Initial Phase 1 Dose Escalation Data for ORIC-533 in Relapsed/Refractory Multiple Myeloma Demonstrates Clinical Activity and Strong Safety Profile Supporting Potential for Combination Development

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Preliminary evidence of clinical antimyeloma activity, including reduction in paraprotein, demonstrated in multiple patients

Clean safety profile with only Grade 1 and 2 treatment related adverse events and no dose limiting toxicities or dose reductions

Clinical activity, safety profile, and dose-dependent increases in immune cell activation support potential for combination studies with other multiple myeloma agents, including BCMA- and CD38-directed therapies

Company to pursue strategic partnership for combination studies, resulting in extension of cash runway into 2026

Company to host conference call and webcast today at 4:30 pm ET

SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, Dec. 11, 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 initial data from the ongoing ORIC-533 Phase 1 dose escalation trial in patients with relapsed/refractory multiple myeloma at the 65th American Society of Hematology (ASH) Annual Meeting (poster here).

“ORIC-533 demonstrated an exceptionally well-tolerated safety profile and preliminary evidence of clinical antimyeloma activity in heavily pretreated relapsed/refractory multiple myeloma patients, which to our knowledge is the first reported single agent activity for a CD73 inhibitor in any oncology indication,” said Pratik Multani, MD, chief medical officer. “We believe the Phase 1 data presented today position ORIC-533 as an ideal candidate for combinations with other immune-based antimyeloma therapies, including bispecific anti-BCMA-CD3 antibodies, CAR-T therapies, and anti-CD38 antibodies.”

“We’re excited that multiple ORIC programs have achieved preliminary proof of concept that justify advancement into later stage studies. Given our desire to advance both ORIC-114, our EGFR/HER2 exon 20 inhibitor for lung cancer, and ORIC-944, our PRC2 inhibitor for prostate cancer, into Phase 2 and beyond, those two programs will require a level of focus from our team that necessitates the prioritization of our clinical pipeline,” said Jacob M. Chacko, MD, chief executive officer. “As such, we intend to complete the single agent dose escalation for ORIC-533 in the coming months, and then combination studies will only be pursued with the operational and financial backing of a future partner for that program. This prioritization extends our projected cash runway into 2026, even with the increased expenses associated with moving ORIC-114 and -944 towards registrational studies.”

ORIC-533 Phase 1 Study Design

ORIC-533 is being evaluated in a Phase 1 dose escalation trial in patients with relapsed/refractory multiple myeloma. The primary objectives of the trial are safety and determination of the recommended Phase 2 dose (RP2D). Additional objectives include characterization of the pharmacokinetics, pharmacodynamics, and preliminary antitumor activity.

ORIC-533 Phase 1 Dose Escalation Data

As of November 28, 2023, a total of 23 patients with multiple myeloma received doses ranging from 400 mg to 2400 mg once daily. The study included a heavily pretreated patient population where 100% of patients were triple-class refractory, 91% were penta-refractory, and 57% also received prior anti-BCMA bispecific antibody and/or CAR-T therapy.

ORIC-533 demonstrated a favorable pharmacokinetic profile with an estimated plasma half-life of ~24 hours, which supports QD dosing. ORIC-533 clinical exposures achieved concentrations associated with efficacy in ex vivo models. ORIC-533 also demonstrated strong inhibition of soluble CD73 enzymatic activity across all dose levels, highlighting good target engagement, including in the bone marrow.

ORIC-533 was well tolerated with only Grade 1 and 2 treatment-related adverse events (TRAEs), without any specific recurrent toxicity. There were no dose limiting toxicities, dose reductions or treatment-related serious adverse events.

ORIC-533 exhibited clear evidence of immune activation in the majority of patients dosed at ≥ 1200 mg, as evidenced by an increased abundance and fraction of activated CD8+ T cells and NK cells. At the 1600 mg dose, there were notable reductions in soluble BCMA levels in serum, indicating that ORIC-533 was having a measurable antimyeloma effect. Soluble BCMA levels have been reported to correlate with clinical response on treatment and predict progression free survival of various therapies. Finally, there were multiple examples of clinical activity, including a confirmed minor response in a patient with penta-refractory myeloma who had progressed on an anti-BCMA bispecific antibody 3 months before study entry.

Next Steps

The company intends to complete dose escalation for ORIC-533 in the first quarter of 2024. Given the overall profile of ORIC-533, it is an ideal candidate for development in combination with other immune-based antimyeloma therapies, and the company intends to evaluate strategic partnerships to enable such development.

Conference Call and Webcast Details

To join the conference call via phone and participate in the live Q&A session, please pre-register online here to receive a telephone number and unique passcode required to enter the call. 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 clinical stage product candidates include (1) 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, (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-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. 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 X 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 continued clinical development of ORIC-533; ORIC-533 clinical outcomes, which may materially change as patient enrollment continues or more patient data become available; ORIC-533's development plans and timelines; the company's intention to evaluate strategic partnerships for ORIC-533; the potential advantages of ORIC-533; plans underlying ORIC's clinical trials and development of ORIC-533 and its other product candidates; the company's cash runway; and statements by the company's chief executive 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's product candidates to differ from preclinical, initial, interim, preliminary or expected results; negative impacts of health emergencies, economic instability or international conflicts 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; the potential market for ORIC's product candidates, and the progress and success of competing therapeutics currently available or in development; ORIC's ability to consummate a strategic partnership for ORIC-533; 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 (SEC) on November 6, 2023, 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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