



ORIC Pharmaceuticals to Present Posters on Four Programs at the 2021 American Association for Cancer Research (AACR) Annual Meeting

March 10, 2021

SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, March 10, 2021 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of resistance in cancer, today announced four preclinical poster presentations at the 2021 American Association for Cancer Research (AACR) virtual annual meeting on April 10-15, 2021.

"We are pleased to present these compelling preclinical data on our four product candidates, which continue to validate our scientific platform focused on overcoming resistance in cancer," said Lori Friedman, chief scientific officer. "In particular, we are encouraged to see our lead program ORIC-101 reversing GR-mediated resistance in a variety of tumor models and contexts. Furthermore, ORIC-533, ORIC-944 and ORIC-114 each continue to show mounting evidence of potential best-in-class differentiation. We look forward to the continued advancements of these programs and our discovery research pipeline as we work to improve the lives of patients with cancer."

ORIC-101: Glucocorticoid Receptor (GR) Antagonist

Title: GR antagonist ORIC-101 overcomes GR-mediated resistance to the combination of AR and AKT inhibition in preclinical prostate cancer cell lines

Date: Poster release on April 10, 2021

Session: Reversal of Drug Resistance

Abstract: 1420

ORIC-101 is a potent and selective GR antagonist, with two distinct mechanisms of action being evaluated in two Phase 1b trials in combination with: (1) Abraxane (nab-paclitaxel) in advanced or metastatic solid tumors and (2) Xtandi (enzalutamide) in metastatic prostate cancer. It has previously been demonstrated that ORIC-101 reverses GR-mediated resistance to enzalutamide and to AR degraders in preclinical prostate cancer cell lines. This preclinical study evaluated whether activated GR confers resistance to the combination of AKT inhibitors with enzalutamide and whether co-treatment with ORIC-101 reverses GR-mediated resistance to the combination. It was observed that GR upregulation and activation, an established resistance mechanism for antiandrogens, may drive resistance when antiandrogens are combined with AKT inhibitors, and our data demonstrated that ORIC-101 was able to overcome this resistance and restore antitumor activity.

ORIC-533: CD73 Inhibitor

Title: Blocking adenosine production with ORIC-533, a CD73 inhibitor with best-in-class properties, reverses immunosuppression in high-AMP environments

Date: Poster release on April 10, 2021

Session: Modifiers of the Tumor Microenvironment

Abstract: LB-163

ORIC-533 is a highly potent, orally bioavailable CD73 inhibitor and has demonstrated greater potency in preclinical studies compared to an antibody approach and other small molecule CD73 inhibitors. In these studies, nanomolar concentrations of ORIC-533 efficiently rescued cytotoxic T-cell function in the presence of high AMP concentrations, reflective of levels observed in tumors. Additionally, inhibitors of adenosine receptors A_{2A} or A_{2A/B} were only able to rescue CD8⁺ T-cell function in the context of low micromolar AMP, thus may be ineffective in tumors with moderate or high AMP and adenosine levels. These preclinical results indicate that ORIC-533 has potential best-in-class properties in reversing immunosuppression in tumors.

ORIC-944: PRC2 Inhibitor

Title: ORIC-944, a potent and selective allosteric PRC2 inhibitor, demonstrates robust in vivo activity in prostate cancer models

Date: Poster release on April 10, 2021

Session: Epigenetic Targets

Abstract: 1131

ORIC-944 is a potent and selective allosteric inhibitor of polycomb repressive complex 2 (PRC2) and targets its regulatory embryonic ectoderm development (EED) subunit. The unique EED targeting strategy may more completely inhibit PRC2, and may address certain resistance mutations in EZH2 and the possible compensatory escape mechanism of EZH1. ORIC-944 has potential best-in-class drug properties compared to first generation PRC2 inhibitors, and superior in vivo efficacy was observed when compared to tazemetostat in a DLBCL model. In prostate cancer, ORIC-944 demonstrated strong tumor growth inhibition as a single agent with once daily dosing in both enzalutamide-responsive and enzalutamide-resistant models.

ORIC-114: EGFR/HER2 Inhibitor

Title: ORIC-114, a brain penetrant, orally bioavailable, irreversible inhibitor selectively targets EGFR and HER2 exon20 insertion mutants and regresses intracranial NSCLC xenograft tumors

Date: Poster release on April 10, 2021

Session: Tyrosine Kinase and Phosphatase Inhibitors

Abstract: 1466

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. Assessment of kinase panels showed ORIC-114 is highly selective to the EGFR family of receptors, with superior kinase selectivity compared to other exon 20 inhibitors. ORIC-114 also demonstrated low nanomolar potency across exon 20 insertion variants in biochemical and cell-based assays. Regressions were observed in multiple EGFR exon 20 patient-derived xenograft models using once daily oral administration. Importantly, ORIC-114 displayed superior brain exposure relative to other compounds targeting exon 20 and significantly regressed established EGFR-driven intracranial NSCLC tumors, commensurate with the superior brain exposure of ORIC-114.

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 in combination with (1) Abraxane (nab-paclitaxel) in advanced or metastatic solid tumors and (2) Xtandi (enzalutamide) in metastatic prostate cancer. 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, (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-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. 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.

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 of ORIC's product candidates and programs, including potential best-in-class differentiation; plans underlying ORIC-101, ORIC-533, ORIC-944, ORIC-114 or any other 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-101 or any other product candidates to differ from preclinical, 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 5, 2020, 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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