ORIC Pharmaceuticals Announces Multiple Presentations at the 2022 American Association for Cancer Research (AACR) Annual Meeting

March 8, 2022

ORIC-533 oral presentation and poster presentation to highlight potential of small molecule inhibitor of CD73 as a treatment for multiple myeloma

ORIC-114 poster presentation to highlight compelling brain penetrant properties of an irreversible inhibitor designed to selectively target EGFR and HER2 with high potency against exon 20 insertion mutations

PLK4 program poster presentation to introduce novel, highly selective inhibitors targeting a synthetic lethality approach as a potential treatment for breast cancer

SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, March 08, 2022 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, today announced three poster presentations and one oral presentation at the 2022 American Association for Cancer Research (AACR) Annual Meeting taking place April 8-13, 2022, in New Orleans, LA. The presentations will highlight preclinical data regarding two Phase 1 programs, including ORIC-533, a highly potent, orally bioavailable CD73 inhibitor, and ORIC-114, a brain penetrant, orally bioavailable, irreversible inhibitor designed to selectively target EGFR and HER2 with high potency against exon 20 insertion mutations. The presentations will also introduce a new program targeting a synthetic lethality pathway in breast cancer.

Details of the presentations are as follows:

Title: 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 myeloma
Session Title: Immunomodulatory Agents and Interventions 1
Date and Time: April 11, 2022, 1:30 p.m. - 5:00 p.m.
Abstract Number: 2074

Abstract Highlights
Using an autologous ex vivo assay, bone marrow aspirates from patients with multiple myeloma were evaluated to assess the impact of CD73 inhibition. The results showed that CD73 inhibition stimulated the activation of plasmacytoid dendritic cells and T cell activation. Moreover, the ORIC CD73 inhibitor as a single agent overcame immune suppression and triggered significant lysis and cell death of multiple myeloma cells by autologous T-cells in the bone marrow microenvironment. Taken together, these results demonstrate that the ORIC small molecule CD73 inhibitor potently inhibits the adenosine pathway, which restores anti-tumor immunity and therefore holds potential for patients with multiple myeloma.

Oral Presentation Title: Optimizations leading to ORIC-533: A potent orally bioavailable CD73 inhibitor that restores anti-tumor immunity in high AMP environments
Session Title: Chemistry to the Clinic, Part 2 of 3: Progress in Small Molecule Cancer Immunology Therapy
Date and Time: April 9, 2022, 11:00 a.m. - 11:30 a.m.

Title: ORIC-114, an orally bioavailable, irreversible kinase inhibitor, has superior brain penetration and antitumor activity in subcutaneous and intracranial NSCLC models
Session Title: Tyrosine Kinase and Phosphatase Inhibitors
Date and Time: April 12, 2022, 1:30 p.m. - 5:00 p.m.
Abstract Number: 3335

Abstract Highlights
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 studies confirmed the brain-penetrance and free unbound exposure in the CNS, which translated to greater anti-tumor activity compared to TAK-788 in an intracranial NSCLC model. Taken together, 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.

Title: Discovery of novel, highly selective inhibitors of PLK4 that demonstrate in vivo regressions in TRIM37 high xenografts
Session Title: Novel Targets and Pathways
Date and Time: April 12, 2022, 9:00 a.m. - 12:30 p.m.
Abstract Number: 2633

Abstract Highlights
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. In contrast, less selective compounds, including from the clinical literature, did not display differential potency in TRIM37 high versus low cancer cell lines. Importantly, cell potency in TRIM37 high cancer cells was rescued with knockdown of TRIM37, illustrating that selective PLK4 inhibitors are synthetic lethal 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.

Abstracts are available for viewing in the AACR Online Itinerary Planner located here, https://www.abstractsonline.com/pp8/#!/10517.

About ORIC Pharmaceuticals, Inc.

ORIC Pharmaceuticals is a clinical stage biopharmaceutical company dedicated to improving patients' lives by *Overcoming Resistance In Cancer.* ORIC's lead product candidate, ORIC-101, is a potent and selective small molecule antagonist of the glucocorticoid receptor, which has been linked to resistance to multiple classes of cancer therapeutics across a variety of solid tumors. ORIC-101 is currently in two separate Phase 1b trials of ORIC-101 in combination with (1) Xtandi (enzalutamide) in metastatic prostate cancer and (2) Abraxane (nab-paclitaxel) in advanced or metastatic solid tumors. ORIC's other 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 the potential advantages ORIC-114 and ORIC-533 may have over other approaches and therapies; and the potential benefits of ORIC-114, ORIC-533 or the company's other product candidates. 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-101, ORIC-533, ORIC-114, ORIC-944 or any other product candidates to differ from preclinical, initial, 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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on November 8, 2021, 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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