UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported)
January 11, 2021

ORIC Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39269**	**47-1787157**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

240 E. Grand Ave, 2nd Floor
South San Francisco, CA 94080
(Address of principal executive offices, including zip code)

(650) 388-5600
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.0001 per share	**ORIC**	**The NASDAQ Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

The information set forth in Item 7.01 is hereby incorporated by reference into this Item 2.02.

Item 7.01 Regulation FD Disclosure.

On January 11, 2021, ORIC Pharmaceuticals, Inc. (the "Company") issued a press release announcing a corporate update, expected milestones for 2021 and the Company's participation in the JP Morgan Healthcare Conference.

A copy of the press release is attached hereto as Exhibit 99.1 and a copy of the Company's current corporate presentation is attached hereto as Exhibit 99.2, which are incorporated herein by reference.

All of the information furnished in this Item 7.01 and Items 2.02 and 9.01 (including Exhibits 99.1 and 99.2) shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated January 11, 2021
99.2	Corporate Presentation dated January 2021

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ORIC PHARMACEUTICALS, INC.

Date: January 11, 2021

By: /s/ Dominic Piscitelli
Dominic Piscitelli
Chief Financial Officer

Exhibit 99.1

ORIC Pharmaceuticals Provides Corporate Update and Highlights Key 2021 Milestones

Lead program ORIC-101 continues patient enrollment investigating two therapeutic mechanisms of action and on track for two initial data readouts in 2021

Three IND/CTA filings for ORIC-533, -944, and -114 expected in 2021

SOUTH SAN FRANCISCO and SAN DIEGO, CA – Jan. 11, 2021 – ORIC Pharmaceuticals, Inc. (Nasdaq: ORIC), a clinical stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, today provided program updates and announced key milestones for 2021, which are expected to substantially expand and advance the company's clinical pipeline.

"2020 was a transformational year for ORIC during which we significantly broadened the pipeline via internal discovery and business development efforts, expanded the team, and strengthened the balance sheet with the completion of an IPO and follow-on financing," said Jacob Chacko, M.D., president and chief executive officer. "These efforts have positioned us for a dynamic 2021, with our first data from two ongoing trials of our lead program ORIC-101 and three INDs/CTAs for our other product candidates, which represents a tremendous amount of development activity for a company at our stage."

Program Updates and 2021 Milestones

ORIC-101: Glucocorticoid Receptor (GR) Antagonist

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

- The company announced today the completion of the Part I dose escalation portion of the Phase 1b trial of ORIC-101 in combination with enzalutamide in metastatic prostate cancer, by identifying the provisional recommended Phase 2 dose (RP2D) that will be used in the Part II expansion portion of the trial. The selection of the provisional RP2D was based upon the totality of safety, pharmacokinetic, and pharmacodynamic data demonstrating a well-tolerated regimen that achieved ORIC-101 exposures leading to demonstrable target engagement and GR inhibition. In the Part I dose escalation portion of the trial, patients were enrolled to evaluate daily dosing of ORIC-101 with doses ranging from 80 to 240 mg, in combination with daily dosing of 160 mg of enzalutamide. In the Part II dose expansion portion of the trial, up to 48 patients are expected to be enrolled and treated at the RP2D of 240 mg of ORIC-101 and 160 mg of enzalutamide on a continuous daily dosing schedule. Patients will be enrolled independent of GR status, with retrospective analysis of GR expression and other potentially predictive biomarkers. The company expects to report interim safety, efficacy, and translational data from this trial in the second half of 2021.

- The Phase 1b trial of ORIC-101 in combination with nab-paclitaxel is now enrolling patients in the Part II dose expansion portion. In December 2020, the company announced the completion of the Part I dose escalation portion of ORIC-101 in combination with nab-paclitaxel in solid tumors, the selection of the RP2D, and the initiation of the dose expansion portion of the trial. For the Part II dose expansion portion of the trial, up to 132 patients are expected to be enrolled across four cohorts, including pancreatic ductal adenocarcinoma, ovarian cancer, triple negative breast cancer, and other advanced solid tumors. Patients in Part II of the trial will be treated at the RP2D of 160 mg of ORIC-101 continuous once daily dosing and 75 mg/m^2 of nab-paclitaxel on days 1, 8, and 15 of a 28-day cycle, without requirement for prophylactic granulocyte colony-stimulating factor. Eligible patients must have previously progressed on a taxane-containing regimen and will be enrolled independent of baseline GR status, with retrospective analysis of GR expression and other potentially predictive biomarkers. The company expects to report interim safety, efficacy, and translational data from this trial in the first half of 2021.

ORIC-533: CD73 Inhibitor

ORIC-533 was designed to be a highly potent, orally bioavailable CD73 inhibitor and has demonstrated more potent adenosine inhibition in preclinical studies compared to an antibody approach and other small molecule CD73 inhibitors. ORIC-533 continues to progress in Investigational New Drug (IND) enabling studies and the company expects to file an IND with the Food and Drug Administration (FDA) in the first half of 2021. Having conducted 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 path in this indication.

ORIC-944: PRC2 Inhibitor

ORIC-944, in-licensed in August 2020, 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 company plans to conduct IND enabling studies and then file an IND with the FDA in the second half of 2021, with initial clinical development as a single agent in treatment-resistant prostate cancer.

ORIC-114: EGFR/HER2 Inhibitor

ORIC-114, in-licensed in October 2020, is a brain penetrant, orally bioavailable, irreversible inhibitor designed to selectively target EGFR and HER2 with high potency against exon 20 insertion mutations. ORIC-114 has demonstrated greater brain exposure in preclinical studies compared to other compounds being developed against exon 20 mutations and has shown strong antitumor activity in an EGFR-driven intracranial lung cancer model. The company plans to conduct IND enabling studies and then file a Clinical Trial Application (CTA) in South Korea in the second half of 2021.

Discovery Pipeline

In addition to the four product candidates, the company is leveraging its resistance platform in pursuit of multiple discovery research programs that focus on its expertise in precision oncology, hormone-dependent cancers, and key tumor dependencies. These programs highlight the company's medicinal chemistry and structure-based drug design proficiency to target drivers of resistance in solid tumors like prostate, breast, and lung cancer that relapse with innate, acquired or bypass mechanisms of resistance. The company recently advanced one of these programs into lead optimization.

Anticipated 2021 Milestones

ORIC anticipates the following milestones in 2021:

- ORIC-101: Report interim safety, efficacy, and translational data from ongoing combination trial with nab-paclitaxel in the first half of 2021
- ORIC-101: Report interim safety, efficacy, and translational data from ongoing combination trial with enzalutamide in the second half of 2021
- ORIC-533: File an IND in the first half of 2021
- ORIC-944: File an IND in the second half of 2021
- ORIC-114: File a CTA in the second half of 2021
- Present additional preclinical and translational research data on ORIC-101, ORIC-533, ORIC-944, and ORIC-114 at scientific conferences in 2021

Financial Guidance

Cash, cash equivalents and marketable securities totaled $293.6 million as of December 31, 2020, which included gross proceeds of $133.3 million from the follow-on financing completed in November 2020. The company expects its cash, cash equivalents and marketable securities will be sufficient to fund its current operating plan into the second half of 2023.

Presentation and Webcast

Jacob Chacko, M.D., president and chief executive officer, will present a corporate overview at the 39th J.P. Morgan Healthcare Conference beginning at 12:40 p.m. PT on Tuesday, January 12, 2021. A live webcast will be available through the investor section of the company's website at https://investors.oricpharma.com/. A replay of the webcast will be available for 90 days following the event.

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 of ORIC-101 in combination with (1) Xtandi (enzalutamide) in metastatic prostate cancer and (2) Abraxane (nab-paclitaxel) in advanced or metastatic solid tumors. 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 ORIC's development plans and timelines; the potential advantages of ORIC's product candidates and programs; plans underlying ORIC-101 clinical trials and development; the expected timing of reporting interim data from the ORIC-101 clinical trials; plans underlying ORIC-533, ORIC-944, ORIC-114 or any other programs; the planned IND filings for ORIC-533 and ORIC-944 and CTA filing for ORIC-114; ORIC's anticipated 2021 milestones; the period over which ORIC estimates its existing cash, cash equivalents and marketable securities will be sufficient to fund its current operating plan; and statements by the company's president and 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-101, ORIC-533, ORIC-944, ORIC-114 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 the Mirati license agreement or the Voronoi license agreement; 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.

Contact:

Dominic Piscitelli, Chief Financial Officer
dominic.piscitelli@oricpharma.com
info@oricpharma.com

Exhibit 99.

ORIC

OVERCOMING RESISTANCE IN CANCER

Company Overview

January 2021

Forward-Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding ORIC Pharmaceuticals, Inc.'s ("ORIC", "we", "us" or "our") future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potentially" "predict," "should," "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: the timing of the initiation, progress and potential results of our preclinical studies, clinical trials and our discovery programs; 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; negative impacts of the COVID-19 pandemic on our operations, including clinical trials; the potential for clinical trials of ORIC-101 or any future clinical trials of other product candidates to differ from preclinical, preliminary or expected results; our ability to advance product candidates into, and successfully complete, clinical trials; the timing or likelihood of regulatory filings and approvals; our estimates of the number of patients who suffer from the diseases we are targeting and the number of patients that may enroll in our clinical trials; the commercializing of our product candidates, if approved; our ability and the potential to successfully manufacture and supply our product candidates for clinical trials and for commercial use, if approved; potential benefits and costs of strategic arrangements, licensing and/or collaborations; the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of the Company's license agreements; our estimates regarding expenses, future revenue, capital requirements and needs for financing and our ability to obtain capital; the sufficiency of our existing cash, cash equivalents and marketable securities to fund our future operating expenses and capital expenditure requirements; our ability to retain the continued service of our key personnel and to identify, hire and retain additional qualified professionals; the implementation of our business model and strategic plans for our business and product candidates; the scope of protection we are able to establish and maintain for intellectual property rights, product candidates and our pipeline; our ability to contract with third-party contract research organizations, suppliers and manufacturers and their ability to perform adequately; the pricing, coverage and reimbursement of our product candidates, if approved; developments relating to our competitors and our industry, including competing product candidates and therapies; general economic and market conditions; and the other risks, uncertainties and assumptions discussed in the public filings we have made and will make with the Securities and Exchange Commission ("SEC"). These risks are not exhaustive. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

We have filed or will file Current Reports on Form 8-K, Quarterly Reports on Form 10-Q, Annual Reports on Form 10-K, and other documents with the SEC. You should read these documents for more complete information about us. You may obtain these documents for free by visiting EDGAR on the SEC website at www.sec.gov.

