ORIC® Pharmaceuticals Reports Selection of Rinzimetostat RP3D in Combination with Darolutamide for Himalayas-1 Phase 3 Global Study with Dose Optimization Data Supporting Its Potential Best-in-Disease Profile

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Rinzimetostat 400 mg once daily selected as RP3D in combination with darolutamide for Himalayas-1 global Phase 3 registrational trial in post-abiraterone mCRPC, with initiation expected in 1H 2026

At a median follow-up of ~5 months, landmark 5-month rPFS of 84% is consistent with competitor PRC2 inhibitor and substantially better than standard of care therapies in mCRPC

Highly differentiated, potential best-in-disease safety profile, with significantly lower frequency and severity of adverse events, nearly all Grade 1 or 2, and far fewer treatment modifications than competitor regimens

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

SOUTH SAN FRANCISCO, Calif. and SAN DIEGO, March 31, 2026 (GLOBE NEWSWIRE) -- ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, today announced a rinzimetostat (ORIC-944) program update and potential best-in-disease efficacy and safety data from the Phase 1b trial of once daily rinzimetostat in combination with darolutamide in patients with metastatic castration-resistant prostate cancer (mCRPC) who were previously treated with abiraterone acetate (abiraterone).

“The combination dose optimization data announced today provide confirmatory evidence that support rinzimetostat’s potential best-in-disease clinical profile, reinforcing its path towards becoming a practice-changing therapy for patients with prostate cancer,” said Jacob M. Chacko, M.D., president and chief executive officer. “The durability observed to date is consistent with the competitor PRC2 inhibitor currently in Phase 3 in mCRPC and appears meaningfully improved relative to other approved standard of care therapies. Notably, rinzimetostat demonstrated this impressive durability with a markedly cleaner safety profile than competitor regimens.”

“These data provide compelling validation for advancing rinzimetostat in combination with darolutamide into Phase 3 registrational trials in patients with prostate cancer,” said Pratik S. Multani, M.D., chief medical officer. “We expect our first Phase 3 trial, Himalayas-1, in patients with mCRPC previously treated with abiraterone, to initiate in the first half of 2026 while we continue to evaluate rinzimetostat in additional indications in prostate cancer and beyond.”

Rinzimetostat Phase 1b Dose Optimization Data in Combination with Darolutamide
Patients were previously treated with a median of two prior lines of therapy, including abiraterone, up to one prior line of chemotherapy, and a variety of other approved and investigational treatment regimens. This median excludes background androgen deprivation therapy or first-generation androgen receptor (AR) inhibitors that the patients may have received. 18 patients were treated with 400 mg of rinzimetostat once daily and 15 patients were treated with 600 mg of rinzimetostat once daily, both in combination with the standard dose of darolutamide at 600 mg twice daily.

Rationale for Selection of the Recommended Phase 3 Dose (RP3D)
At the 400 mg dose, rinzimetostat in combination with darolutamide continues to be well tolerated and demonstrates a safety profile supportive of long-term administration and sustained patient adherence. As of the January 16, 2026 data cutoff, the vast majority of treatment-related adverse events (TRAEs) were Grade 1 in severity and consistent with PRC2 and AR inhibition. The most common TRAEs were fatigue (39%; 17% Grade 1 and 22% Grade 2), diarrhea (22%; 17% Grade 1 and 6% Grade 2) and nausea (22%; all Grade 1). A single Grade 3 TRAE was observed, and no Grade 4 or 5 AEs were attributed to rinzimetostat or darolutamide. Dose modifications were rare (one interruption and one discontinuation), with no dose reductions required. The 600 mg dose of rinzimetostat in combination with darolutamide was associated with a modestly higher rate of adverse events and dose modifications. In a broader dataset of post-ARPI (androgen receptor pathway inhibitor) patients (n=72, inclusive of the post-abiraterone patients), the safety and tolerability profile was consistent with the post-abiraterone cohort.

To support the selection of the recommended Phase 3 dose in accordance with the FDA's Project Optimus initiative, the company conducted a comprehensive exposure-response (E-R) analysis in over 100 patients across both the single-agent and combination data evaluating the relationship between rinzimetostat drug exposure versus efficacy and safety outcomes. The analysis demonstrated that 400 mg and 600 mg once daily provided comparable efficacy. In contrast, the E-R analysis identified statistically significant relationships between higher drug exposure and toxicities as well as increased rates of treatment modifications, clearly favoring the 400 mg dose on the basis of safety. Based on these findings 400 mg once daily in combination with darolutamide has been selected as the RP3D for rinzimetostat.

