ORIC® Pharmaceuticals Announces Potentially Best-In-Class Preliminary Efficacy and Safety Data from Ongoing Phase 1b Trial of ORIC-944 in Combination with AR Inhibitors for the Treatment of Patients with mCRPC

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Broad and deep PSA responses achieved, with 59% PSA50 response rate (confirmed rate of 47%, and one additional response pending confirmation) and 24% PSA90 response rate (all confirmed) in patients with mCRPC

PSA responses were observed across all ORIC-944 dose levels and at comparable rates in combination with apalutamide and with darolutamide; majority of patients are still ongoing with multiple patients approaching one year or more

Both combination regimens demonstrated a safety profile compatible with long term dosing, with the vast majority of adverse events Grade 1 or 2

Announced concurrent $125 million financing, which extends cash runway into 2H 2027 and through anticipated primary endpoint readout from first Phase 3 trial

SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, May 28, 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 potentially best-in-class preliminary efficacy and safety data from the ongoing Phase 1b trial of once daily ORIC-944 in combination with androgen receptor (AR) inhibitors in patients with metastatic castration-resistant prostate cancer (mCRPC).

"These ORIC-944 combination data demonstrate substantial clinical activity with both AR inhibitors, apalutamide and darolutamide, through early measures of efficacy (PSA50 and PSA90 response rates) and a safety profile consisting almost entirely of mild to moderate GI related adverse events, making it highly suitable for potential long term dosing," said Pratik S. Multani, M.D., chief medical officer.

"The data generated to date continue to demonstrate the potential of ORIC-944 to be 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 efficacy and safety data presented today compare favorably to other PRC2 inhibitor data presented earlier this year. We look forward to subsequent updates from the dose exploration and dose optimization portion of the Phase 1b trial over the next three quarters as we move towards initiating our first global registrational trial in 1H 2026."

ORIC-944 Phase 1b Trial Design

ORIC-944 is being evaluated in a Phase 1b dose exploration 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 objectives of the trial are to determine the recommended Phase 2 dose (RP2D), and additional objectives include safety, tolerability, pharmacokinetics, and preliminary clinical activity.

ORIC-944 Phase 1b Dose Exploration Data

Data include 17 patients with mCRPC previously treated with a median of three lines of prior therapy, including abiraterone, up to one prior line of chemotherapy, and a variety of other approved and investigational treatment regimens. This median does not include androgen deprivation therapy or first-generation androgen receptor deprivation therapy. Patients were treated once daily with 400 mg, 600 mg, or 800 mg of ORIC-944 in combination with 240 mg of apalutamide once daily or with 600 mg of darolutamide twice daily. PSA response data are as of May 9, 2025.

Preliminary activity analysis

59% of patients (10/17) achieved a PSA50 response and nearly all patients with a PSA50 response were confirmed one month later, for a confirmed PSA50 response rate of 47% (8/17), which does not include one additional PSA response pending confirmation. 24% of patients (4/17) achieved a PSA90 response, all of which were subsequently confirmed.

PSA responses were observed across all ORIC-944 dose levels and were also observed at comparable rates in combination with apalutamide or with darolutamide. The majority of patients are still ongoing with multiple patients approaching one year or more on therapy. Further dose exploration is ongoing.

Preliminary safety analysis

ORIC-944 in combination with apalutamide or with darolutamide has been generally well tolerated to date, with a vast majority of adverse events (AEs) Grade 1 or 2 in severity and consistent with PRC2 and AR inhibition. As of April 22, 2025, diarrhea was the most common treatment-related AE, occurring in 53% of patients (9/17) across all dose levels with only one patient experiencing a Grade 3 event. There were no Grade 4 or Grade 5 treatment-related AEs attributed to ORIC-944 with apalutamide or with darolutamide.

Next Steps

Following completion of the Phase 1b dose exploration portion of the trial expected in mid-2025, the company plans to evaluate two candidate RP2Ds for each combination in the dose optimization portion of the trial in 2H 2025. 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 that the company expects to initiate in 1H 2026.

Corporate Update

The company announced a concurrent $125 million private placement financing that it expects will extend cash runway into the second half of 2027 and through the anticipated primary endpoint readout from the first ORIC-944 Phase 3 registrational trial in mCRPC. The financing is expected to close

on May 29, 2025, subject to customary closing conditions.

Conference Call and Webcast Details
ORIC will host a conference call and webcast today at 4:30 p.m. 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 the company's website at www.oricpharma.com. The webcast will be available for replay for 90 days following the presentation.

About ORIC-944
ORIC-944 is a potent and selective allosteric inhibitor of the polycomb repressive complex 2 (PRC2) via the embryonic ectoderm development (EED) subunit that demonstrates best-in-class drug properties in preclinical studies, including potency, solubility, and pharmacokinetics, with half-life supporting once daily dosing. ORIC-944 was initially evaluated as a single agent in a Phase 1b trial in patients with advanced prostate cancer and demonstrated potential best-in-class drug properties, including clinical half-life of approximately 20 hours, robust target engagement and a favorable safety profile. ORIC-944 continues to further demonstrate a potential best-in-class profile with positive interim PSA response data generated in an ongoing Phase 1b trial in combination with ERLEADA® (apalutamide) and in combination with NUBEQA® (darolutamide) for prostate cancer (NCT05413421).

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) ORIC-114, a brain penetrant inhibitor that selectively targets EGFR exon 20, HER2 exon 20 and EGFR atypical mutations, being developed across multiple genetically defined cancers. Beyond these two product candidates, ORIC® is also developing multiple precision medicines targeting other hallmark cancer resistance mechanisms. 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; the anticipated timing of the primary endpoint readout from the first ORIC-944 Phase 3 registrational trial in mCRPC; the timing and expectation of the closing of the private placement financing; the satisfaction of customary closing conditions related to the private placement financing; the period over which ORIC estimates the proceeds from the private placement, combined with its existing cash, cash equivalents and marketable securities, will be sufficient to fund its current operating plan; 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 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's 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 titled "Risk Factors" in ORIC's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on May 5, 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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