This presentation discusses our product candidates that are under pre-clinical or clinical study, and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of our product candidates for the therapeutic use for which they are being studied.

ORIC Pharmaceuticals: Dedicated to **O**vercoming **R**esistance **I**n **C**ancer

Experienced Leadership	• Heritage of discovering and developing multiple approved oncology medicines at Ignyta, Medivation, Aragon and Genentech
Lead Program Targeting Multiple Large Indications	• Two clinical trials focused on resistance to anti-androgen treatment in prostate cancer and resistance to chemotherapy in solid tumors • Preliminary POC by competitor compound not optimized for oncology
Broad Pipeline	• Fully integrated R&D team advancing internally-discovered and externally-sourced pipeline beyond lead program
Multiple Upcoming Catalysts	• Data from multiple clinical trials evaluating distinct mechanisms of resistance expected in 2021 • Three IND/CTAs expected in 2021
Strong Financial Foundation	• Existing cash, cash equivalents and marketable securities expected to fund current operating plan into 2H 2023

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Note: IND, investigational new drug. CTA, clinical trial application. POC, proof of concept.

Founders and Board Members with Significant Oncology Experience

Distinguished Founders and Scientific Advisors

Charles Sawyers, MD
Founder, SAB
- MSKCC and HHMI Investigator
- Key role in discovery and development of Gleevec, Sprycel, Xtandi and Erleada
- National Academy of Sciences
- Board member at Novartis

Scott Lowe, PhD
Founder, SAB
- MSKCC and HHMI Investigator
- Chair, Cancer Biology & Genetics and Cancer Research at MSKCC
- Expert in tumor networks and molecular determinants of treatment response

Rich Heyman, PhD
Founder, BOD Chair, SAB
- CEO/founder Aragon (sold to Johnson & Johnson)
- CEO/founder Seragon (sold to Roche)
- Board member at Gritstone, Vividion, Metacrine, Yumanity and Amunix

Richard Scheller, PhD
BOD Member, SAB
- Chairman of R&D BridgeBio
- Previously CSO Genentech and 23andMe
- National Academy of Sciences
- Board member at BridgeBio, Alector and Maze

Board of Directors

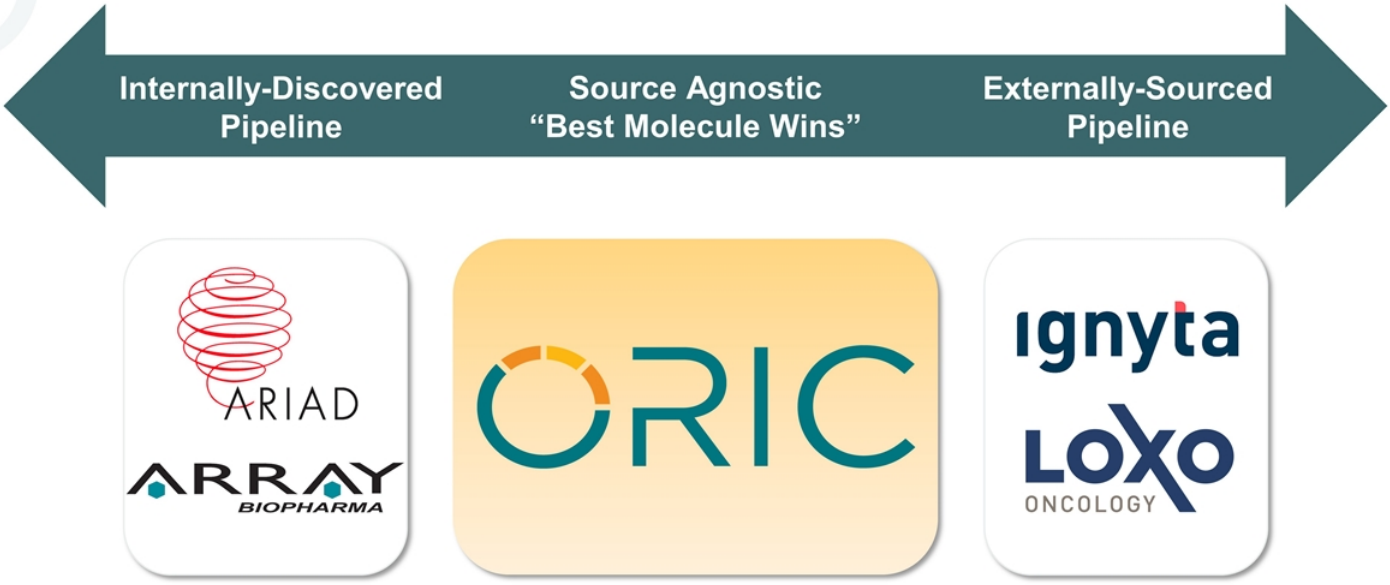
- Richard Heyman, PhD - *Chairman and Founder*
- Mardi C. Dier - *EVP and CFO Ultragenyx Pharmaceuticals*
- Carl L. Gordon, PhD, CFA - *Managing Partner, OrbiMed*
- Lori Kunkel, MD - *Former CMO Loxo, Pharmacyclics and Proteolix*
- Richard Scheller, PhD - *Chairman of R&D, BridgeBio*
- Peter Svennilson - *Managing Partner, The Column Group*
- Jacob Chacko, MD - *President and CEO*

Executive Team with Expertise in Building Leading Oncology Companies

Jacob Chacko, MD Chief Executive Officer	• Previously CFO of Ignyta (acquired by Roche), raised over $500mm in capital • TPG Capital (completed $10bn of aggregate acquisitions) and McKinsey • Board member of Turning Point Therapeutics and 4D Molecular Therapeutics; previously Bonti, RentPath, EnvisionRx, Par Pharma, IMS and Quintiles	ignyta TPG McKinsey&Company
Lori Friedman, PhD Chief Scientific Officer	• Previously Head of Translational Oncology at Genentech; advanced over 20 drug candidates into development, two approvals to date • Director of Signal Transduction at Exelixis; led new target discovery and collaboration with BMS • Inventor on 24 issued patents and author on 88 peer-reviewed publications	Genentech EXELIXIS
Pratik Multani, MD Chief Medical Officer	• Previously CMO of Ignyta, led development and regulatory for entrectinib • CMO of Fate Therapeutics; contributed to development of Rituxan and Zevalin at Idec, and Treanda at Salmedix; earlier at Dana Farber and MGH • Board member of Erasca and Chimerix	ignyta biogen idec DANA-FARBER CANCER INSTITUTE
Matt Panuwat Chief Business Officer	• Previously SVP of Business Development at Prothena, established Celgene collaboration for up to $2.2bn • Head of BD at Medivation (acquired by Pfizer), led M&A including the acquisition of talazoparib • Global Healthcare Investment Banking at Merrill Lynch	prothena MEDIVATION Bank of America Merrill Lynch
Dominic Piscitelli Chief Financial Officer	• Previously CFO of AnaptysBio, raised over $500mm in capital (IPO and follow-on financing) • VP of Finance, Strategy and Investor Relations at Medivation • VP of Treasury and Finance at OSI Pharmaceuticals (acquired by Astellas) • Board member of Celyad Oncology	AnaptysBio MEDIVATION (OSI) pharmaceuticals
Christian Kuhlen, MD General Counsel	• Previously General Counsel at Synthorx (acquired by Sanofi), completed $151 million IPO • General Counsel at Ignyta and Genoptix (acquired by Novartis), executed multiple financings and M&A • Attorney at Cooley LLP	synthorx ignyta GENOPTIX
Edna Chow Maneval, PhD SVP Clinical Development	• Previously SVP at Ignyta; clinical lead for entrectinib, led transition team through global filings • VP of Clinical Development at Seragon and Aragon, clinical lead for apalutamide • Led pivotal Phase 3 study in RCC for Sutent at Pfizer	ignyta SERAGON PHARMACEUTICALS ARAGON PHARMACEUTICALS

ORIC

Full Slate of Capabilities Enables “Best of Breed” Hybrid Approach to Company Building



Leveraging Areas of Expertise and Proven Track Records of Success

ORIC

Overcoming Resistance Cancer

Precision Oncology

- Biomarker-driven, patient-selected trials
- Purpose-built targeted therapeutics

Key Tumor Dependencies

- Mechanisms responsible for treatment relapse:
  - Innate resistance
  - Acquired resistance
  - Bypass resistance

