Iambic Presents Updated IAM1363 Clinical Data at ESMO 2026, Showing Durable Responses with a Favorable Tolerability Profile in Heavily Pretreated Participants with HER2-Driven Cancers

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- *IAM1363, now in a Phase 1/1b study, was designed using Iambic's molecular superintelligence platform and brought to clinical development in approximately two years*
- *Data presented at ESMO 2026 demonstrates IAM1363 was well tolerated with low rates of Grade 3 or higher treatment-related adverse events, serious adverse events, and dose modifications*
- *More than half of participants dosed at 960 mg remain on study with some participants on treatment beyond one year*
- *Intracranial responses were observed in participants with HER2-positive breast cancer who have previously received T-DXd and tucatinib*

SAN DIEGO--(BUSINESS WIRE)--Oct. 26, 2026-- Iambic Therapeutics, Inc. (Iambic) (Nasdaq: IAM), a clinical-stage life sciences and technology company developing novel medicines using its AI-driven platform, today announced updated clinical data for IAM1363, a selective and brain-penetrant HER2 tyrosine kinase inhibitor (TKI), from its ongoing Phase 1/1b clinical trial. The data, which showed durable anti-tumor activity, intracranial responses and a favorable tolerability profile in heavily pretreated participants with HER2-altered advanced cancers, were presented in a poster at the European Society for Medical Oncology (ESMO) Congress 2026 in Madrid on October 23, 2026.

IAM1363 was discovered using Iambic's molecular superintelligence platform and progressed from project initiation to clinical development in approximately two years.

"Last year at ESMO we shared the first clinical data for IAM1363. Today's update shows that data set maturing in the ways that matter most for patients: durability, higher rate of best overall response, and consistent tolerability at the recommended dose," said Tom Miller, PhD, Co-Founder and CEO, Iambic. "The intracranial responses, including in participants with extensive brain metastases who had already been treated with T-DXd and tucatinib, reflect what we set out to build: a potentially differentiated selective HER2 inhibitor that is brain penetrant, brought to the clinic years faster than industry norm."

Updated Clinical Results (data cutoff August 31, 2026)

As of the data cutoff, 122 participants had received IAM1363 across Parts 1-4 of the study, including 103 treated with monotherapy at doses of ≥960 mg and 68 treated at the recommended dose of 960 mg once daily (QD). Participants were heavily pretreated, with a median of three prior regimens in the metastatic setting; 61% had received prior trastuzumab deruxtecan (T-DXd) and 36% prior tucatinib. Breast cancer (38%) and non-small cell lung cancer (NSCLC) (19%) were the most common tumor types, and 44% of participants had central nervous system (CNS) metastases.

In participants with targetable HER2 alterations dosed at ≥960 mg QD:

- **Systemic activity:** Best overall response by RECIST v1.1 was partial response (PR) in 36% (19/53), stable disease (SD) in 38% (20/53) and progressive disease (PD) in 26% (14/53).
- **Intracranial activity:** Best overall response by modified RANO-BM was PR in 41% (9/22), SD in 55% (12/22), and PD in 5% (1/22).
- **Durability:** More than half of participants dosed at 960 mg QD remain on study treatment. Responses are ongoing beyond 12 months in a participant with HER2-mutant NSCLC who had received prior T-DXd, and in a participant with HER2-mutant renal cell cancer; a separate participant with HER2-mutant NSCLC has

maintained disease control for more than 10 months.

- **Breadth of activity:** Responses were observed across HER2-positive, HER2-mutant, and HER2-amplified cancers, including breast cancer, NSCLC, biliary tract cancer, gastroesophageal adenocarcinoma, and renal cell cancer, among others. Three participants with NGS-detected HER2-amplified cancers had durable responses.
- **Intracranial responses:** Three participants with HER2-positive breast cancer, all previously treated with T-DXd and tucatinib, achieved confirmed intracranial partial responses per RANO-BM, and all remain on treatment. This included one participant with more than 50 brain metastases who had received prior treatment with seven different HER2-directed agents
- **Tolerability:** IAM1363 monotherapy was generally well tolerated. In participants dosed at 960 mg QD (n=68), few experienced grade 3 treatment-related adverse events (TRAEs) or TRAEs that led to dose modifications (5.9% for each) and none experienced a grade 4 or 5 TRAE. Across all participants dosed at >=960 mg QD (n=103), most treatment-emergent adverse events (TEAEs) were low grade, with the most common TEAEs of any grade being diarrhea (59%), nausea (53%), and vomiting (49%). There were no Grade 4 TEAEs and no Grade 5 TRAEs.

"We believe that these data support continued development of IAM1363, which has been generally well-tolerated and has shown anti-tumor activity across a wide range of HER2 altered cancers at the recommended monotherapy dose of 960 mg," said Neil Josephson, MD, Chief Medical Officer, Iambic. "Especially promising are the intracranial responses in participants with HER2-positive breast cancer who had previously received T-DXd and tucatinib. Patients with brain metastases have limited options, so we are encouraged by early evidence of anti-tumor activity in this setting with a significant unmet need. We are grateful to the participants and investigators who are taking part in this Phase 1/1b study and look forward to continuing evaluation of IAM1363 as a monotherapy and in combination with standard of care therapies."

The Phase 1/1b trial (NCT06253871) is an open-label, multicenter study evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of IAM1363 in participants with HER2-altered advanced cancers. The study comprises four parts: dose escalation (Part 1) and dose optimization (Part 2), both completely enrolled; monotherapy expansion cohorts at 960 mg (Part 3); and combination cohorts (Part 4). Parts 3 and 4 are open to enrollment at sites in the U.S., Europe and Asia.

About Iambic

Iambic's mission is to make better technology for better medicines. By utilizing molecular superintelligence — integrating proprietary AI with automated, scalable chemistry and biology experimentation — our platform is designed to address the totality of drug discovery and development. We believe the utility of our platform is demonstrated by the discovery of IAM1363, a novel drug candidate advanced to clinic in approximately two years, along with a diverse preclinical pipeline. Our leading AI technologies include Enchant and NeuralPLexer for multimodal endpoint prediction designed to improve the speed, precision, and success rates of drug discovery and clinical development. At Iambic, we are building an engine that is designed to power the future of medicine. | iambic.ai

Forward-Looking Statements

This press release contains forward-looking statements as that term is defined in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Statements in this press release that are not purely historical are forward-looking statements. Such statements include, but are not limited to, statements regarding the potential therapeutic effects of IAM1363, including its potential activity against CNS disease and in heavily pretreated patients, the potential durability of responses observed, the safety and tolerability profile of IAM1363, the potential for IAM1363 to be differentiated from other therapies, and Iambic's plans to continue evaluating IAM1363 in ongoing monotherapy expansion and combination cohorts. These

statements are based on numerous assumptions and involve substantial risks, uncertainties and other factors that may cause actual results, levels of activity, performance or achievement to be materially different from the information expressed or implied by these forward-looking statements, including that data from an ongoing early-phase trial with a limited number of participants may change as the study continues and may not be predictive of results in later trials, and the other risks described under “Risk Factors” in Iambic’s final prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) on October 15, 2026, and in Iambic’s subsequent filings with the Securities and Exchange Commission. The forward-looking statements in this press release are as of the date of this press release. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this press release. These forward-looking statements are made as of the date of this press release, and Iambic assumes no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law.

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