NEWS RELEASE

Systematic Review and Meta-Analysis Confirms TissueCypher® Outperforms Traditional Pathology or Clinical Factors Alone to Identify Patients at Increased Risk of Developing Esophageal Cancer

2025-12-12

Across multiple published studies, the test consistently identifies high-risk patients whose progression rates exceed guideline-based actionable thresholds for intensified care

FRIENDSWOOD, Texas, Dec. 12, 2025 (GLOBE NEWSWIRE) -- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced the publication of a new systematic review and meta-analysis (SRMA) demonstrating that the TissueCypher® Barrett's Esophagus test provides clinically validated risk stratification for patients with Barrett's esophagus (BE). The findings confirm that TissueCypher can outperform traditional pathology or clinical factors alone to identify patients at increased risk of developing esophageal cancer.

The paper, titled "The Tissue Systems Pathology Test Predicts Risk of Progression in Patients With Barrett's Esophagus: Systematic Review and Meta-Analysis," was published in the **Journal of Clinical Gastroenterology**. The analysis consolidated data from six previously published studies and found that TissueCypher consistently identifies patients at greater risk of progression to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC), a key step toward enabling personalized, risk-aligned patient management aimed at preventing cancer.

"Our findings provide strong evidence that TissueCypher delivers meaningful risk stratification for patients with Barrett's esophagus," said Caitlin C. Houghton, M.D., board-certified foregut surgeon at Keck Medicine of USC in Los Angeles, California, and lead author of the study. "By identifying which patients are truly at high risk for progression to esophageal cancer — and which are not — TissueCypher can help physicians personalize care, flagging those

who may benefit from earlier intervention and providing confidence in continuing routine surveillance for those at low risk."

SRMAs represent rigorous, high-quality evidence for clinical validation because they synthesize findings across multiple studies to provide overall estimates of performance. The results of this SRMA represent the most comprehensive validation of the TissueCypher test to date, reinforcing its value as an evidence-based tool for risk stratification in BE. The study demonstrates TissueCypher's predictive performance across patients with non-dysplastic BE (NDBE), indefinite for dysplasia (IND) and low-grade dysplasia (LGD), and shows that the test outperforms histologic assessment in identifying patients at greatest risk of progression.

Key findings of the SRMA indicate TissueCypher can help physicians:

- Identify patients at highest risk: Across six published studies, patients with high-risk TissueCypher results were 6.7 times more likely to progress to HGD or EAC within five years than those with low-risk results ($p<0.0001$).
- Guide care with confidence: Patients with high or intermediate-risk results had an annual progression rate of 2.8%, and those with high-risk results had a rate of 5.6% per year, both above the 1.7% annual progression rate typically reported for patients with LGD, a clinical benchmark for therapeutic intervention.

By integrating data across multiple studies, this analysis confirms that TissueCypher provides consistent, reproducible performance and supports its potential to help physicians deliver risk-aligned care, identifying patients most likely to progress and tailoring management strategies that can improve outcomes while reducing unnecessary procedures.

About TissueCypher Barrett's Esophagus Test

TissueCypher is a precision medicine test designed and extensively validated to predict a patient's personalized risk of progression from Barrett's esophagus to high-grade dysplasia or esophageal adenocarcinoma. Indicated for patients with non-dysplastic BE, indefinite for dysplasia or with low-grade dysplasia, TissueCypher's five-year risk assessment is designed to help physicians tailor care to each patient's risk of developing HGD or EAC.

Backed by 17 peer-reviewed publications and studied in biopsies from more than 8,000 patients, TissueCypher has been shown to be the strongest independent predictor of progression compared with traditional histopathological risk assessment. Using an AI-driven spatialomics approach, the test identifies molecular signatures that often precede the development of dysplasia, which can enable earlier identification, treatment, and management of patients at increased risk of cancer. TissueCypher is designed to integrate seamlessly into routine endoscopic practice by analyzing standard esophageal pinch biopsies, delivering actionable insights without requiring

additional procedures. Learn more at **www.CastleBiosciences.com/TissueCypher**.

About Castle Biosciences

Castle Biosciences (Nasdaq: CSTL) is a leading diagnostics company improving health through innovative tests that guide patient care. With a primary focus in dermatologic and gastroenterological disease, we develop personalized, clinically actionable solutions that help improve disease management and patient outcomes.

We put people first—empowering patients and clinicians and informing care decisions through rigorous science and advanced molecular tests that support more confident treatment planning. To learn more, visit **www.CastleBiosciences.com** and connect with us on **LinkedIn**, **Instagram**, **Facebook** and **X**.

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 provide risk insights beyond pathology or clinical factors alone and enable more personalized surveillance and treatment strategies for BE patients that may help prevent cancer, including supporting earlier intervention for those at higher risk for progression to esophageal cancer, reducing unnecessary procedures for those at lower risk of progression, and supporting risk-aligned management of patients with a finding of indefinite for dysplasia. The words "believe," "may," "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 our Quarterly Report on Form 10-Q for the quarter ended September 30, 2025, each as filed with the SEC, 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.

Source: Castle Biosciences, Inc.