Hormone-Dependent Cancers

- Nuclear hormone receptor targets
- Prostate and breast cancer indications

Broad Pipeline Targeting Multiple Resistance Mechanisms

Substantial Progress in 2020: Well Positioned to Build Value in 2021 and Beyond

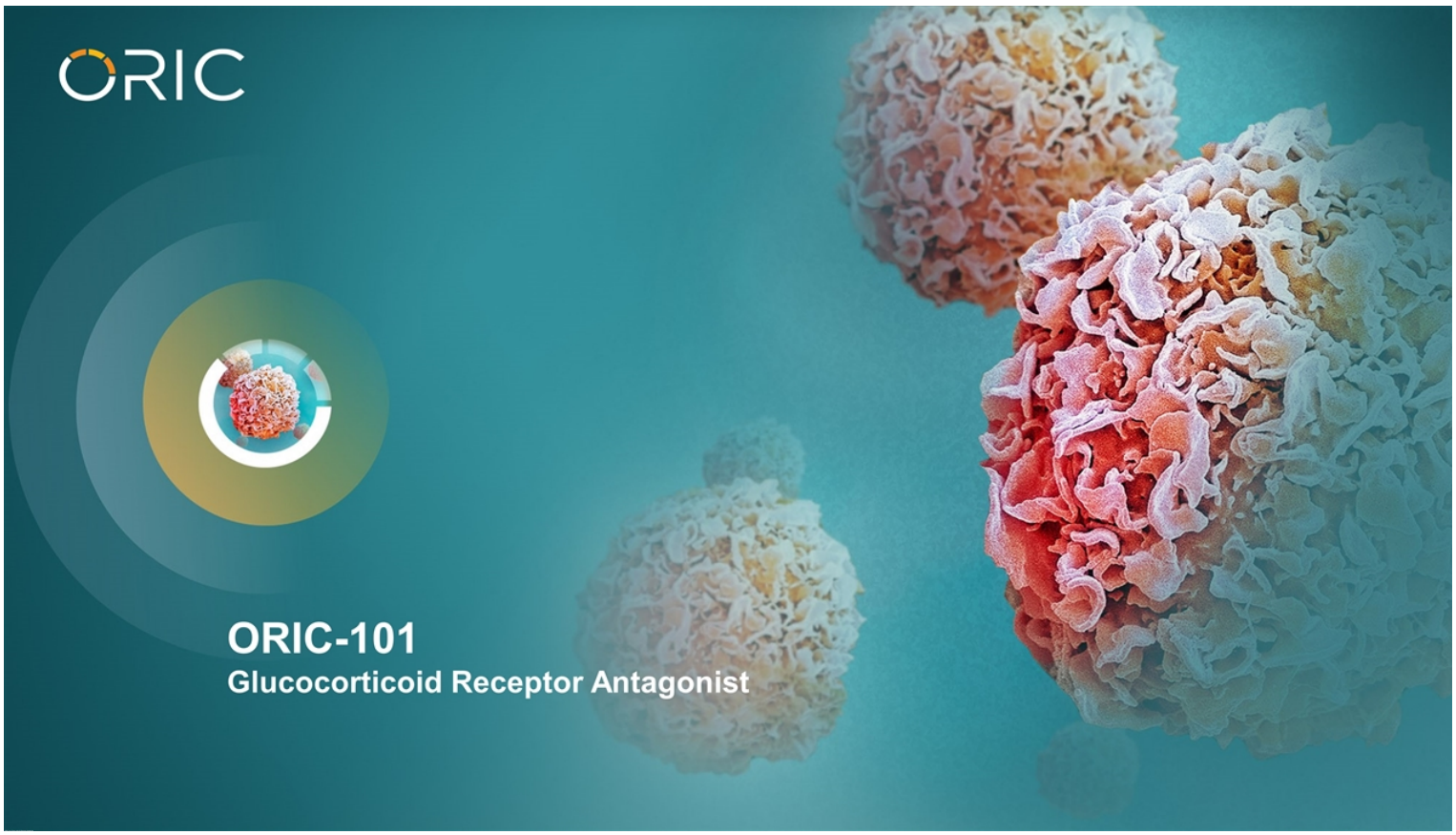
	2020 Accomplishments
ORIC-101 (GR Antagonist)	✓ Combination with Abraxane: initiated multiple expansion cohorts ✓ Combination with Xtandi: selected provisional RP2D
ORIC-533 (CD73 Inhibitor)	✓ Demonstrated potential best-in-class preclinical profile ✓ Generated compelling preclinical package with leading KOL to support single agent clinical development path
ORIC-944 (PRC2 Inhibitor)	✓ In-licensed program from Mirati Therapeutics
ORIC-114 (EGFR/HER2 Inhibitor)	✓ In-licensed program from Voronoi
Discovery	✓ Continued to progress multiple oncology discovery programs ✓ Advanced one program into lead optimization
Corporate	✓ Raised $271 million through IPO and follow-on offering

Expected Milestones

- **2** Trials to Report Initial Phase 1b Data in 2021
- **3** IND / CTA Filings Expected in 2021
- **4** Programs in Clinical Development by Early 2022
- Discovery Pipeline Advancing and Potential New Programs from Business Development

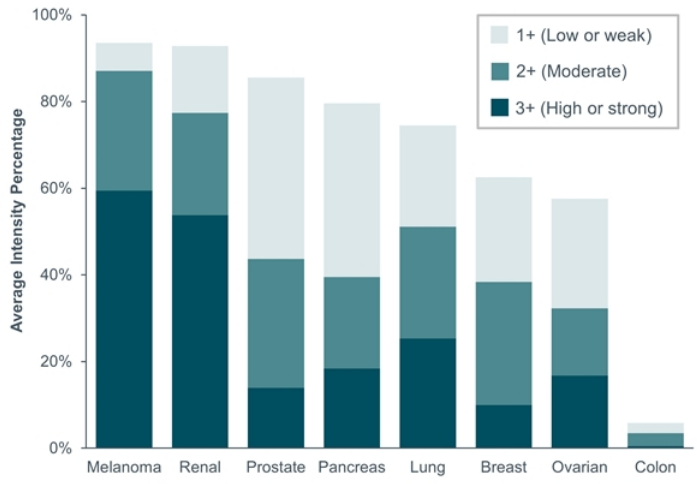
ORIC

Note: RP2D, recommended Phase 2 dose. KOL, key opinion leader.

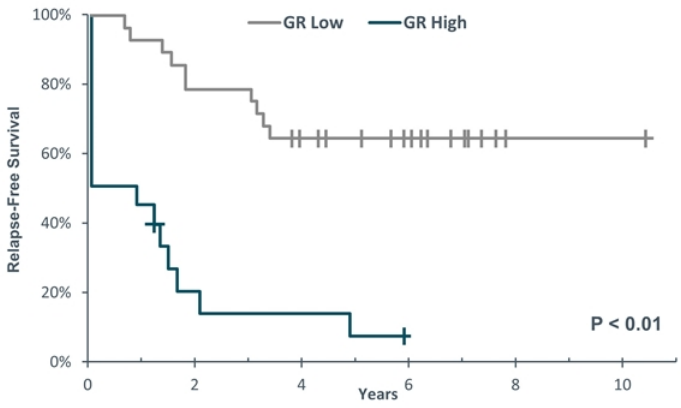

ORIC
ORIC-101
Glucocorticoid Receptor Antagonist

Glucocorticoid Receptor (GR) Is Overexpressed in Solid Tumors and Associated with Therapy Resistance

GR Is Overexpressed in Multiple Solid Tumors [1]



Elevated GR Expression Correlated with Worse Clinical Outcomes in ER-Negative Breast Cancer [2]

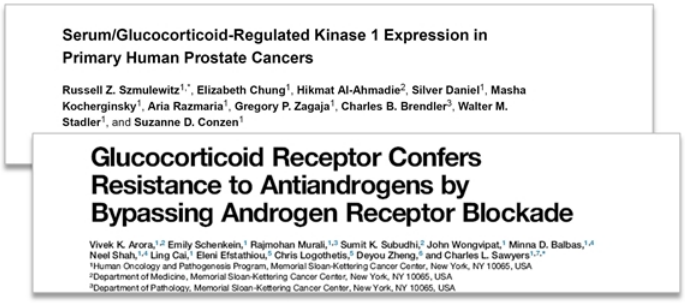


- Elevated GR expression also correlated with worse clinical outcomes in:
  - Endometrial cancer [3]
  - CRPC treated with enzalutamide [4]

(1) Block et al. Canc Man Res (2017). (2) Pan et al. Clin Cancer Res (2011). (3) Tangen et al. Gynecol Oncol (2017). (4) Arora et al. Cell (2013). Note: Left figure: Melanoma n=11, Renal n=10, Prostate n=11, Pancreas n=16, Lung n=17, Breast (non-TNBC) n=10, Ovarian n=11 and Colon n=16. Right figure: GR high n=18 and GR low n=28; post-adjuvant chemotherapy.

