NEWS RELEASE

New Data Demonstrate that the Utilization of TissueCypher® Barrett's Esophagus Test Results Can Significantly Improve the Management of Low-Grade Dysplasia in Patients with Barrett's Esophagus over the Standard of Care Alone

10/25/2022

Data presented at the 2022 American College of Gastroenterology (ACG 2022) Annual Scientific Meeting

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced new data showing that the use of TissueCypher® Barrett's Esophagus Test results can significantly improve management decisions for Barrett's esophagus (BE) patients with low-grade dysplasia (LGD)to improve health outcomes. TissueCypher is Castle's precision medicine test designed to predict future development of high-grade dysplasia (HGD) and/or esophageal adenocarcinoma (EAC) within five years for patients diagnosed with BE.

Overall, the study results suggest that TissueCypher may be used to standardize the management of BE patients with LGD to improve health outcomes, by helping ensure that patients at a high risk of progression receive earlier interventions and by potentially reducing unnecessary use of endoscopic eradication therapy (EET) and endoscopies for lower risk patients.

"A diagnosis of low-grade dysplasia in Barrett's esophagus warrants expert pathology review, as these patients may have a significant risk of developing esophageal cancer. However, expert pathology review lacks standard criteria, is highly variable and is fraught with logistical challenges," said Lucas C. Duits, M.D., Ph.D., Department of

Gastroenterology and Hepatology at University Medical Center in Amsterdam, The Netherlands. “The use of TissueCypher test results can reduce inconsistencies in management decisions for Barrett’s esophagus patients with low-grade dysplasia. We believe there are potential implications to this finding, including a reduction in the incidence and mortality of esophageal cancer and a reduction in the use of unnecessary clinical treatments, when appropriate.”

The study results were shared in a podium presentation at the 2022 American College of Gastroenterology (ACG2022) Annual Scientific Meeting, being held Oct. 21-26 in Charlotte, North Carolina. The presentation was titled “An Objective Spatialomics Test Standardizes Management Decisions with Potential to Improve Outcomes for Barrett’s Esophagus Patients,” and was given by Lucas C. Duits, M.D., Ph.D.

The study involved a cohort of 154 real patients with known outcomes who were followed prospectively as part of the SURF trial. Twenty-four of these patients progressed to HGD/EAC within five years. Each patient’s baseline specimens were independently reviewed by 30 pathologists from five countries and also tested with TissueCypher in a blinded manner. Management decision simulations were performed, where each patient's baseline specimens were first evaluated by a generalist pathologist, and then referred to an expert pathologist from the same country for any diagnoses of LGD. In one arm of the study, management for the patients was determined by the current standard of care, which includes pathology review of tissue samples and management according to current guidelines. In the other arm, patients were managed by the current standard of care with additional guidance from TissueCypher test results. The percentage of patients receiving appropriate management per their known outcome was compared between the two study arms, with appropriate management defined as:

- Three- to five-year surveillance for patients who did not progress to HGD/EAC during surveillance; and
- Either surveillance in less than one year or EET for patients who did progress to HGD/EAC during surveillance.

The study results showed the following:

- Using TissueCypher test results to guide patient management decisions significantly increased the likelihood of BE patients with LGD receiving appropriate management per their known outcome ($p=0.0007$). 58.4% of patients had a 100% chance of receiving appropriate management when TissueCypher test results were used to guide decisions despite different pathologists reviewing their baseline specimens, compared to 9.1% of patients who were managed according to the standard of care pathology review alone.
- Use of TissueCypher test results improved the consistency of management decisions for BE patients with LGD by reducing the impact of variable pathology review ($p<0.0001$). 57.1% of patients whose care was guided with the addition of TissueCypher test results had no deviation in management decisions when different pathologists reviewed their baseline specimens, compared to 7.1% of patients whose management was guided only by the current standard of care.

About TissueCypher® Barrett's Esophagus Test

The TissueCypher Barrett's Esophagus test is Castle's precision medicine test designed to predict future development of high-grade dysplasia (HGD) and/or esophageal cancer in patients with Barrett's esophagus (BE). TissueCypher is indicated for use in patients with endoscopic biopsy confirmed BE that is graded non-dysplastic (ND), indefinite for dysplasia (IND) or low-grade dysplasia (LGD); its clinical performance has been supported by nine peer-reviewed publications of BE progressor patients with leading clinical centers around the world. The TissueCypher Barrett's Esophagus Assay is a proprietary Laboratory Developed Test with its own unique CPT PLA code (0108U) and has been on the Medicare Clinical Laboratory Fee Schedule since January 2021. Additionally, the test received Advanced Diagnostic Laboratory Test (ADLT) status from the Centers for Medicare & Medicaid Services (CMS) in March 2022.

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 predict systemic therapy response in patients with moderate-to-severe psoriasis, atopic dermatitis and related conditions. To learn more, please visit **www.CastleBiosciences.com** and connect with us on **LinkedIn**, **Facebook**, **Twitter** 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 potential of TissueCypher test results to (i) significantly improve the management of LGD in patients with BE over the standard of care alone to improve health outcomes, (ii) standardize the management of BE patients with LGD to improve health outcomes by helping ensure that patients at a high risk of progression receive earlier interventions and by potentially reducing unnecessary use of EET and endoscopies for lower risk patients; (iii) reduce inconsistencies in management decisions for BE patients with LGD; and (iv) reduce

the incidence and mortality of esophageal cancer and the use of unnecessary clinical treatments, when appropriate. The words “can,” “may,” “potential” 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 this study, including with respect to the discussion of TissueCypher 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 Quarterly Report on Form 10-Q for the three months ended June 30, 2022, 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.

Investor Contact:

Camilla Zuckero

czuckero@castlebiosciences.com

Media Contact:

Allison Marshall

amarshall@castlebiosciences.com

Source: Castle Biosciences, Inc.