ORIC® Pharmaceuticals Presents Data Further Supporting Potential Best-In-Class Profile of ORIC-114 to Treat EGFR Exon 20 Insertions and Other Atypical Mutations at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics

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SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, Oct. 23, 2024 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, today announced the company presented a poster highlighting certain best-in-class properties of ORIC-114, a brain penetrant, orally bioavailable, irreversible EGFR/HER2 inhibitor, to treat EGFR exon 20 insertions and other atypical mutations at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics.

“Preclinical data presented today underscore ORIC-114’s superior potency and selectively across EGFR mutational classes compared to other EGFR inhibitors,” said Lori Friedman, PhD, chief scientific officer. “These results build on clinical findings that highlight ORIC-114’s potential best-in-class profile, showing notable systemic and CNS responses, along with a favorable safety profile, even in heavily pre-treated NSCLC patients. We are continuing to evaluate ORIC-114 in multiple Phase 1b expansion cohorts for NSCLC patients with EGFR exon 20, HER2 exon 20, and atypical EGFR mutations, with updated data expected in the first half of 2025.”

Poster presentation details:

ORIC-114, a highly selective, brain penetrant EGFR and HER2 inhibitor, demonstrates best-in-class properties against exon 20 insertions and other atypical EGFR mutations

ORIC-114 previously demonstrated systemic and intracranial clinical responses in heavily pre-treated patients with EGFR and HER2 exon 20 insertion mutations. Key findings of this poster presentation:

- Demonstrates regressions in all EGFR mutant in vivo models tested, including cell-derived xenografts, patient-derived xenografts and intracranial models that encompass exon 20 insertion and atypical mutant models. An in vivo model with complex atypical mutant EGFR dosed with ORIC-114 notably shows 100% tumor regressions and all tumors experienced a complete response.
- In an expanded preclinical comparative analysis of exon 20 insertion, atypical PACC and other mutations, overall ORIC-114 is the most potent across EGFR mutational classes whilst displaying comparative wild-type selectivity in cell-based assays, relative to firmonertinib, zipalertinib, lazertinib and BDTX-1535.
- In head-to-head comparisons with firmonertinib, zipalertinib, lazertinib and BDTX-1535, ORIC-114 has superior kinome selectivity with no off-target kinase liabilities identified.
- Shows complete molecular responses in ctDNA from patients with EGFR exon 20 insertion and PACC mutations from Phase 1 dose escalation study. Evidence of molecular responses observed across dose escalation cohorts supports broad therapeutic window for ORIC-114.
- ORIC-114 is a promising therapeutic candidate with best-in-class potential for patients with non-small cell lung cancer harboring exon 20 insertions and atypical mutations in EGFR, including those presenting with active CNS metastases, and is being evaluated in a global clinical trial (NCT05315700).

About ORIC-114
ORIC-114 is a highly selective, brain penetrant, orally bioavailable, irreversible inhibitor that selectively targets EGFR exon 20, HER2 exon 20 and EGFR atypical mutations, making it a promising therapeutic candidate to address the unmet medical need of having both meaningful systemic as well as CNS antitumor 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-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, (2) ORIC-944, an allosteric inhibitor of the polycomb repressive complex 2 (PRC2) via the EED subunit, being developed for prostate cancer, and (3) ORIC-533, an orally bioavailable small molecule inhibitor of CD73, a key node in the adenosine pathway believed to play a central role in resistance to chemotherapy- and immunotherapy-based treatment regimens, being developed for multiple myeloma. Beyond these three 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 best-in-class properties of ORIC-114; the continued clinical development of ORIC-114; the potential advantages of ORIC-114 and ORIC’s other product candidates and programs; timing of updated data from the clinical trial of ORIC-114; development plans for ORIC’s product candidates and programs; 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 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 August 12, 2024, 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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