GR Potentially Drives Resistance Across Large Oncology Indications Through Two Distinct Mechanisms

1 GR Implicated in Anti-Androgen Resistance in Prostate Cancer



Serum/Glucocorticoid-Regulated Kinase 1 Expression in Primary Human Prostate Cancers

Russell Z. Szmulewitz[1,*], Elizabeth Chung[1], Hikmat Al-Ahmadie[2], Silver Daniel[1], Masha Kocherginsky[1], Aria Razmaria[1], Gregory P. Zagaja[1], Charles B. Brendler[3], Walter M. Stadler[1], and Suzanne D. Conzen[1]

Glucocorticoid Receptor Confers Resistance to Antiandrogens by Bypassing Androgen Receptor Blockade

Vivek K. Arora,[1,2] Emily Schenkein,[1] Rajmohan Murali,[1,3] Sumit K. Subudhi,[2] John Wongvipat,[1] Minna D. Balbas,[1,4] Neel Shah,[1,4] Ling Cai,[1] Eleni Efstathiou,[5] Chris Logothetis,[5] Deyou Zheng,[6] and Charles L. Sawyers[1,7,*]

[1]Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA
[2]Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA
[3]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA

2 GR Implicated in Chemotherapy Resistance in Solid Tumors

Microarray Analysis Reveals Glucocorticoid-Regulated Survival Genes That Are Associated With Inhibition of Apoptosis in Breast Epithelial Cells

Wei Wu,[1] Shamita Chaudhuri,[1] Deanna R. Brickley,[1] Diana Pang,[1] Theodore Karrison,[2] and Suzanne D. Conzen[1,3]

Departments of [1]Medicine and [2]Health Studies and [3]Committee on Cancer Biology, University of Chicago, Chicago, Illinois

Glucocorticoid receptor activation inhibits chemotherapy-induced cell death in high-grade serous ovarian carcinoma☆

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	Therapeutic Area	US Patient Population(1)	Anti-Cancer Treatment	Resistance Mechanism	Potential Solution
1	Prostate cancer	~175,000	AR modulators (e.g., Xtandi, Erleada)	GR bypasses AR signaling	GR Antagonist
2	Solid tumors	~180,000	Chemotherapy (e.g., Abraxane)	GR drives tumor survival and proliferation	

GR antagonist could address two potential distinct mechanisms of resistance to anti-androgen treatment for prostate cancer and chemotherapy treatment for solid tumors, targeting potential patient populations of over 350,000 in the US alone

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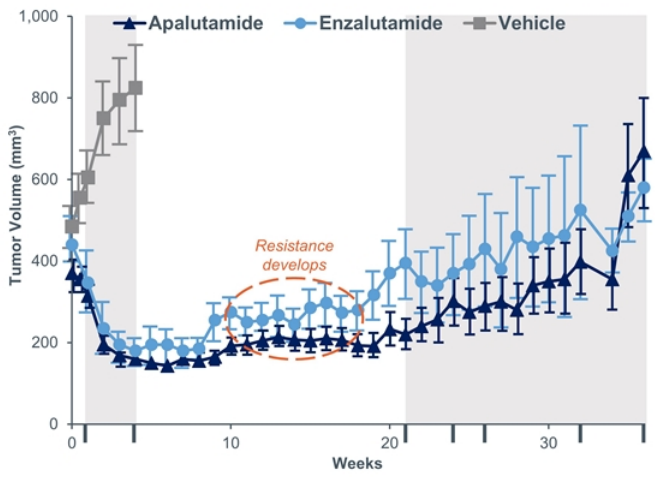
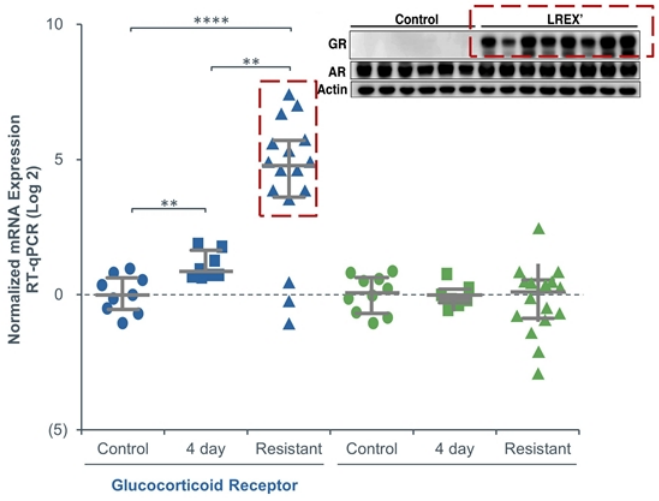
(1) American Cancer Society, Cancer Facts & Figures (2019). US patient population for solid tumors includes ~62,000 endometrial, ~57,000 pancreatic, ~22,500 ovarian and ~41,000 triple negative breast (estimated as 15% of breast) cancers.

Acquired Resistance to Anti-Androgen Treatment Correlated with Upregulation of GR Expression

Long-Term Anti-Androgen Treatment Led to Resistance In Vivo…



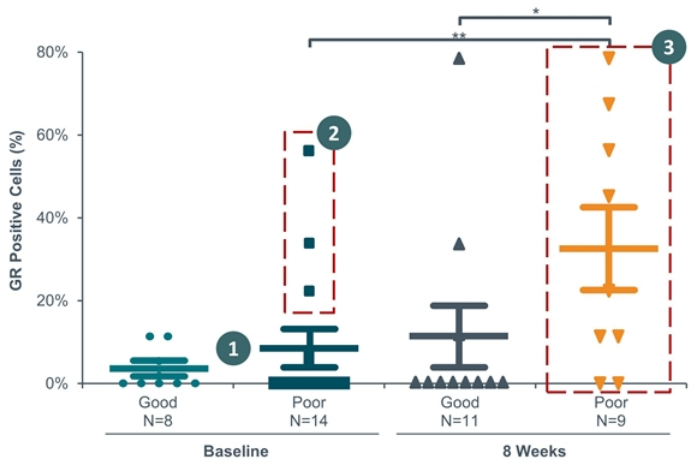
…This Resistance Correlated to Increased GR mRNA and GR Protein Expression



Source: Arora et al. Cell (2013). Note: Left graph's grey shading indicates treatment period when tumors were harvested (as annotated by long hash marks on the x axis). LREX' is a prostate cancer model that was derived from an enzalutamide-resistant tumor with high GR expression. Actin was used to verify consistent sample loading for the western blot experiment. **: $p < 0.01$, ****: $p < 0.0001$.

GR Expression Is Associated with Clinical Resistance to Enzalutamide in the Treatment of Prostate Cancer

Elevated GR Expression in Tumors of Patients Responding Poorly to Enzalutamide



1. Baseline levels of GR expression were low prior to enzalutamide treatment in both groups, but slightly higher in the group with poor responses
2. All patients with high GR expression at baseline had poor response to enzalutamide
3. After 8 weeks of enzalutamide treatment, GR expression levels increased significantly in patients who had a poor response to enzalutamide

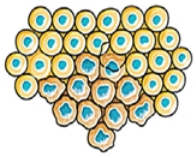
Initial observations from Sawyers' lab demonstrated a correlation between increased GR expression and poor clinical response to enzalutamide, and suggest that AR inhibition may induce GR expression in some patients

Source: Arora et al. Cell (2013). Note: Patients who continued to benefit from enzalutamide for greater than six months were classified as "good" responders. Patients who discontinued enzalutamide earlier than six months due to a lack of clinical benefit were classified as "poor" responders. *: $p < 0.05$, **: $p < 0.01$.

GR May Also Impede Therapeutic Response to Chemotherapy by Enabling Pro-Survival Mechanisms

GR Acts as a Pro-Survival Mechanism in Tumors

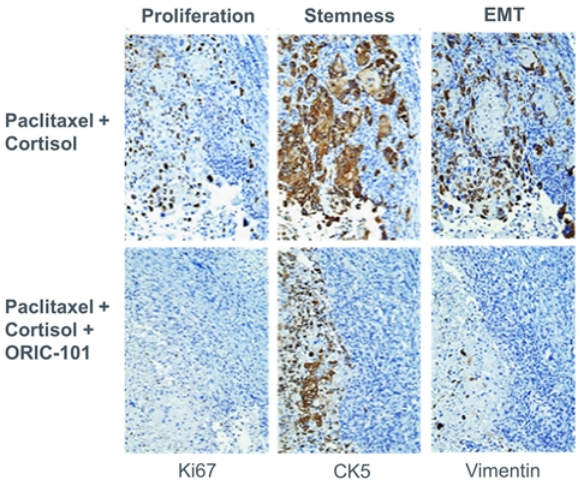
Glucocorticoids



Pro-Survival Mechanisms

- ↓ Apoptosis
- ↓ Adhesion
- ↓ Inflammation
- ↑ EMT
- ↑ "Stemness" (Metabolic changes)

GR Inhibition Reversed EMT-Like Phenotype In Vivo



Counteracting GR is expected to block the transcriptional program driving tumor cell survival and therapy escape

Source: Zhou et al. AACR (2019).
Note: HCC1806 xenografts. EMT, epithelial-mesenchymal transition.

Preliminary Proof-of-Concept Demonstrated with a Competitor GR Antagonist in Combination with Chemotherapy in Patients with Solid Tumors

Relacorilant Plus Abraxane Phase 1 Data in Advanced Solid Tumors

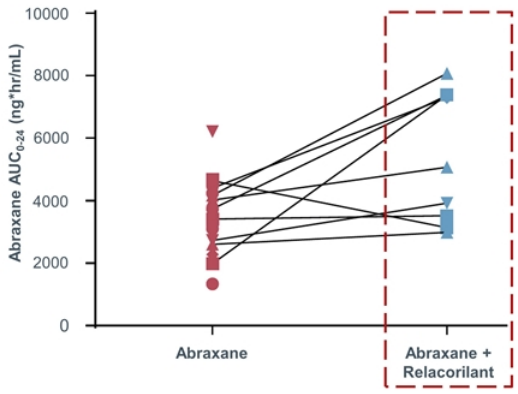
	Total (response evaluable)[a]		
	PDAC (n=25)	Ovarian cancer (n=11)	Other solid tumors (n=13)
CR, n	0	1	0
PR, n	4	2	3
SD, n	8	5	8
PD, n	13	3	2
DCR >16 wks, n/N (%) [range, wks]	7/25 (28.0) [17-52+]	5/11 (45.5) [18-65+]	7/13 (53.8) [17-80+]

Relacorilant plus Abraxane demonstrated ORR in PDAC of 4/25 (16%) and ORR in ovarian cancer of 3/11 (27%); historical ORR is typically 0% in third-line PDAC and <15% in third-line ovarian cancer [1]

Source: Munster et al. ASCO Poster (2019). Note: CR, complete response; DCR, disease control rate; PDAC, pancreatic ductal adenocarcinoma; PR, partial response; PD, progressive disease; SD, stable disease; wks, weeks. a Patients who received at least one dose of study drug and had at least one post-baseline tumor assessment. (1) Peddi et al. J Gastrointest Oncol (2013). Macarulla et al. J of Clinical Oncology (2017). Bruchim et al. Eur J Obstet Gynecol Reprod Biol (2013).

