NEWS RELEASE

New Data at American College of Gastroenterology Annual Meeting Show TissueCypher® Provides Actionable Risk Insights that Influence Clinical Management and Prompt Risk-Aligned Intervention in Barrett's Esophagus

2025-10-26

Research on TissueCypher by Horvath et al. honored with a Presidential Poster Award from the ACG Abstract Selection Committee, a distinction awarded to only 5-7% of abstracts for research deemed high quality, novel or unique

FRIENDSWOOD, Texas, Oct. 26, 2025 (GLOBE NEWSWIRE) -- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced new data demonstrating that its TissueCypher® Barrett's Esophagus test can provide risk insights beyond pathology alone, influencing clinical management to support earlier intervention for those at higher risk of progression to esophageal cancer and potentially reducing unnecessary procedures for those at lower risk. The research will be presented in three posters at the American College of Gastroenterology (ACG) 2025 Annual Scientific Meeting, taking place Oct. 27–29, 2025, in Phoenix, Arizona, including one selected for a Presidential Poster Award.

"Our findings being presented at ACG highlight how difficult it can be to accurately assess progression risk in patients with Barrett's esophagus when relying on pathology alone," said Edward Horvath, M.D., board-certified gastroenterologist at Gastro Health West Boynton in Boynton Beach, Florida. "By identifying patients at higher risk who may otherwise be missed, the TissueCypher test provides objective, individualized risk information that supports more personalized decisions around surveillance and intervention, helping clinicians act sooner to potentially reduce the risk of progression to esophageal cancer."

More than 6,400 scientific abstracts will be presented during ACG 2025. Only a small percentage of these received a Presidential Poster Award, recognizing high quality, novel, unique or interesting research, including the abstract by Horvath et al. highlighted below.* Two additional posters on TissueCypher will also be presented (all times Pacific Daylight Time).

P0689: The Tissue Systems Pathology Test (TSP-9) Informs Management of Patients That Are Indefinite for Dysplasia to Predict Missed Prevalent Neoplasia

- Presenting Author: Ronen Arai, M.D., Gastro Health North Broward, Coral Springs, Florida
- Date: Sunday, Oct. 26
- Time: 3:30-7:00 p.m.; author available to answer questions from 5:15-6:30 p.m.
- Summary: Pathologists may issue a finding of indefinite for dysplasia (IND) when active inflammation makes it unclear whether dysplasia or early neoplasia is present. Although guidelines recommend repeat endoscopy in three to six months after high-dose proton pump inhibitor (PPI) therapy, patients with IND remain at increased risk of progression to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC). New data from two case studies show that TissueCypher returned high-risk results corresponding to five-year probabilities of progression to HGD/EAC of 34% and 62%, respectively, exceeding the published rates of progression from HGD to EAC (33% over five years). These results prompted the use of advanced imaging and/or earlier follow-up, leading to detection of HGD in one patient and HGD and intramucosal cancer in another, enabling timely and more aggressive intervention. These findings illustrate how TissueCypher can deliver clinically valuable insights that support more risk-aligned management of patients with IND to reduce the risk of mortality from EAC.

ACG Presidential Poster Award Winner*
P4977: High-risk Tissue Systems Pathology Test (TSP-9) Results Enable Risk-aligned Management of Patients With Presumed Clinically Low-Risk Non-Dysplastic Barrett's Esophagus

- Presenting Author: Edward Horvath, M.D., Gastro Health West Boynton, Boynton Beach, Florida
- Date: Tuesday, Oct. 28
- Time: 10:30 a.m.-4 p.m.; author available to answer questions from 1-2:15 p.m.
- Summary: Patients with non-dysplastic Barrett's esophagus (NDBE) are considered at low risk for progression to HGD/EAC under current guidelines, which recommend surveillance every three to five years. Despite this classification, patients with NDBE can still progress to HGD or EAC within that interval. New data from two case studies show that TissueCypher identified patients with NDBE at high-risk of progression to HGD/EAC, with five-year probabilities of 43% and 45%, respectively, exceeding the published rates of progression from HGD to EAC (33% over five years). Guided by these results, clinicians recommended earlier intervention with

endoscopic eradication therapy, and both patients were subsequently confirmed to have progressed to low grade dysplasia (LGD). These findings support the role of TissueCypher in providing individualized risk stratification to help inform more risk-aligned decision making and potentially earlier interventions to help prevent disease progression at an early, treatable stage.

P4930: Impact of Spatialomics Utilization on the Management of Non-Dysplastic Barrett's Esophagus in a Rural Community

- Presenting Author: Stephen Thai, M.S., Texas Medical Center, The Colony, Texas
- Date: Tuesday, Oct. 28
- Time: 10:30 a.m.-4 p.m.; author available to answer questions from 1-2:15 p.m.
- Summary: In a rural Texas study of 114 patients with NDBE, TissueCypher stratified patients into low, intermediate and high-risk groups. Seven patients identified as intermediate- or high-risk by the TissueCypher test received ablation therapy, while 99 low-risk patients had their surveillance interval safely extended from two to three years to five years. Overall, the test influenced clinical management in 93% of cases, supporting its potential to help ensure timely intervention for higher-risk patients while reducing unnecessary procedures and burden for lower-risk patients.

All posters are available on the **ACG 2025 website** and in an online issue of The American Journal of Gastroenterology. For more information on TissueCypher, visit Castle at booth 358.

About TissueCypher Barrett's Esophagus Test
The TissueCypher Barrett's Esophagus test is Castle's precision medicine test designed to predict future development of HGD and/or EAC 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 NDBE, IND, or LGD; its clinical performance has been supported by 14 peer-reviewed publications of BE progressor patients with leading clinical centers around the world. 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, Barrett's esophagus and uveal melanoma. Additionally, the Company has active research and development programs for tests in these and other diseases with high clinical need, including its test in development to help guide treatment decisions for patients with moderate-to-severe atopic dermatitis. To learn more, please visit **www.CastleBiosciences.com** and connect with us

on **LinkedIn**, **Facebook**, **X** 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 provide risk insights beyond pathology 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," "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 June 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.

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Source: Castle Biosciences, Inc.

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