ORIC Pharmaceuticals Announces Multiple Presentations at the 2023 American Association for Cancer Research (AACR) Annual Meeting

March 14, 2023 at 4:30 PM EDT

ORIC-944 preclinical poster presentation to highlight comprehensive biomarker strategy for ongoing Phase 1 trial in metastatic prostate cancer

PLK4 poster presentation to spotlight the high selectivity required for synthetic lethality in breast cancer models

SOUTH SAN FRANCISCO and SAN DIEGO, March 14, 2023 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, today announced that two abstracts have been accepted for poster presentations at the 2023 American Association for Cancer Research (AACR) Annual Meeting taking place April 14-19, 2023, in Orlando, FL. The presentations will highlight:

- preclinical biomarker results for ORIC-944, a potent and selective allosteric inhibitor of PRC2 currently in Phase 1 for patients with metastatic prostate cancer; and
- preclinical data from ORIC's selective PLK4 inhibitor discovery program

Details of the presentations are as follows:

Title:	Biomarker strategy for a phase 1 study of ORIC-944, a potent and selective allosteric PRC2 inhibitor, in patients with metastatic
Session Category:	Experimental and Molecular Therapeutics
Session Title:	Pharmacokinetics, Pharmacodynamics, and Molecular Pharmacology
Session Date & Time:	Monday, April 17, 2023, 1:30 p.m. - 5:00 p.m. ET
Location:	Poster Section 18
Abstract Number:	2791

Abstract Highlights
ORIC-944 is a potent, highly selective allosteric small molecule inhibitor of PRC2, the complex which tri-methylates histone H3 and lysine 27 (H3K27me3) leading to transcriptionally silenced genes. Preclinical pharmacology studies in mice showed that H3K27me3 levels significantly decreased in response to ORIC-944 in a dose- and time-dependent manner, in epidermis, monocytes, and plasma. Assays included immunohistochemistry, alphaLISA, and cell-free nucleosomal bead-based sandwich immunoassay. Additionally, putative PRC2 target genes were identified in xenograft tumors profiled by RNA-sequencing and H3K27me3 chromatin immunoprecipitation sequencing. The establishment of these assays represent a comprehensive biomarker strategy of target engagement and pharmacodynamic biomarkers for use in the ongoing Phase 1 trial of ORIC-944 in patients with metastatic prostate cancer.

Title:	Selective PLK4 inhibition demonstrates synthetic lethality in TRIM37 amplified neuroblastoma and breast cancer models while less selective inhibitors do not
Session Category:	Experimental and Molecular Therapeutics
Session Title:	Targeting Protein Kinases and Phosphatases for Therapy 1
Session Date & Time:	Tuesday, April 18, 2023, 1:30 p.m. - 5:00 p.m. ET
Location:	Poster Section 17
Abstract Number:	4998

Abstract Highlights
The synthetic lethal interaction of PLK4 with 17q23 amplicon-driven overexpression of TRIM37 (Metinger et al. 2020, Yeow et al. 2020) is only observed with highly selectivity inhibitors of PLK4 in preclinical studies. Cell viability assessment in cancer cell lines revealed that highly selective PLK4 inhibitors showed differential potency in TRIM37 high cancer cell lines, while less selective compounds, including clinical compounds, did not. Additionally, selective PLK4 inhibition induced significantly greater apoptosis in a caspase 3/7 assay in TRIM37 high cancer cells vs other cells. In a PLK4 stabilization assay, a measure of target engagement, selective PLK4 inhibitors showed strong correlation between cell viability and target engagement, while non-selective inhibitors did not. Importantly using a genetically engineered PLK4 cell line variant (PLK4 G95L) that prevents compound-mediated inhibition of PLK4, it was confirmed that only highly selective PLK4-targeting compounds require PLK4 inhibition for activity, while the cell potency of less selective inhibitors did not require PLK4 inhibition. Together these mechanistic data confirm the potential of selective PLK4 inhibition as a synthetic lethal therapy for TRIM37 high cancers.

Abstracts are available for viewing via the AACR Online Itinerary Planner located here, https://www.abstractsonline.com/pp8/#!/10828.

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 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 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 benefits of a comprehensive biomarker strategy for clinical trials of ORIC-944; the potential advantages selective inhibitors of PLK4 may have over less selective inhibitors; target indications for ORIC's product candidates; the potential advantages or benefits of ORIC's product candidates; and plans underlying ORIC's clinical trials and development. 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, 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 and collaboration 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 7, 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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