Competitor GR Antagonist Is Limited by Significant Drug-Drug Interactions and Serious Adverse Events When Combined with Chemotherapy

Abraxane Exposure Following Abraxane +/- Relacorilant Treatment



Relacorilant + Abraxane Grade ≥3 Adverse Events

Adverse event, n (%)	Continuous-dosing regimen (n=49)	Intermittent-dosing regimen (n=19)	Overall (N=68)
Patients Reporting at Least One Grade ≥3 Adverse Event	33 (67.4)	13 (68.4)	46 (67.7)
Neutropenia	7 (14.3)	6 (31.6)	13 (19.1)
Abdominal pain	4 (8.2)	1 (5.3)	5 (7.4)
Anemia	3 (6.1)	2 (10.5)	5 (7.4)
Hyponatremia	3 (6.1)	1 (5.3)	4 (5.9)
Hypophosphatemia	3 (6.1)	1 (5.3)	4 (5.9)
Vomiting	2 (4.1)	2 (10.5)	4 (5.9)
Diarrhea	2 (4.1)	1 (5.3)	3 (4.4)
Febrile neutropenia	3 (6.1)	0	3 (4.4)
Hypokalemia	2 (4.1)	1 (5.3)	3 (4.4)
Malignant neoplasm progression	3 (6.1)	0	3 (4.4)
Mucosal inflammation	1 (2.0)	2 (10.5)	3 (4.4)
Pulmonary embolism	3 (6.1)	0	3 (4.4)

In a Phase 1 clinical study, relacorilant increased the exposure of Abraxane, resulting in high rate of neutropenia (despite mandatory prophylactic G-CSF) among other serious adverse events

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Source: Munster et al. ASCO Poster (2018) and (2019).

ORIC-101 Is a Potent and Selective GR Antagonist Designed for Oncology

	Mifepristone (steroidal)	Relacorilant (non-steroidal)	**ORIC-101** (steroidal)
GR antagonism IC_{50} (nM)	2.9	16	**7.3**
AR agonism IC_{50} (nM)	25	>2500	**>2500**
PR antagonism IC_{50} (nM)	0.4	>2500	**22**
CYP inhibition IC_{50} (nM)	Inhibitor of CYP2C8, CYP2C9 and CYP3A4	Inhibitor of CYP2C8, CYP2C9 and CYP3A4	**Inhibitor of CYP3A4**

ORIC-101 Advantages

- ✓ No AR agonism
- ✓ Potential for reduced CYP inhibition

Less favorable than ORIC-101
More favorable than ORIC-101

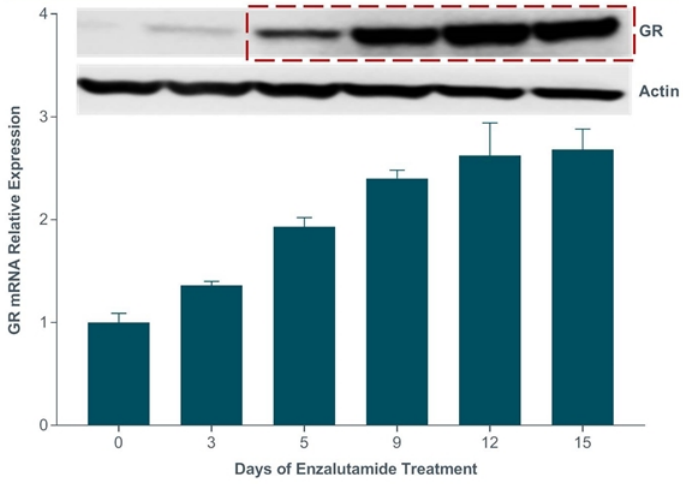
ORIC-101 is a potent and selective GR antagonist with reduced potential for drug-drug interaction versus other GR antagonists (CYP2C8 plays a critical role in metabolism of taxanes and enzalutamide)

Source: ORIC data. Note: In vitro experiments conducted by ORIC evaluating ORIC-101, mifepristone and relacorilant across a variety of properties ORIC believes to be important in developing a potent and selective GR antagonist. The determination of more favorable or less favorable relates to the ideal properties of a GR antagonist for a combination therapy in oncology. GR antagonism, AR agonism and PR antagonism measured by luciferase assay. GR, glucocorticoid receptor. AR, androgen receptor. PR, progesterone receptor.

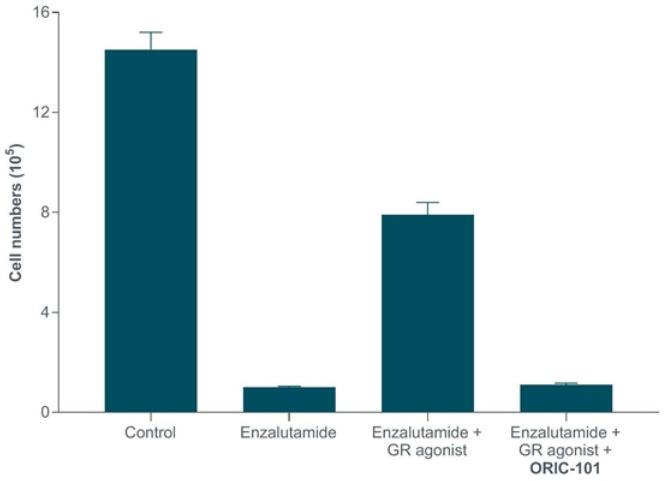
ORIC-101 Reverses Enzalutamide Resistance in an In Vitro Prostate Cancer Model

In Vitro Prostate Cancer Model

AR Inhibition Upregulates GR in Prostate Cancer Cells



ORIC-101 Reverses GR-Driven Enzalutamide Resistance

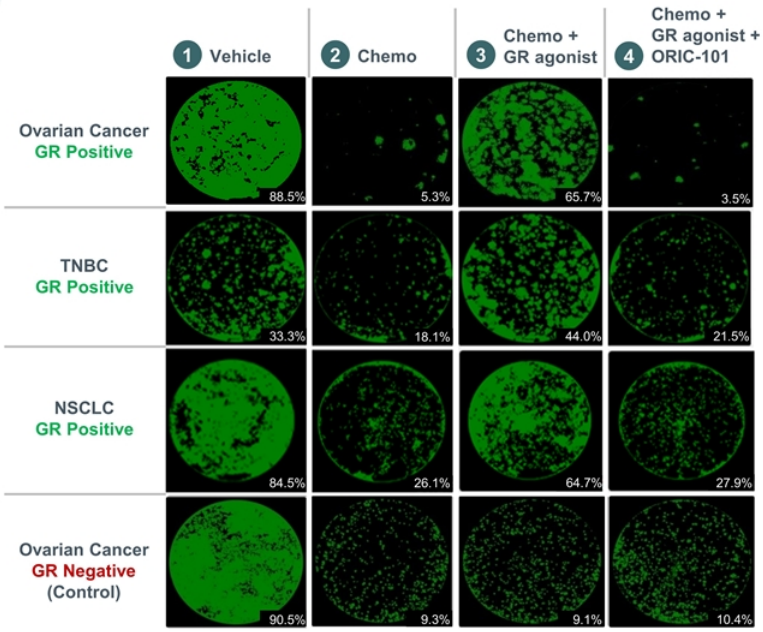


GR activation by glucocorticoid treatment (i.e., dexamethasone) drives enzalutamide resistance in vitro; ORIC-101 resensitizes these prostate cancer cells to enzalutamide

ORIC

Source: Zhou et al. AACR-NCI-EORTC (2019). Note: CWR22PC cells. Left graph: GR mRNA levels relative to untreated samples shown with GR protein levels shown as inset. Actin was used to verify consistent sample loading for the western blot experiment. Right graph: AR agonist R1881 (synthetic AR ligand) added to media. GR agonist used was dexamethasone.

ORIC-101 Overcomes GR-Driven Chemotherapy Resistance Across a Wide Range of Human Cancer Cell Lines



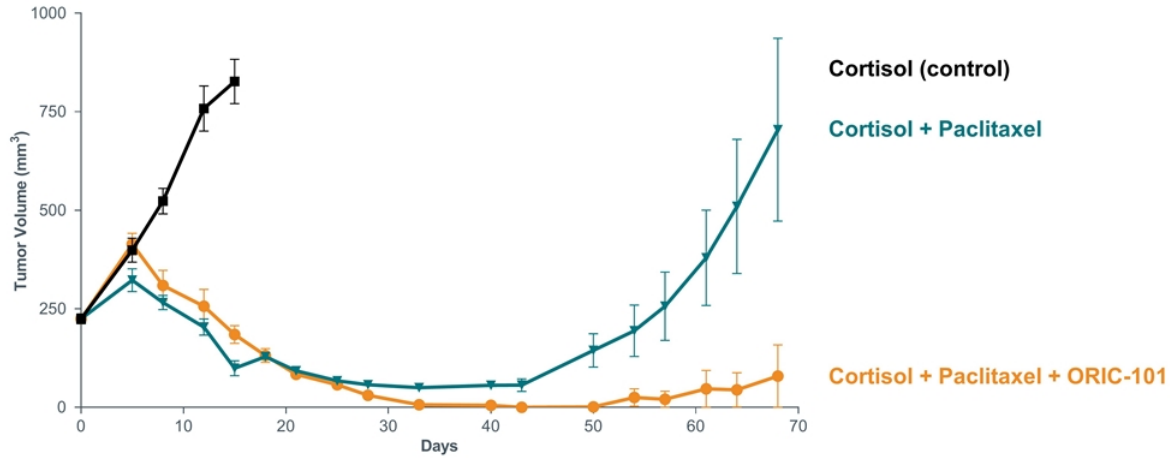
1. Baseline growth of tumor cell colonies in vehicle
2. Chemotherapy alone significantly reduced the number of tumor cell colonies
3. However, chemotherapy in the presence of GR agonist was significantly less effective
4. ORIC-101 reversed this GR-driven chemoprotection in GR-positive cell lines

Green = Tumor cell colony
% = Percentage of plate covered with tumor cell colonies

Source: Jahchan et al. AACR-NCI-EORTC (2017) and additional ORIC data.
Note: Chemotherapeutic agent is gemcitabine for ovarian cancer and paclitaxel for TNBC and NSCLC. GR agonist is dexamethasone.

