



ORIC Pharmaceuticals Announces Update on ORIC-533, a Highly Potent, Orally Bioavailable Small Molecule CD73 Inhibitor

September 21, 2021

SOUTH SAN FRANCISCO and SAN DIEGO, Sept. 21, 2021 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, today announced an update on its CD73 inhibitor program. ORIC recently announced the U.S. Food and Drug Administration (FDA) has cleared the company's Investigational New Drug Application (IND) for ORIC-533 to proceed into a first-in-human clinical trial in which ORIC-533 will be tested as a single agent in an undisclosed tumor type not currently known to be under clinical evaluation with any other CD73 inhibitor. ORIC-533 was discovered internally at ORIC, is wholly owned, and is a highly potent, 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.

In preclinical studies, ORIC-533 has demonstrated higher potency in a high AMP environment compared to all CD73 and adenosine receptor inhibitors against which it was compared, including both small molecules and antibodies, such as oleclumab. Preclinical data suggest ORIC-533 binds CD73 with high affinity and effectively blocks adenosine-driven immunosuppression. In preclinical studies, nanomolar concentrations of ORIC-533 efficiently rescued cytotoxic T-cell function in the presence of high AMP concentrations, reflective of AMP levels observed in tumors.

Based on a preclinical collaboration with an academic key opinion leader that generated compelling single agent activity in patient derived model systems in an undisclosed tumor type, the company plans to pursue a single agent clinical development plan in this indication. ORIC expects to enroll its first patient in this trial during the fourth quarter of 2021. Also during the fourth quarter of 2021, ORIC plans to host an R&D event during which it will disclose the tumor indication along with the supporting preclinical rationale and data.

The second quarter ORIC-533 IND filing was the first of three planned IND/CTA filings by ORIC in 2021, with the IND filing for ORIC-944 (allosteric inhibitor of PRC2) and CTA filing for ORIC-114 (brain penetrant inhibitor of EGFR and HER2, including exon 20 insertion mutations) expected in the fourth quarter of 2021.

About ORIC-533

ORIC-533 is a highly potent, 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. ORIC-533 has demonstrated greater potency in preclinical studies compared to an antibody approach, other small molecule CD73 inhibitors and inhibitors of adenosine receptors. Preclinical data suggest ORIC-533 binds CD73 with high affinity and effectively blocks adenosine-driven immunosuppression in a high AMP environment. In preclinical studies, nanomolar concentrations of ORIC-533 efficiently rescued cytotoxic T-cell function in the presence of high AMP concentrations, reflective of AMP levels observed in tumors.

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, 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 clinical development of ORIC-533 in an undisclosed tumor type; potential advantages ORIC-533 may have over other CD73 and adenosine receptor inhibitors in development; the expected timing of initiation of the Phase 1 clinical trial of ORIC-533; the expected timing of an IND filing for ORIC-944 and a CTA filing for ORIC-114; and the potential benefits of 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-944, ORIC-114 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 August 10, 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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