Preliminary Efficacy Analysis at RP3D
As of March 6, 2026, radiographic progression-free survival (rPFS) was assessed in 18 efficacy-evaluable patients. PSA responses were assessed in a subset of 15 patients with at least one post-baseline assessment as of the January 16, 2026 clinical cutoff. ctDNA molecular response was evaluated in 14 patients with detectable ctDNA at baseline.

Early efficacy data, including landmark rPFS rates, PSA reductions and ctDNA responses, are suggestive of meaningful and durable clinical benefit for rinzimetostat in combination with darolutamide compared to competitor data and historical outcomes with approved therapies. Rinzimetostat 400 mg once daily in combination with darolutamide demonstrated compelling efficacy across multiple endpoints:

- With a median follow up of 4.9 months, landmark rPFS rates of 93%, 84%, and 84% at 3, 4, and 5 months, respectively,

are consistent with the competitor PRC2 inhibitor currently in Phase 3 in post-abiraterone mCRPC patients and superior to available standard-of-care therapies, including Xtandi®, Jevtana®, Taxotere®, and Pluvicto®. For reference, the 5-month landmark rPFS for these approved therapies ranges from approximately 60% to 75%.

- 47% of patients (7/15) achieved a PSA50 response, with 33% (5/15) confirmed.
- Impressive ctDNA reductions observed across a range of AR mutations, with 71% of patients (10/14) achieving >50% ctDNA reduction.

Himalayas-1 Phase 3 Trial

The company expects to initiate the Himalayas-1 global Phase 3 registrational trial in mCRPC patients previously treated with abiraterone in the first half of 2026. This proposed trial will enroll approximately 600 patients from over 250 sites in over 20 countries, randomized 1:1 to receive the RP3D of 400 mg QD rinzimetostat in combination with darolutamide versus physician's choice of an AR inhibitor or chemotherapy. The primary endpoint is rPFS, the key secondary endpoint is overall survival, and additional secondary endpoints include PSA response rate, objective response rate and patient reported outcomes.

In the US, the annual incidence of mCRPC patients previously treated with abiraterone is approximately 17,000, with an estimated addressable market of greater than $3.5 billion and total global addressable market of $7 billion. This market lacks oral, well-tolerated therapies with meaningful efficacy.

Next Steps

Rinzimetostat 400 mg QD plus darolutamide is currently being evaluated in a food effect cohort. Thus far, there does not appear to be a significant food effect, consistent with previous single agent studies. Furthermore, as of March 6, 2026, early efficacy and safety are consistent with fasted results, with two confirmed PSA50 responses and one confirmed PSA90 response in the first five patients dosed, and all TRAEs reported being Grade 1 with a single Grade 2 TRAE.

The company is also evaluating additional prostate cancer populations for future potential Phase 3 trials in mCRPC and mCSPC. Early data from rinzimetostat in 19 patients with mCRPC previously treated with AR inhibitors demonstrated compelling landmark rPFS rates of 93%, 85%, and 85% at 3, 4, and 5 months, respectively, with a median follow-up of 4.8 months.

Rinzimetostat Phase 1b Trial Design

Rinzimetostat is being evaluated in a Phase 1b dose optimization trial in combination with ERLEADA® (apalutamide), Johnson & Johnson's AR inhibitor, and NUBEQA® (darolutamide), Bayer's AR inhibitor, in patients with mCRPC. Patients are eligible if they have received prior treatment with an ARPI and up to one prior chemotherapy. The primary objective of the trial is to determine the RP3D, and additional objectives include safety, tolerability, pharmacokinetics, and preliminary clinical activity.

Conference Call and Webcast Details

ORIC will host a conference call and webcast today at 4:30 p.m. ET. 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 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) rinzimetostat (ORIC-944), an allosteric inhibitor of the polycomb repressive complex 2 (PRC2) via the EED subunit, being developed for prostate cancer, and (2) enozertinib (ORIC-114), a brain-penetrant inhibitor targeting EGFR exon 20 and EGFR PACC mutations, being developed for NSCLC. 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, the continued clinical development of rinzimetostat (ORIC-944); statements regarding the potential best-in-class and best-in-disease properties of rinzimetostat; clinical outcomes from combination studies with rinzimetostat, which may materially change as patient enrollment continues or more patient data become available; the development plans and timelines for rinzimetostat; the potential advantages of rinzimetostat; plans underlying ORIC's clinical trials and development; next steps and anticipated program milestones, including the initiation of rinzimetostat's first global Phase 3 registrational trial in mCRPC; estimated patient population and market data; and statements by the company's chief executive officer and chief medical 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 rinzimetostat or any other 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 or its clinical trial collaboration and supply agreements; the potential market for rinzimetostat, and the progress and success of competing therapeutics currently available or in development; 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (the SEC) on February 23, 2026, 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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