



ORIC® Pharmaceuticals Presents Potential Best-in-Class Data for Enozertinib in 1L NSCLC Patients with EGFR Atypical Mutations at ESMO Congress 2026 and Plans to Advance Enozertinib into a Global Phase 3 Trial

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In a 1L EGFR atypical population with more than double the rate of baseline CNS metastases as competitor datasets, enozertinib demonstrates a potential best-in-class 84% confirmed systemic ORR and 70% confirmed intracranial ORR, with multiple intracranial complete responses

88% 6-month landmark PFS compares favorably to current standards of care and to investigational therapies; follow-up ongoing with majority of patients continuing on treatment

Competitive safety profile with no significant off-target toxicity and no treatment-related discontinuations

Redwood-1 global Phase 3 registrational trial initiation in 1L EGFR atypical NSCLC expected in 1H 2027

Company to host a conference call and webcast today at 8:00 am ET featuring Dr. Joshua Sabari

SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, Oct. 23, 2026 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing and commercializing treatments that address mechanisms of therapeutic resistance, today presented potential best-in-class data for enozertinib in first-line NSCLC patients with EGFR atypical mutations at ESMO Congress 2026 and announced plans to advance enozertinib into a global Phase 3 trial.

"These enozertinib systemic and intracranial response data set a new benchmark in 1L EGFR atypical NSCLC," said Pratik S. Multani, M.D., chief medical officer. "The data are particularly impressive given that nearly two-thirds of our patients had baseline brain metastases, which is more than double the rate seen in competitor datasets, and which has historically been associated with poorer outcomes."

"Supported by these potential best-in-class data and having successfully completed End-of-Phase 1 interactions with FDA, we are rapidly advancing enozertinib into a global Phase 3 registrational trial," said Jacob M. Chacko, M.D., president and chief executive officer. "With rinzimetostat's first Phase 3 trial in prostate cancer initiated earlier this year and enozertinib's first Phase 3 trial in lung cancer planned for 1H 2027, ORIC has become a diversified, late-stage oncology company with two programs offering opportunities for broader development across indications with significant unmet need and meaningful commercial potential."

Enozertinib Phase 1b Data in 1L EGFR Atypical NSCLC

Enozertinib is being evaluated in an ongoing Phase 1b trial in patients with locally advanced or metastatic NSCLC with EGFR atypical and EGFR exon 20 insertion mutations. Notably, enrollment allows patients with previously untreated brain metastases (i.e., active, untreated brain metastases). Key objectives of the trial included safety and determination of the recommended Phase 2 dose, along with assessment of antitumor activity based on investigator-assessed objective response rate (ORR), blinded independent central review (BICR)-assessed ORR, CNS-ORR according to modified RECIST 1.1 and/or Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM), as well as DOR and PFS.

As of the September 4, 2026 cutoff date, data are presented for 26 patients who were treated with 80 mg once daily oral enozertinib, including 23 patients with P-loop and alpha C-helix compressing (PACC) mutations and 3 patients with L861Q mutations without a co-occurring PACC mutation. Brain metastases were present in 65% of patients at baseline, which is more than double the rate versus competitor datasets. Notably, 46% of all patients had previously untreated brain metastases.

Safety Analysis

Enozertinib was well tolerated with predominantly Grade 1 or 2 treatment-related adverse events (TRAEs) and no significant off-target toxicities. Most frequent TRAEs included diarrhea, paronychia, and dermatitis acneiform. Six patients (23%) experienced Grade 3 TRAEs, all of which were resolved with dose modifications. There were no Grade 4 or 5 TRAEs and no treatment discontinuations related to TRAEs.

Meaningful Systemic Antitumor Activity

Tumor reductions were observed across all response-evaluable patients¹. Reductions were also observed across a wide range of mutations, including the most prevalent PACC mutations (e.g., G719X, S768I), a broad spectrum of PACC complex mutations, and L861Q mutations. Enozertinib demonstrated meaningful systemic activity, including:

- **84% (21 of 25) confirmed systemic ORR by investigator.**
- **80% (20 of 25) confirmed systemic ORR by BICR.**

Deep EGFR-mutant ctDNA molecular responses were achieved by Cycle 3 Day 1 in all response-evaluable patients across diverse mutations²:

- **100% of patients achieved MR90**, defined as a $\geq 90\%$ EGFR-mutant ctDNA reduction.
- **82% of patients achieved full clearance**, which has been associated with improved long-term survival outcomes in prior Phase 3 NSCLC trials.

