



NEWS RELEASE

Data from Independent, Pooled Analysis Show Significantly Improved Risk Predictions Over Clinical Variables for TissueCypher® Barrett's Esophagus Test and Ability to Identify Patients at High Risk of Progressing to Esophageal Cancer

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The study data reinforce the value of TissueCypher in helping physicians and patients make more informed management decisions based on the unique biology of individual patients' esophageal biopsies

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced an independent, peer-reviewed article published in Clinical Gastroenterology and Hepatology. The study, which can be viewed [here](#), reinforces the ability of TissueCypher® to significantly improve predictions of progression to esophageal cancer in patients with Barrett's esophagus (BE), compared to predictions based on clinical and pathology variables alone, allowing for more informed disease management decisions.

"One of the most critical challenges in the management of the nearly 384,000 patients with Barrett's esophagus who undergo an endoscopy each year is determining which are at risk of progression to esophageal cancer," said Derek Maetzold, president and chief executive officer of Castle Biosciences. "In this study, TissueCypher outperformed expert pathologist evaluations, which relied solely on commonly used clinical and pathologic variables, in risk-stratifying patients for progression, particularly those at highest risk of developing esophageal cancer."



“Of particular importance in this study was the ability of the test to identify high-risk patients who progressed to high-grade dysplasia (HGD) or esophageal cancer, yet were initially diagnosed as non-dysplastic BE (NDBE),” said Prasad G. Iyer, M.D., M.Sc., lead study author and professor of medicine in the Barrett’s Esophagus Unit of the Division of Gastroenterology and Hepatology at the Mayo Clinic, Rochester, Minn. “In clinical practice, the majority of BE patients who develop esophageal cancer are diagnosed as NDBE at their baseline endoscopy. Many of these are missed by traditional standard of care, and importantly, miss the opportunity of early interventions that could potentially prevent their progression to the highly lethal esophageal cancer, or at a minimum, increase their chances of survival.”

“TissueCypher has the potential to help change this,” added Maetzold.

In the manuscript titled, “Prediction of Progression in Barrett’s Esophagus Using a Tissue Systems Pathology Test: A Pooled Analysis of International Multicenter Studies,” Iyer et al. at Mayo Clinic and Case Western Reserve University evaluated the risk-stratification performance of TissueCypher using patient-level data from five published clinical validation studies that included a total of 552 patients with BE.

In the study, 51.8% (n=58) of the 112 patients diagnosed as NDBE who progressed to HGD or esophageal cancer received an intermediate- or high-risk TissueCypher score, representing a sensitivity of 52% in detecting this subset of progressors who are often missed by the current standard of care. Further, a TissueCypher high-risk score was associated with a strong (Odds Ratio (OR)=14.3) independent risk of progression in NDBE patients. When incorporated with expert pathologist review and clinical risk variables, TissueCypher was associated with further improved risk predictions versus those made without the test’s results (c-statistic=0.72 with TissueCypher versus 0.63 without, $p<0.0001$).

In the study, a TissueCypher high-risk score independently predicted increased risk of progression to HGD/esophageal cancer (OR=6.0, 95% Confidence Interval (CI)=2.99-12.01, $p<0.001$), with improved accuracy over expert pathologist diagnoses of low-grade dysplasia (LGD) (OR=2.92, 95% CI=1.18-7.24, $p<0.021$) and indefinite for dysplasia (IND) (OR=2.13, 95% CI=0.76-5.99, $p=0.15$). Additionally, when the TissueCypher score was incorporated with expert pathologist review of biopsied tissue and other clinical risk variables, the risk prediction accuracy was significantly improved (c-statistic=0.75 with TissueCypher versus 0.68 without, $p<0.0001$), which suggests that TissueCypher can be added into existing clinical care plans to help guide more personalized and risk-aligned management of BE patients.

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). The

TissueCypher Barrett's Esophagus test is indicated for use in patients with endoscopic biopsy confirmed BE that is graded non-dysplastic (NDBE), indefinite for dysplasia (IND) or low-grade dysplasia (LGD); its clinical performance has been supported by eight 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.

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](#).

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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: TissueCypher's ability to identify patients with a high risk of progressing to HGD or esophageal cancer and provide opportunities for early interventions that could potentially prevent progression to esophageal cancer or increase chances of survival; the test's ability to help physicians and patients make more informed management decisions based on the unique biology of individual patients' esophageal biopsies by risk-stratifying patients for progression. The words "potential," "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: the effects of the COVID-19 pandemic on our business and our efforts to address its impact on our business; subsequent study results and findings may contradict earlier study results and findings, including with respect to the TissueCypher test discussed 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 fiscal year ended Dec. 31, 2021, 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

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