ORIC-101 Overcomes GR-Driven Resistance to Chemotherapy In Vivo

TNBC Xenograft Model



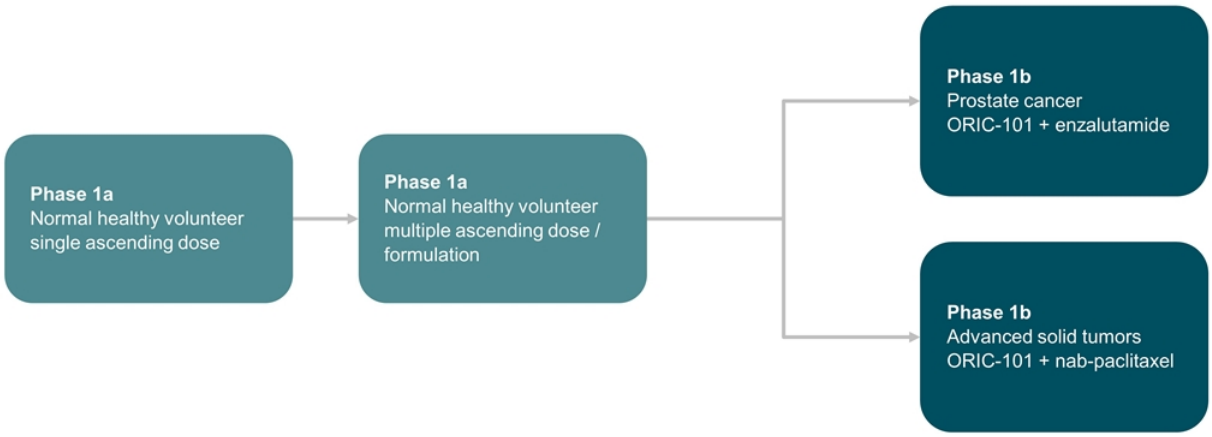
Comparable activity demonstrated in xenograft models of ovarian cancer, TNBC and in combination with other classes of chemotherapy

Source: ORIC data. Note: HCC1806 tumor growth curves. Mice were treated with paclitaxel (20 mg/kg IP, Q3D×8), cortisol (100 mg/L in drinking water, ad libitum) and/or ORIC-101 (75 mg/kg of ORIC-101, PO, BID) starting on Day 0 for the duration of the study. Data is displayed as mean ± SEM. Cortisol supplementation required to activate human GR since primary glucocorticoid utilized by rodents is corticosterone. Cortisol levels intended to simulate physiological corticosteroid levels in humans. TNBC, triple negative breast cancer.

ORIC-101 Is Currently Being Studied in Two Phase 1b Studies

Phase 1a: Single Agent PK, PD, and Safety (Complete)

Phase 1b: Multiple Indications and Combinations



Initial data from nab-paclitaxel combination trial expected in 1H 2021 and from enzalutamide combination trial in 2H 2021

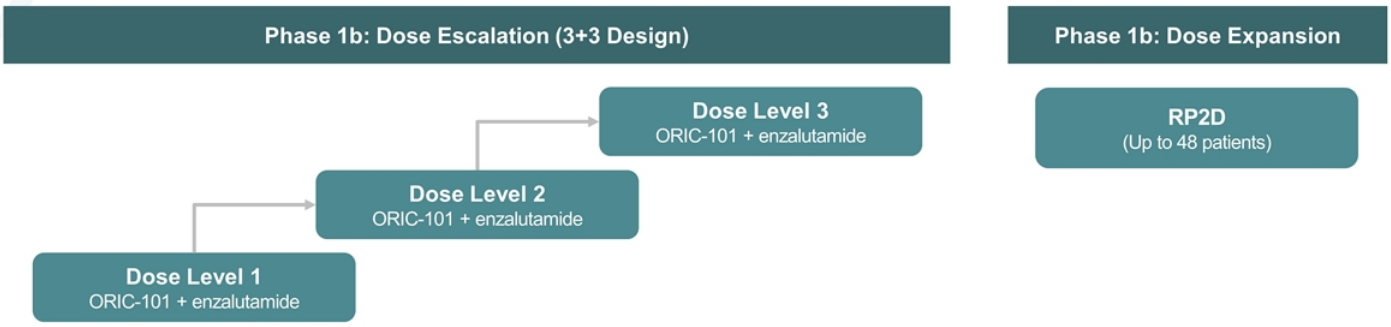
ORIC-101 Demonstrated a Favorable Safety and Tolerability Profile in Phase 1a

Treatment-Emergent AEs	All Doses (n=56)	Multiple Ascending Dose			
		200 mg (n=6)		350 mg (n=6)	
		Grade 1	Grade ≥2	Grade 1	Grade ≥2
Nausea	7	–	–	3	–
Diarrhea	3	–	–	1	–
Abdominal pain	2	–	–	1	–
Dysgeusia	2	–	–	2	–
Dyspepsia	2	–	–	2	–
Fatigue	2	–	–	2	–
Back pain	1	–	–	–	–
Catheter site swelling	1	–	–	–	–
Decreased appetite	1	–	–	1	–
Dry eye	1	–	–	–	–
Gastroesophageal reflux disease	1	–	–	1	–
Headache	1	–	–	–	–
Hot flush	1	–	–	1	–
Insomnia	1	–	–	–	–
Musculoskeletal chest pain	1	1	–	–	–
Pain in extremity	1	–	–	–	–
Proctalgia	1	–	–	1	–
Somnolence	1	–	–	1	–
Vomiting	1	1	–	–	–

All adverse events observed across Phase 1a studies were limited to Grade 1;
higher rate of GI events at 350 mg attributed, at least in part, to pill burden of the early clinical formulation (7 capsules)

Source: ORIC data.
Note: Severity grade as per the National Cancer Institute Common Terminology Criteria for Adverse Events (CTAE) v.5.0.

Phase 1b Trial of ORIC-101 in Combination with Enzalutamide in Patients with Metastatic Prostate Cancer



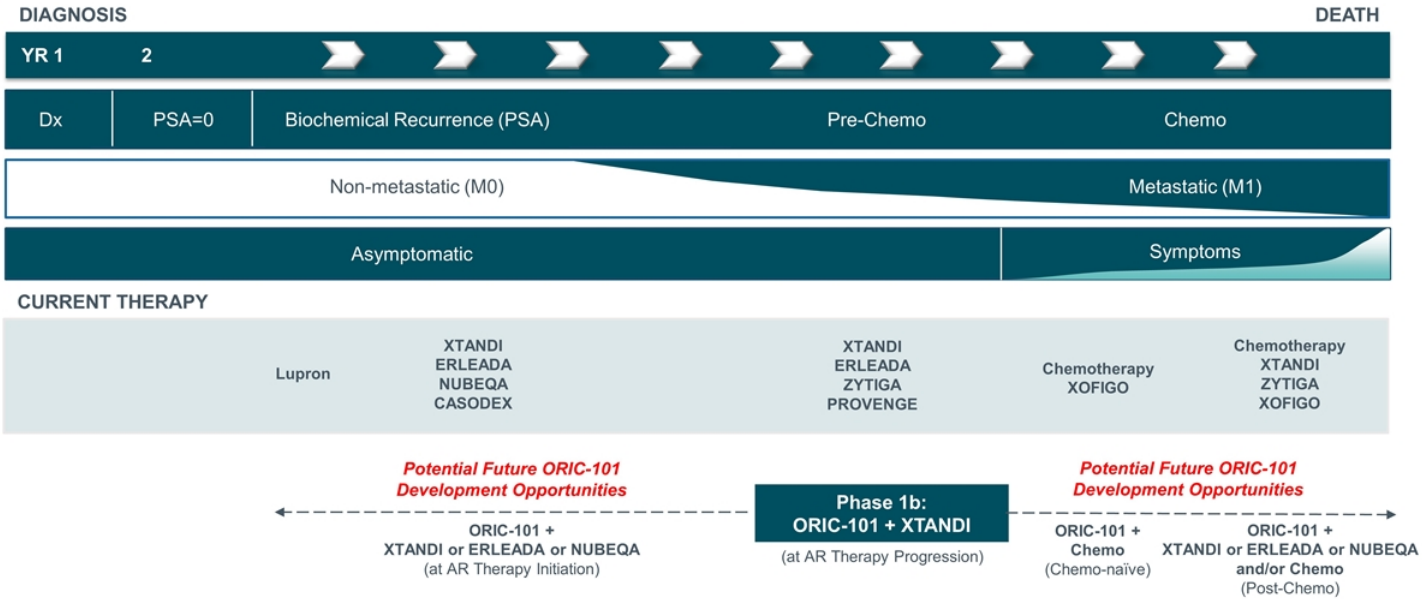
- **Patients:** Chemo-naïve metastatic prostate cancer with evidence of disease progression on enzalutamide
  - Patients will enroll while remaining on enzalutamide (i.e., no treatment-free period)
  - Exclusion of patients with rapid progression on enzalutamide (1)
  - Enrollment not limited by baseline GR status
- **Objectives:** Safety, PK, PD and initial evidence of clinical activity (e.g., PSA decline, imaging, CTC conversion)
  - Exploratory GR, AR and other biomarker data generated from archival tumor tissue; pre-, post- and end-of treatment biopsies and blood
- **Collaboration:** Trial is being conducted under a clinical trial collaboration with Astellas
- **Provisional Recommended Phase 2 Dose (RP2D):** ORIC-101 (240 mg QD) + enzalutamide (160 mg QD)

Interim safety, efficacy and translational data expected in 2H 2021

Note: IHC, immunohistochemistry. PSA, prostate-specific antigen. CTC, circulating tumor cell.
(1) Rapid progression defined as progression within 3 months of starting enzalutamide therapy.

