ORIC Pharmaceuticals Presents Promising Preclinical Data on Three Programs at the 2022 American Association for Cancer Research (AACR) Annual Meeting

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SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, April 12, 2022 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, presented three preclinical poster presentations and one preclinical oral presentation at the 2022 American Cancer Research Association (AACR) Annual Meeting.

“Our four presentations at AACR reflect the broad and diverse pipeline of differentiated programs at ORIC,” said Jacob M. Chacko, MD, chief executive officer. “Preclinical data further demonstrate the potential of CD73 inhibitor ORIC-533 as a treatment for multiple myeloma, as well as the compelling brain penetrant properties of ORIC-114 with its high potency against exon 20 insertion mutations. We also introduced our highly selective inhibitors of PLK4 as a potential treatment for breast cancer by leveraging a synthetic lethal liability. We look forward to the continued advancement of these programs as well as ORIC-944, with initial data for our three clinical programs expected in the first half of 2023.”

Presentation details:

ORIC-533: CD73 Inhibitor
ORIC-533 is a highly potent, orally bioavailable small molecule inhibitor of CD73 that has demonstrated more potent adenosine inhibition in preclinical studies compared to an antibody approach and other small molecule inhibitors of the adenosine pathway and is currently being studied in a Phase1b trial in multiple myeloma.

Poster Presentation:
ORIC-533, a small molecule CD73 inhibitor with best-in-class properties, reverses immunosuppression and has potential as an immunomodulatory therapy in patients with multiple

Oral Presentation:
Optimizations leading to ORIC-533: A potent orally bioavailable CD73 inhibitor that restores anti-tumor immunity in high AMP environments

Key findings of the presentations:

- Target candidate profile for best-in-class CD73 inhibitor was met by ORIC-533 in preclinical analyses.
- In an autologous ex vivo assay using bone marrow aspirates from patients with relapsed or refractory multiple myeloma, CD73 inhibition stimulated plasmacytoid dendritic cells and activated T cells.
- ORIC-533, across multiple dose levels, overcame immune suppression and triggered significant lysis and cell death of multiple myeloma cells in an assay comprised of autologous bone marrow microenvironment.
- These results demonstrate that single agent ORIC-533 potently inhibits the adenosine pathway, which restores anti-tumor immunity and therefore holds potential as a treatment for patients with multiple myeloma.

ORIC-114: EGFR/HER2 Inhibitor
ORIC-114 is a brain penetrant, orally bioavailable, irreversible inhibitor designed to selectively target EGFR and HER2 with high potency against exon 20 insertion mutations, and is currently being studied in a Phase 1b trial in patients with advanced solid tumors with EGFR or HER2 exon 20 alterations or HER2 amplifications.

Poster Presentation:
ORIC-114, an orally bioavailable, irreversible kinase inhibitor, has superior brain penetration and antitumor activity in subcutaneous and intracranial NSCLC models

Key findings of the presentation:

- Oral administration of ORIC-114 resulted in tumor regressions in an EGFR exon 20 NSCLC model, with superior efficacy relative to CLN-081 and BDTX-189.
- Additional preclinical studies confirmed the brain-penetrance and free unbound exposure in the CNS, which translated to greater anti-tumor activity compared to mobocertinib (TAK-788) in an intracranial NSCLC model.
- These data confirm ORIC-114 as a potent, selective, irreversible, brain penetrant EGFR exon 20 inhibitor, and a promising therapeutic candidate, including for patients with CNS metastases.

PLK4 Inhibitor Program:
The PLK4 Inhibitor program is a small molecule therapeutic program intended to address a mechanism of innate resistance found in a subset of breast cancers, specifically a synthetic lethal interaction of polo-like kinase 4 (PLK4) inhibition in tumors bearing a TRIM37 DNA amplification.

Poster Presentation:
Discovery of novel, highly selective inhibitors of PLK4 that demonstrate in vivo regressions in TRIM37 high xenografts

Key findings of the presentation:

- ORIC discovered novel, potent, orally bioavailable small molecule inhibitors of PLK4 that are highly selective, including against the closely related aurora kinases and PLK1-3.
- Cell viability assessment across a cancer cell line panel revealed that the highly selective ORIC PLK4 inhibitors showed greater potency in TRIM37 high cancer cell lines as compared to TRIM37 low cell lines.
- Importantly, cell potency in TRIM37 high cancer cells was rescued with knockdown of TRIM37, illustrating that selective PLK4 inhibitors exhibit synthetic lethality with TRIM37 amplification.
- Oral administration of ORIC PLK4 inhibitors resulted in strong anti-tumor activity of TRIM37 high xenograft tumors, with corresponding pharmacodynamic effects and no body weight loss.

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-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, (2) ORIC-114, a brain penetrant inhibitor designed to selectively target EGFR and HER2 with high potency against exon 20 insertion mutations, being developed across multiple genetically defined cancers, and (3) ORIC-944, an allosteric inhibitor of the polycomb repressive complex 2 (PRC2) via the EED subunit, being developed for prostate cancer. Beyond these four 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 Twitter 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 ORIC's development plans; the potential advantages of ORIC's product candidates and programs; the expected timing of reporting initial data from the ORIC-533, ORIC-114 and ORIC-944 clinical trials; plans underlying any of ORIC's other programs; 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-533, ORIC-114, ORIC-944 or any other product candidates to differ from preclinical, interim, preliminary or expected results; negative impacts of the COVID-19 pandemic 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 agreements; 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC") on March 21, 2022, 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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