ORIC Pharmaceuticals Presents Data Supporting the Therapeutic Potential of ORIC-533 in Multiple Myeloma at the American Society of Hematology (ASH) Annual Meeting

December 13, 2021

CD73 inhibition overcomes immunosuppression and demonstrates activity in assays derived from relapsed or refractory multiple myeloma patients, offering the potential for single agent activity in the clinic

Phase 1 trial of single agent ORIC-533, a highly potent, orally bioavailable small molecule inhibitor of CD73, expected to initiate in 4Q 2021 in patients with multiple myeloma

Conference call and webcast today at 5:30 p.m. ET

SOUTH SAN FRANCISCO and SAN DIEGO, Calif., Dec. 13, 2021 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance presented preclinical data with ORIC's small molecule inhibitor of CD73 in multiple myeloma at the American Society of Hematology (ASH), in collaboration with Dr. Kenneth Anderson's research laboratory at Dana-Farber Cancer Institute. The abstract and presentation are available for online viewing via the ASH Annual Meeting website.

"ORIC-533 has a differentiated profile, demonstrating stronger potency in a high AMP environment compared to benchmark CD73 inhibitors and adenosine receptor antagonists in preclinical studies," said Lori Friedman, chief scientific officer. "Based on a strong mechanistic rationale and compelling single agent activity in patient-derived autologous ex vivo assays, we are excited to pursue clinical development in multiple myeloma."

Multiple myeloma patient samples have demonstrated that the tumor environment is adenosine rich, and studies have shown that high CD73 and adenosine levels are associated with poor prognosis and therapeutic resistance.

The ASH presentation focused on the role of adenosine signaling in immunosuppression in patients with relapsed or refractory multiple myeloma and the ability of ORIC's small molecule inhibitor of CD73 to restore antitumor immune activity.

Key highlights from a series of experiments utilizing bone marrow aspirates from patients with multiple myeloma include:

- CD73 inhibition addressed adenosine mediated immunosuppression, which stimulated T-cell proliferation, T-cell activation, and activation of plasmacytoid dendritic cells in ex vivo assays derived from patients with multiple myeloma.
- ORIC's small molecule inhibitor of CD73 overcame immunosuppression and triggered significant lysis and cell death of multiple myeloma cells by autologous T-cells from the bone marrow microenvironment.
- ORIC's CD73 inhibitor demonstrated single agent activity, comparing favorably to standard of care therapies, in bone marrow-derived mononuclear cell assays from relapsed or refractory myeloma patients.

The company plans to pursue a single agent clinical development plan for ORIC-533 in multiple myeloma and initiate a Phase 1 trial in the fourth quarter of 2021.

Additional Pipeline Updates:

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. The company recently disclosed that ORIC-114 induced tumor regressions in a subcutaneous HER2 positive breast cancer xenograft model. In a new study, ORIC-114 demonstrated significant tumor growth inhibition in an intracranial HER2 positive breast cancer model, with superior antitumor activity versus tucatinib. The CTA has been filed in South Korea, and initiation of a Phase 1 trial is expected in early 2022.

ORIC-944 PRC2 Inhibitor

ORIC-944 is a potent and selective allosteric inhibitor of polycomb repressive complex 2 (PRC2) that targets its regulatory embryonic ectoderm development (EED) subunit and has demonstrated single agent efficacy in multiple enzalutamide-resistant prostate cancer models in preclinical studies. The IND was cleared by the FDA in December, and initiation of a Phase 1 trial is expected in early 2022.

Webcast and Conference Call Details

ORIC will host a conference call and webcast, today at 5:30 p.m. ET. To participate in the conference call, please dial (833) 651-0991 (domestic) or (918) 922-6080 (international) and refer to conference ID 7989199. A live webcast and audio archive of the conference call will be available through the investor section of the company's website at www.oricpharma.com. The webcast will be available for replay for 90 days following the presentation.

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, as well as other small molecule inhibitors of CD73 and adenosine receptor antagonists. Preclinical data

demonstrated that ORIC-533 binds CD73 with high affinity and effectively blocks adenosine-driven immunosuppression in a high AMP environment, reflective of AMP levels observed in tumors. In preclinical studies, nanomolar concentrations of ORIC-533 efficiently rescued cytotoxic T-cell function in the presence of high AMP concentrations, as well as in ex vivo bone marrow aspirates from relapsed or refractory multiple myeloma patients.

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, being developed for multiple myeloma, (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 ability of a single agent CD73 inhibitor to overcome immune suppression and demonstrate antitumor activity; the potential advantages ORIC-533 may have over other approaches and therapies; the expected timing of initiation of the Phase 1 trial of ORIC-533 in patients with multiple myeloma; the expected timing of initiation of the Phase 1 trials of ORIC-944 and ORIC-114; the potential advantages and benefits of ORIC-533, ORIC-944 and ORIC-114; 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, 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 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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