Multiple Pathways Exist for Future Development of ORIC-101 in Prostate Cancer

Illustrative Prostate Cancer Treatment Landscape



Potential Future ORIC-101 Development Opportunities

ORIC-101 + XTANDI or ERLEADA or NUBEQA
(at AR Therapy Initiation)

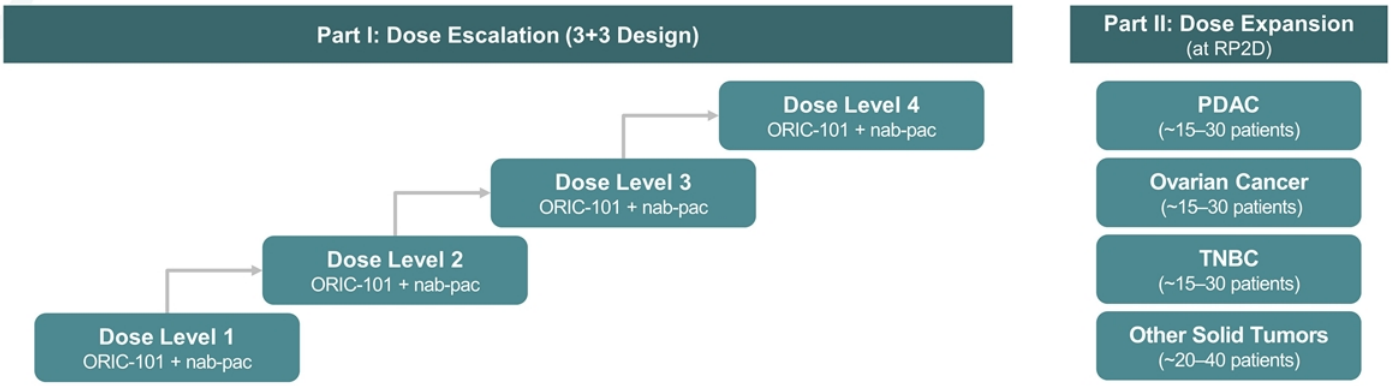
Phase 1b: ORIC-101 + XTANDI
(at AR Therapy Progression)

Potential Future ORIC-101 Development Opportunities

ORIC-101 + Chemo
(Chemo-naïve)

ORIC-101 + XTANDI or ERLEADA or NUBEQA and/or Chemo
(Post-Chemo)

Expansion Portion of Phase 1b Trial of ORIC-101 in Combination with Abraxane in Advanced Solid Tumors Ongoing



- **Patients:**
  - Part I (dose escalation): Advanced solid tumors completed
  - Part II (dose expansion): Previous progression on taxane-containing regimen, independent of baseline GR status
- **Objectives:** Safety, PK, PD and preliminary antitumor activity
  - Exploratory GR and other biomarker data generated from archival tumor tissue; pre-, post- and end-of treatment biopsies and blood
- **Recommended Phase 2 Dose (RP2D):** ORIC-101 (160 mg QD) + nab-paclitaxel (75 mg/m^2); no prophylactic G-CSF required

Interim safety, efficacy and translational data expected in 1H 2021

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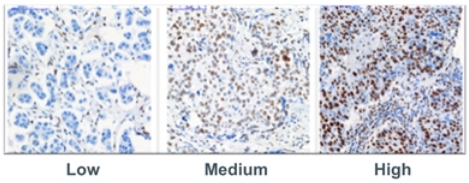
Note: For the RP2D, ORIC-101 will be dosed once-daily on a continuous dosing regimen from day 1 through day 21. Nab-paclitaxel will be dosed on day 1, day 8 and day 15 of a 28-day cycle.
PDAC, pancreatic ductal adenocarcinoma. TNBC, triple negative breast cancer.

ORIC Expects to Broadly Explore Predictive Biomarkers and PD Activity to Determine Patient Selection and Confirm Target Engagement in Phase 1b

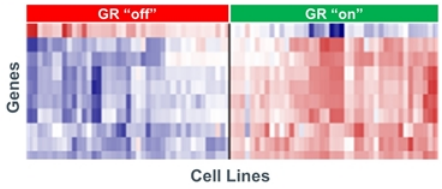
Precision Medicine Strategies Being Explored for ORIC-101

1. **Physiologic biomarkers** to assess GR pathway modulation (e.g., cortisol levels in plasma)
2. **Protein expression** of GR to stratify patient population (e.g., expression in tumors and CTCs by ORIC's IHC)
3. **Transcriptional activation** of GR to monitor pharmacodynamic activity (e.g., activation of ORIC's gene signature in tumors and PBMCs)
4. **Imaging** of GR occupancy to confirm target engagement (e.g., imaging by PET)
5. **Genetic biomarkers** to investigate GR resistance mechanisms (e.g., gene mutations in ctDNA)

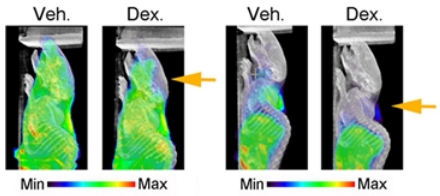
Protein Expression of GR



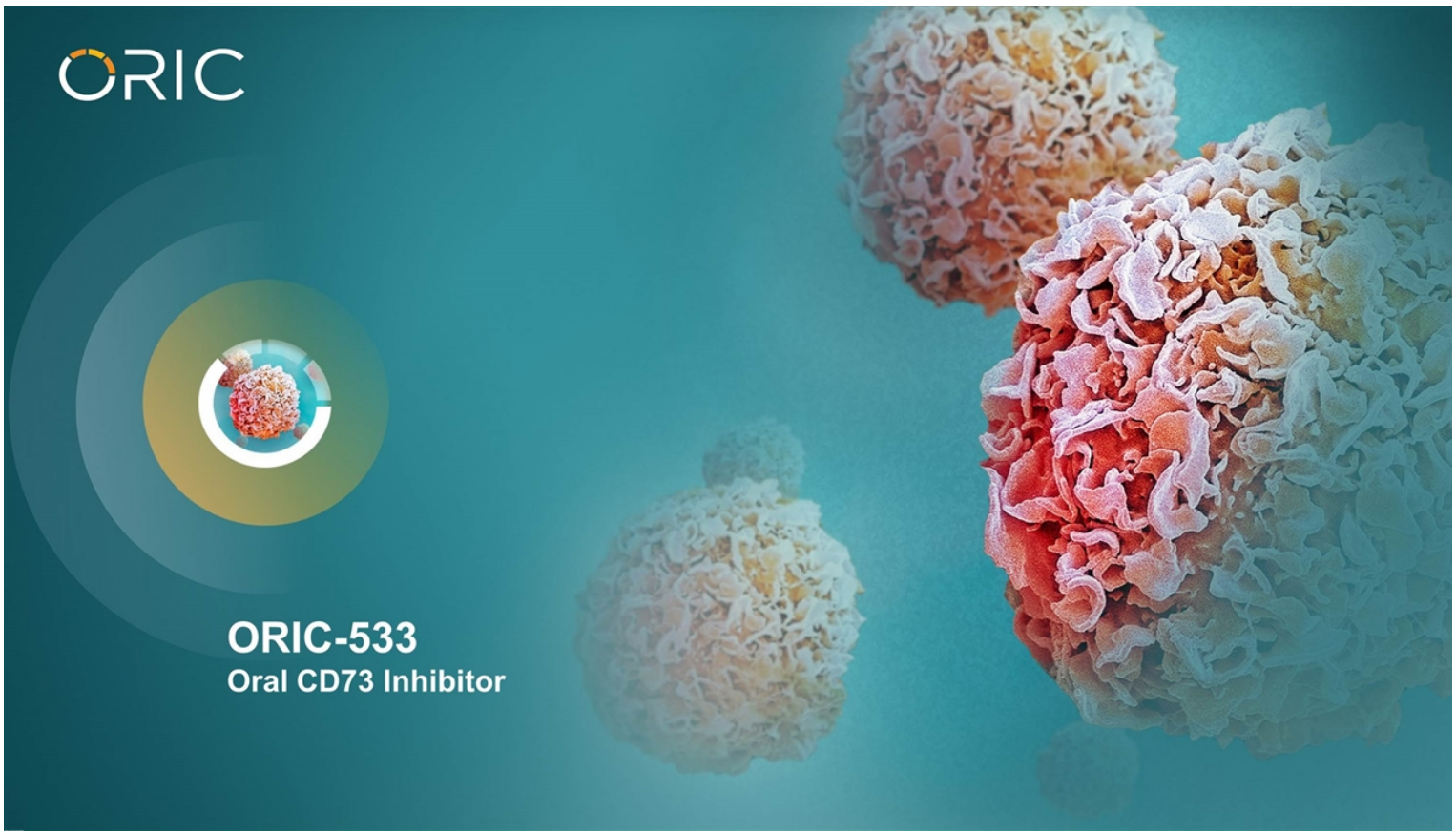
Transcriptional Activation of GR



Imaging of GR (1)