Compelling Intracranial Antitumor Activity

Enozertinib continues to demonstrate potential best-in-class intracranial efficacy. Notably, no new CNS lesions were observed in patients with or without baseline CNS metastases.

All response-evaluable patients with measurable CNS disease (90% without prior treatment for their CNS metastases) achieved CNS tumor reductions per investigator-assessment³. Enozertinib demonstrated compelling intracranial activity, including:

- **70% confirmed intracranial ORR by investigator.**

Intracranial efficacy was also evaluated utilizing the more stringent BICR RANO-BM assessment criteria. Based on this assessment, CNS tumor reductions were observed in nearly all response-evaluable patients, including in patients with previously untreated CNS metastases⁴. Enozertinib demonstrated compelling intracranial activity, including:

- **67% (10 of 15) intracranial ORR by BICR RANO-BM.**
- **40% (6 of 15) intracranial complete response rate by BICR RANO-BM**, including in three patients with non-measurable CNS disease.

Promising Early Durability

Median progression-free survival and median duration of response data are immature. The Kaplan-Meier 6-month landmark PFS is 88%. Follow-up is ongoing with the majority of patients continuing on treatment.

Redwood-1 Phase 3 Initiation

Supported by potential best-in-class data presented at ESMO Congress 2026 and based on End-of-Phase 1 interactions with the FDA, ORIC plans to initiate Redwood-1, a global Phase 3 registrational trial in EGFR atypical NSCLC in 1H 2027. This trial plans to enroll approximately 360 patients with PACC and L861X mutations, including those with untreated brain metastases, randomized to receive 80 mg once daily oral enozertinib or physician's choice of osimertinib or afatinib. Dual primary endpoints include ORR by BICR for potential accelerated approval as well as PFS by BICR for full approval. Key secondary endpoints include overall survival and intracranial ORR by BICR RANO-BM.

Poster Details

Enozertinib (ORIC-114), a Brain Penetrant, Highly Selective EGFR Inhibitor, in Treatment-Naive Metastatic NSCLC with EGFR Atypical Mutations

Presentation Number: 2627P

Session Date & Time: Monday, October 26, 2026; 12:00 – 12:45 p.m. CET

Session Title: Metastatic NSCLC

The poster presentation can be found on the ESMO Congress website [here](#), and in the publication section of ORIC's website [here](#).

Conference Call and Webcast Details

The conference call and webcast will take place on Friday, October 23, 2026, at 8:00 a.m. ET. ORIC leadership plans to have Dr. Joshua Sabari, Assistant Professor of Medicine at NYU Grossman School of Medicine, join the call to share his perspective on the enozertinib clinical data and the potential of enozertinib to treat first-line NSCLC patients with EGFR atypical mutations. 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. The live webcast and an 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.

¹ n=25 patients with opportunity for two post-baseline tumor assessments.

² n=22 patients with EGFR mutation in baseline plasma and opportunity for two post-baseline systemic tumor assessments. September 15, 2026 cutoff.

³ n=10 patients with measurable target CNS lesions per investigator assessment.

⁴ n=15 patients with baseline CNS metastases per BICR assessment.

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) rinzimetostat, an allosteric inhibitor of the polycomb repressive complex 2 (PRC2) via the EED subunit, being developed for prostate cancer, and (2) enozertinib, a brain-penetrant inhibitor targeting EGFR atypical and EGFR exon 20 mutations, being developed for NSCLC. 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, the continued clinical development of enozertinib; the potential advantages of enozertinib; statements regarding the potential best-in-class profile of enozertinib; clinical outcomes from studies of enozertinib, which may materially change as patient enrollment continues or more patient data become available; the development plans and timelines for rinzimetostat and enozertinib, including the expected initiation of the Redwood-1 trial; plans underlying ORIC's clinical trials and development; and statements by the company's chief medical officer and chief executive officer. 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 a 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 rinzimetostat, 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 August 3, 2026, 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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