ORIC® Pharmaceuticals Announces Completion of Dose Exploration Portion of ORIC-944 Phase 1b Clinical Trial and Continues to Demonstrate Potential Best-in-Class Efficacy and Safety

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Efficacy data remain consistent with prior disclosure and continue to demonstrate broad and deep PSA responses, with 55% PSA50 response rate and 20% PSA90 response rate

Rapid and deep ctDNA reductions were observed in 76% of patients and ctDNA clearance was observed in 59% of patients, underscoring potential for long-term treatment and survival benefit

PSA responses and ctDNA reductions were observed across all ORIC-944 dose levels and at comparable rates in combination with apalutamide or with darolutamide

Both combination regimens continue to demonstrate a safety and tolerability profile compatible with long-term dosing, with the vast majority of adverse events Grade 1 or 2 and consistent with PRC2 and AR inhibition

SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, Nov. 13, 2025 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, today announced additional efficacy and safety data from the Phase 1b trial of once daily ORIC-944 in combination with androgen receptor (AR) inhibitors in patients with metastatic castration-resistant prostate cancer (mCRPC).

“We continue to be encouraged by ORIC-944 combination data, which further demonstrate its potential as a best-in-class PRC2 inhibitor that may benefit a broad range of patients with prostate cancer,” said Jacob M. Chacko, M.D., president and chief executive officer. “The tolerability and efficacy data to date provide compelling validation for the doses we’ve selected for the dose optimization portion of the Phase 1b trial. We look forward to sharing dose optimization data in 1Q 2026 ahead of initiating our first global Phase 3 registrational trial in mCRPC in the first half of next year.”

ORIC-944 Phase 1b Dose Exploration Data
Patients were previously treated with a median of three prior lines of therapy, including abiraterone acetate, up to one prior line of chemotherapy, and a variety of other approved and investigational treatment regimens. This median does not include background androgen deprivation therapy or first-generation AR inhibitors that the patients may have received. Patients were treated once daily with 400 mg, 600 mg, 800 mg, or 1,200 mg of ORIC-944 in combination with 240 mg of apalutamide once daily or with 600 mg of darolutamide twice daily. PSA data for 20 patients with mCRPC includes 17 patients previously reported in May 2025. Circulating tumor DNA (ctDNA) was assessed for 17 patients with mCRPC who had available ctDNA samples and evidence of ctDNA at baseline prior to study entry. PSA response data and ctDNA data are as of September 22, 2025.

Preliminary antitumor activity analysis
PSA responses and ctDNA reductions were observed across all ORIC-944 dose levels and were also observed at comparable rates in combination with apalutamide or with darolutamide.

PSA activity

- 55% of patients (11/20) achieved a PSA50 response, confirmed in 40% (8/20).
- 20% of patients (4/20) achieved a PSA90 response (all confirmed).

ctDNA activity
ctDNA serves as a useful biomarker to predict the duration of treatment benefit and survival in prostate cancer. Detectable ctDNA at baseline is associated with poor prognosis, and non-detectable ctDNA at baseline or upon treatment is associated with longer progression-free survival and overall survival. In the Phase 1b trial, 88% of patients had detectable ctDNA at baseline (higher than precedent trials with standard of care agents in comparable mCRPC patient populations), and ORIC-944 in combination with apalutamide or with darolutamide demonstrated:

- Rapid and deep ctDNA responses across a breadth of AR mutations and other gene alterations, with 76% of patients (13/17) achieving >50% ctDNA reduction.
- 59% of patients (10/17) achieved ctDNA clearance, which is greater than clearance rates observed in precedent trials with standard of care agents in comparable mCRPC patient populations.

Preliminary safety analysis
ORIC-944 in combination with apalutamide or with darolutamide continues to be well tolerated to date. Both combination regimens demonstrated a safety profile compatible with long-term dosing, with the vast majority of treatment-related adverse events (TRAEs) Grade 1 or 2 in severity and consistent with PRC2 and AR inhibition. As of the September 22, 2025 cutoff date, only one patient experienced a Grade 3 TRAE, and there were no Grade 4 or Grade 5 AEs attributed to ORIC-944, apalutamide or darolutamide.

Next Steps
Based on these efficacy and safety results, ORIC has selected provisional recommended Phase 2 doses (RP2Ds) of ORIC-944 to be tested in

combination with the approved doses of darolutamide and apalutamide in the dose optimization portion of the Phase 1b trial: 400 mg and 600 mg once daily of ORIC-944 in combination with 600 mg twice daily of darolutamide; and 600 mg, 800 mg and 1,200 mg once daily of ORIC-944 in combination with 240 mg once daily of apalutamide. Enrollment in the dose optimization portion of the trial is ongoing, and the company plans to announce preliminary dose optimization data in 1Q 2026. Data from the dose optimization portion of the trial will inform the choice of ORIC-944 dose to advance in combination with apalutamide or with darolutamide in the first global Phase 3 registrational trial in mCRPC, which the company expects to initiate in 1H 2026.

ORIC-944 Phase 1b Trial Design
ORIC-944 is being evaluated in a Phase 1b dose optimization trial in combination with ERLEADA® (apalutamide), Johnson & Johnson's AR inhibitor, and NUBEQA® (darolutamide), Bayer's AR inhibitor, in patients with mCRPC. Patients are eligible if they have received prior treatment with an androgen receptor pathway inhibitor (ARPI) and up to one prior chemotherapy. The primary objective of the trial is to determine the recommended Phase 2 dose (RP2D), and additional objectives include safety, tolerability, pharmacokinetics, and preliminary clinical activity.

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 continued clinical development of ORIC-944; statements regarding the potential best-in-class properties of ORIC-944; clinical outcomes from combination studies with ORIC-944, which may materially change as patient enrollment continues or more patient data become available; the development plans and timelines for ORIC-944 and ORIC's other product candidates; the potential advantages of ORIC-944 and ORIC's other product candidates and programs; plans underlying ORIC's clinical trials and development; next steps and anticipated program milestones, including timing of program and data updates and the initiation of the first ORIC-944 Phase 3 registrational trial in mCRPC; and statements by the company's 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 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 ORIC-944, 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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