ORIC® Pharmaceuticals Presented Preclinical Data at the EORTC-NCI-AACR International Conference on Molecular Targets and Cancer Therapeutics Supporting Best-in-Class Potential of ORIC-944 to Treat Patients With Prostate Cancer and Other Solid Tumors

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SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, Oct. 27, 2025 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, presented posters at the 2025 EORTC-NCI-AACR International Conference on Molecular Targets and Cancer Therapeutics highlighting preclinical data that further illustrate the potential for ORIC-944, a potent and selective allosteric inhibitor of the polycomb repressive complex 2 (PRC2) via the embryonic ectoderm development (EED) subunit, to treat prostate cancer and various other solid tumors.

“These preclinical data underscore the potential of ORIC-944 to overcome resistance not only in prostate cancer but in other solid tumors and highlight that the therapeutic potential of PRC2 inhibition may be maximized in combination with inhibitors of key tumor drivers, including AR inhibitors and KRAS inhibitors,” said Lori Friedman, PhD, chief scientific officer. “Based on these data and clinical findings to date, we continue to believe ORIC-944 is a potential best-in-class PRC2 inhibitor with potential in both castration-resistant and castration-sensitive prostate cancer, as well as multiple other tumor types.”

Key findings of posters presented at the 2025 EORTC-NCI-AACR International Conference on Molecular Targets and Cancer Therapeutics:

PRC2 inhibition enhances AR inhibitor response to delay treatment relapse in castration-sensitive prostate cancer by restricting adaptation of tumor cells in preclinical studies

- ORIC-944 is a potential best-in-class PRC2 inhibitor that, when combined with androgen receptor (AR) inhibition, synergistically impaired tumor growth, significantly improved survival and extended the duration of response to AR inhibitors in vivo by restricting cellular plasticity and delaying prostate tumor adaptation in castration-sensitive prostate cancer (CSPC).
- Transcriptional effects induced by combining ORIC-944 and AR inhibitors were comparable across all AR inhibitors tested (i.e., darolutamide, apalutamide or enzalutamide), and consistent with transcriptional effects of mevrometostat and AR inhibitor combination.
- Mechanistically, ORIC-944 in combination with AR inhibition in CSPC was linked to increased luminal cell state, and the restriction of lineage adaptation through reduced chromatin accessibility at binding sites of transcription factors associated with lineage diversification and cell plasticity such as FOXA, HNF1A and ONECUT2. These results were reproduced with mevrometostat and AR inhibitor combination and are consistent with what was previously reported in preclinical studies of CRPC.

PRC2 inhibition enhances KRAS inhibitor response to delay treatment relapse in KRAS-mutant preclinical lung and colorectal cancer models

- ORIC-944 is a potential best-in-class PRC2 inhibitor that, when combined with KRAS inhibition, significantly improved efficacy and progression-free survival in KRAS G12C mutant non-small cell lung cancer (NSCLC) and colorectal cancer (CRC) models, demonstrating that PRC2 inhibition can deepen and extend responses by preventing or delaying resistance to KRAS inhibition.
- PRC2 activity is increased in tumors from KRAS-mutant NSCLC and CRC patients, and transcriptional analysis from in vivo studies of CRC demonstrated that PRC2 inhibition drives tumor cell differentiation.
- ORIC-944 combined with the KRAS inhibitor adagrasib, regressed 100% of tumors in KRAS-mutant adenocarcinoma and squamous NSCLC xenograft models in vivo. The combination also prevented adagrasib tumor relapse and extended progression-free survival in a KRAS G12C adenocarcinoma NSCLC xenograft model.

About ORIC-944
ORIC-944 is a potent and selective allosteric PRC2 inhibitor via 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 embryonic ectoderm development (EED) subunit, being developed for prostate cancer, and (2) enozertinib (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. 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 ORIC-944 and its best-in-class potential; the potential advantages of ORIC-944, including in combination with KRAS inhibitors in lung and colorectal cancers; the development plans and timelines for ORIC-944; plans underlying ORIC's clinical trials and development; and statements by the company's chief scientific 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; the potential market for our 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 12, 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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