ORIC® Pharmaceuticals Presents Enozertinib Data in NSCLC Patients with HER2 Exon 20 Mutations at the ESMO Asia Congress 2025

December 5, 2025 at 1:00 AM EST

Systemic activity of 35% ORR in 2L+ patients, including in patients with active brain metastases

Manageable safety profile with low discontinuation rate

Enrollment completed; no further development planned in this patient population

Company to host a conference call and webcast on Saturday, December 6, 2025, at 8:00 pm ET

SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, Dec. 05, 2025 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, announced data from a Phase 1b trial of enozertinib (ORIC-114) at the ESMO Asia Congress 2025. Data in previously treated NSCLC patients with HER2 exon 20 mutations were presented at a poster session, and the poster can be found in the publication section of ORIC's website here.

Enozertinib Phase 1b Trial Design
Enozertinib is being evaluated in a Phase 1b trial in patients with locally advanced or metastatic NSCLC with HER2 exon 20 mutations. Notably, enrollment allows patients with active untreated brain metastases. Prior therapies include chemotherapy and HER2 targeted therapies. The primary endpoint of the trial is to determine the recommended Phase 2 dose (RP2D), and secondary endpoints include investigator-assessed objective response rate (ORR), disease control rate (DCR), and safety.

Previously Treated NSCLC Patients with HER2 Exon 20 Mutations
As of the August 29, 2025 cutoff date, 49 patients were dosed — 26 patients received 80 mg QD oral enozertinib and 23 patients received 120 mg QD. Patients were treated with up to 4 prior therapies, with 80% of patients having received prior chemotherapy and 35% having received a prior HER2 targeted therapy. Brain metastases were present in 47% of patients at baseline, including those with active brain metastases.

Preliminary Safety Analysis
Enozertinib was well tolerated with mostly Grade 1 or 2 treatment-related adverse events (TRAEs), and no significant off-target toxicities. Most frequent TRAEs included paronychia, diarrhea, and dermatitis acneiform. Only 2 patients discontinued treatment due to TRAEs. Higher rates of dose reductions occurred in the 120 mg cohort compared to the 80 mg cohort.

Preliminary Activity Analysis
Tumor responses were observed in both the 80 mg and 120 mg cohorts, including in patients with baseline brain metastases. Patients in the 80 mg cohort experienced deeper tumor regressions potentially due to the lower rate of dose reductions.

- 35% ORR (26% confirmed ORR) and 100% DCR in the 80 mg cohort
- As of the data cutoff (at a median follow-up of 50 weeks), 32% of patients remained on treatment in both the 80 mg and 120 mg cohorts

Next Steps
Based on data generated in patients with EGFR exon 20 and EGFR atypical mutations, 80 mg QD oral enozertinib has been selected as the dose for potential Phase 3 development. Enrollment and follow-up continues in 1L NSCLC patients with EGFR exon 20 and EGFR P-loop and alpha C-helix compressing (PACC) mutations, with the next update expected in mid-2026, ahead of initiation of potential Phase 3 trial(s). Enrollment in HER2 exon 20 has been completed with no further development planned in this patient population.

Conference Call and Webcast Details
In conjunction with the ESMO Asia Congress, ORIC will host a conference call and webcast on Saturday, December 6, 2025, at 8:00 pm ET. To join the conference call via phone and participate in the live Q&A session, please pre-register online here to receive a telephone number and unique passcode required to enter the call. A live webcast and audio archive of the conference call will be available through the investor section of ORIC's website at www.oricpharma.com. The webcast will be available for replay for 90 days following the presentation.

About ORIC Pharmaceuticals, Inc.
ORIC Pharmaceuticals is a clinical stage biopharmaceutical company dedicated to improving patients' lives by *Overcoming Resistance In Cancer*. ORIC's clinical stage product candidates include (1) ORIC-944, an allosteric inhibitor of the polycomb repressive complex 2 (PRC2) via the EED subunit, being developed for prostate cancer, and (2) enozertinib (ORIC-114), a brain-penetrant inhibitor that selectively targets EGFR exon 20, EGFR atypical, and HER2 exon 20 mutations, being developed across multiple genetically defined cancers. ORIC has offices in South San Francisco and San Diego, California. For more information, please go to www.oricpharma.com, and follow us on X or LinkedIn.

Cautionary Note Regarding 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 forward-looking statements include, among other things, statements regarding the clinical development of enozertinib; clinical outcomes from studies of enozertinib, which may materially change as patient enrollment continues or more patient data become available; the potential advantages of enozertinib; and plans underlying ORIC's clinical trials and development. Words such as "believes," "anticipates," "plans," "expects," "intends," "will," "goal," "potential"

and similar expressions are intended to identify forward-looking statements. The forward-looking statements contained herein are based upon ORIC's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those projected in any forward-looking statements due to numerous risks and uncertainties, including but not limited to: risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and operating as an early clinical stage company; ORIC's ability to develop, initiate or complete preclinical studies and clinical trials for, obtain approvals for and commercialize any of its product candidates; changes in ORIC's plans to develop and commercialize its product candidates; the potential for clinical trials of enozertinib or any other product candidates to differ from preclinical, initial, interim, preliminary or expected results; negative impacts of health emergencies, economic instability or international conflicts on ORIC's operations, including clinical trials; the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of ORIC's license and collaboration agreements or its clinical trial collaboration and supply agreements; the potential market for ORIC's product candidates, and the progress and success of competing therapeutics currently available or in development; ORIC's ability to raise any additional funding it will need to continue to pursue its business and product development plans; regulatory developments in the United States and foreign countries; ORIC's reliance on third parties, including contract manufacturers and contract research organizations; ORIC's ability to obtain and maintain intellectual property protection for its product candidates; the loss of key scientific or management personnel; competition in the industry in which ORIC operates; general economic and market conditions; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in ORIC's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the SEC) on November 13, 2025, and ORIC's future reports to be filed with the SEC. These forward-looking statements are made as of the date of this press release, and ORIC 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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