DM rates compared to Class 1A (lowest risk) patients across all sites: CNS (7.4% vs. 0.9%, p<0.001), lung (7.4% vs. 1.2%, p<0.001), liver (4.5% vs. 0.6%, p<0.001) and bone (3.0% vs. 0.8%, p<0.05). Notably, Class 2B patients had significantly lower five-year DM-free survival and elevated metastasis risk persisted several years after diagnosis, particularly to CNS and lung. These results support combining DecisionDx-Melanoma with AJCC staging to potentially identify high-risk patients for tailored surveillance and treatment strategies, which may enable earlier metastasis detection and potentially improve survival outcomes.

DecisionDx-UM

- **Abstract LB262**: Development of a clinically feasible aqueous proteomic signature to assess the malignant potential of small uveal melanocytic tumors
- Session Title: Late-Breaking Research: Clinical Research 2 / Endocrinology
- Location: Poster Section 51
- Poster Board Number: 11
- Date & Time: April 29, 9 a.m.-12 p.m.
- Summary: UM, though rare, is the most common eye cancer, with up to 50% of patients developing metastatic disease. While tumor biopsy-based molecular testing is widely utilized to identify high-risk biology, repeated intraocular tumor biopsies are not feasible for monitoring small uveal melanocytic tumors of indeterminate malignant potential (UMTIMP). This study seeks to address this unmet clinical need by evaluating aqueous humor (AH) protein biomarkers—obtainable through a minimally invasive office-based liquid biopsy from the anterior chamber of the eye—to help identify high-risk lesions early to help inform the decision to biopsy. Among 79 UM patients assessed with the DecisionDx-UM test (the current standard of care for evaluating metastatic risk in UM), 72% (57/79) were classified as low risk (Class 1) and 28% (22/79) as high risk for developing metastasis. The study identified proteins in the AH with significant differences between risk classes (N=386, p<0.0001) for the development of several risk prediction models. The proteins from the highest-performing models may be further evaluated for their ability to detect high-risk UMTIMPs with a goal of enabling more timely clinical decisions, determining the need for further prognostic testing

(DecisionDx-UM, -PRAME, -UMSeq), and potentially allowing for earlier therapeutic intervention to improve patient outcomes.

About DecisionDx-Melanoma

DecisionDx-Melanoma is a 31-gene expression profile (31-GEP) 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 50 peer-reviewed and published studies, providing confidence in disease management plans that incorporate the test's results. Through Dec. 31, 2024, DecisionDx-Melanoma has been ordered more than 191,000 times for patients diagnosed with cutaneous melanoma. Learn more at **www.CastleBiosciences.com**.

About DecisionDx-UM

DecisionDx-UM is Castle Biosciences' 15-gene expression profile (15-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. Learn more at **www.CastleBiosciences.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, 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 seeking biologic treatment. 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: the ability of DecisionDx-Melanoma to identify early-stage melanoma patients at high risk of DM to enable risk-appropriate surveillance and treatment; Castle's ability to continuously innovate; the ability of new data to further advance Castle's mission to improve health through innovative tests that can help guide personalized treatment strategies designed to enhance patient outcomes; the ability of Castle's tests to enable more personalized treatment and improve patient outcomes; the ability of DecisionDx-Melanoma, combined with AJCC staging, to identify high-risk patients and enable earlier metastasis detection and improve survival outcomes; and the ability of the DecisionDx-UM test to detect high risk UMTIMP's and to allow earlier therapeutic intervention to improve patient outcomes. The words "believe," "can" 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 these studies, including with respect to the discussion of our tests 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, 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.

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Source: Castle Biosciences, Inc.