Source: ORIC data. (1) Courtesy of Evans Lab, UCSF.
Note: CTCs, circulating tumor cells. IHC, immunohistochemistry. PBMCs, peripheral blood mononuclear cells. PET: positron emission tomography. ctDNA, circulating tumor DNA.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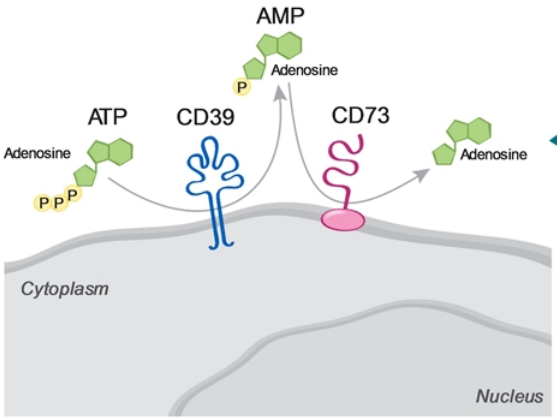
ORIC-533
Oral CD73 Inhibitor

CD73, a Cell Surface Enzyme in the Adenosine Pathway, Has Been Linked to Therapy Resistance

Adenosine Pathway Overview



Increased Adenosine Inhibits:
- T cell priming
- T cell activation / cytolytic activity
- NK degranulation
- Macrophage M1 polarization
- DC maturation / activation

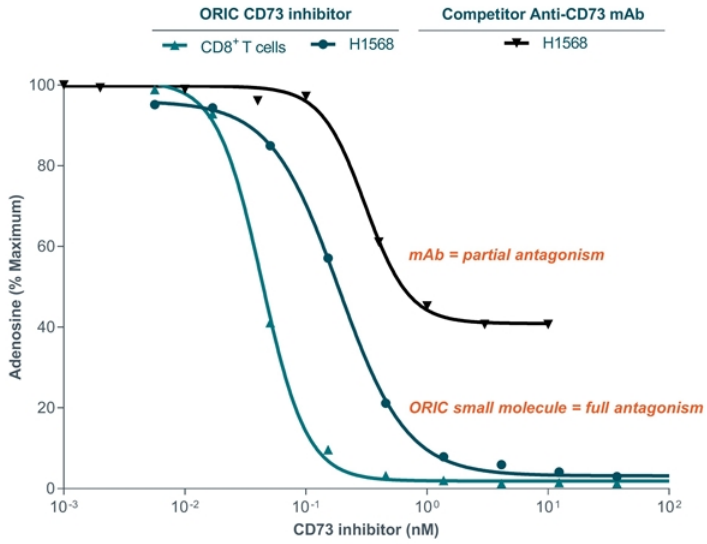
CD73 Background

- Overexpressed across cancer types driving local elevation of adenosine
- Expression is correlated with poor prognosis
- Mediates immunosuppression and chemoresistance via adenosine production
- Upregulated in response to PD-1/L1 and CTLA-4 inhibition

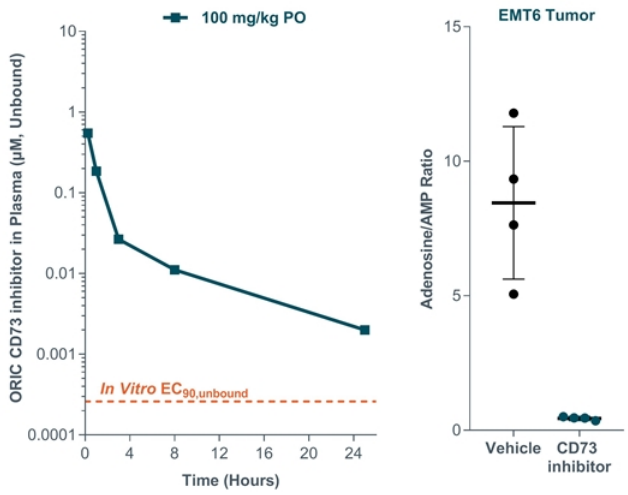
Therapeutic Hypothesis
- ***CD73 inhibition may enhance activity of chemotherapy and immunotherapy***
- ***Small molecule approach is mechanistically distinct from antibodies and may differentiate in safety profile, dosing regimen and tumor penetration***

ORIC Oral CD73 Inhibitors Demonstrate Potent Adenosine Inhibition with Enhanced Activity Over an Antibody-Based Approach

ORIC-533 Analogue Suppresses Adenosine Production In Vitro



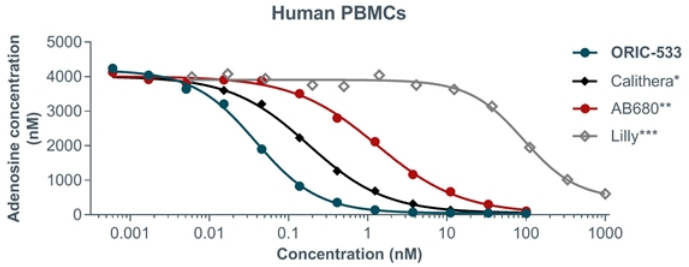
Oral Administration of ORIC-533 Analogue Maintains Exposure and Reduces Adenosine in Tumors In Vivo



Source: ORIC data. In vivo data shown using in EMT6 model.

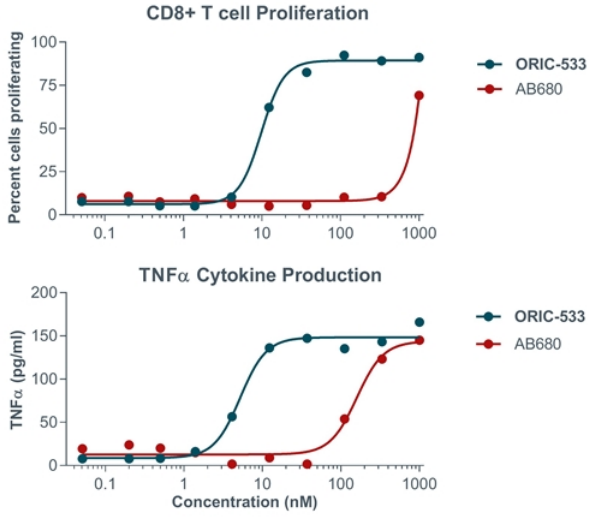
Preliminary Evidence of ORIC-533 Differentiation versus Competitor Small Molecule Compounds

ORIC-533 Potently Blocks Adenosine Production from AMP



Compound	Biochem IC50 (nM)	H1568 ADO EC50 (nM)	CD8+ ADO EC50 (nM)
ORIC-533	**0.1**	**0.1**	**0.1**
Calithera*	0.2	1.3	0.2
AB680**	0.8	5.3	5
Lilly***	48	88	125

ORIC-533 Rescues CD8+ T Cells in 1mM High AMP Environment

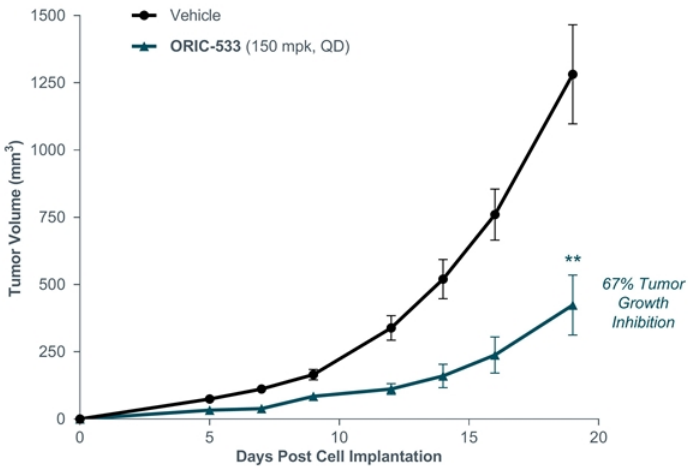


ORIC-533 binds CD73 with high affinity and effectively blocks adenosine-driven immunosuppression high AMP environment

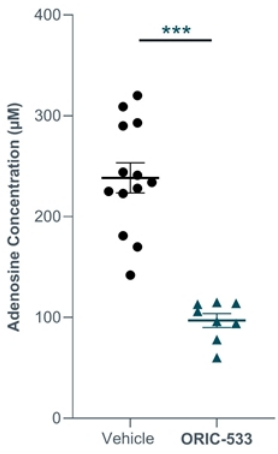
Source: Zavorotinskaya et al. AACR Poster (2020).
Note: *: WO2019246403A1 Compound 9. **: Bowman *et al*, 2019. ***: WO2019168744A1 Example 2. PBMC, peripheral blood mononuclear cell.

CD73 Inhibitor ORIC-533 Demonstrates Significant Single Agent Inhibition of Tumor Growth and Reverts Intratumor Immunosuppression with Oral Dosing In Vivo

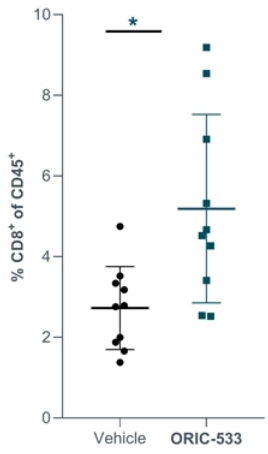
Once-Daily Oral ORIC-533 Showed Single Agent Efficacy



Tumor Adenosine

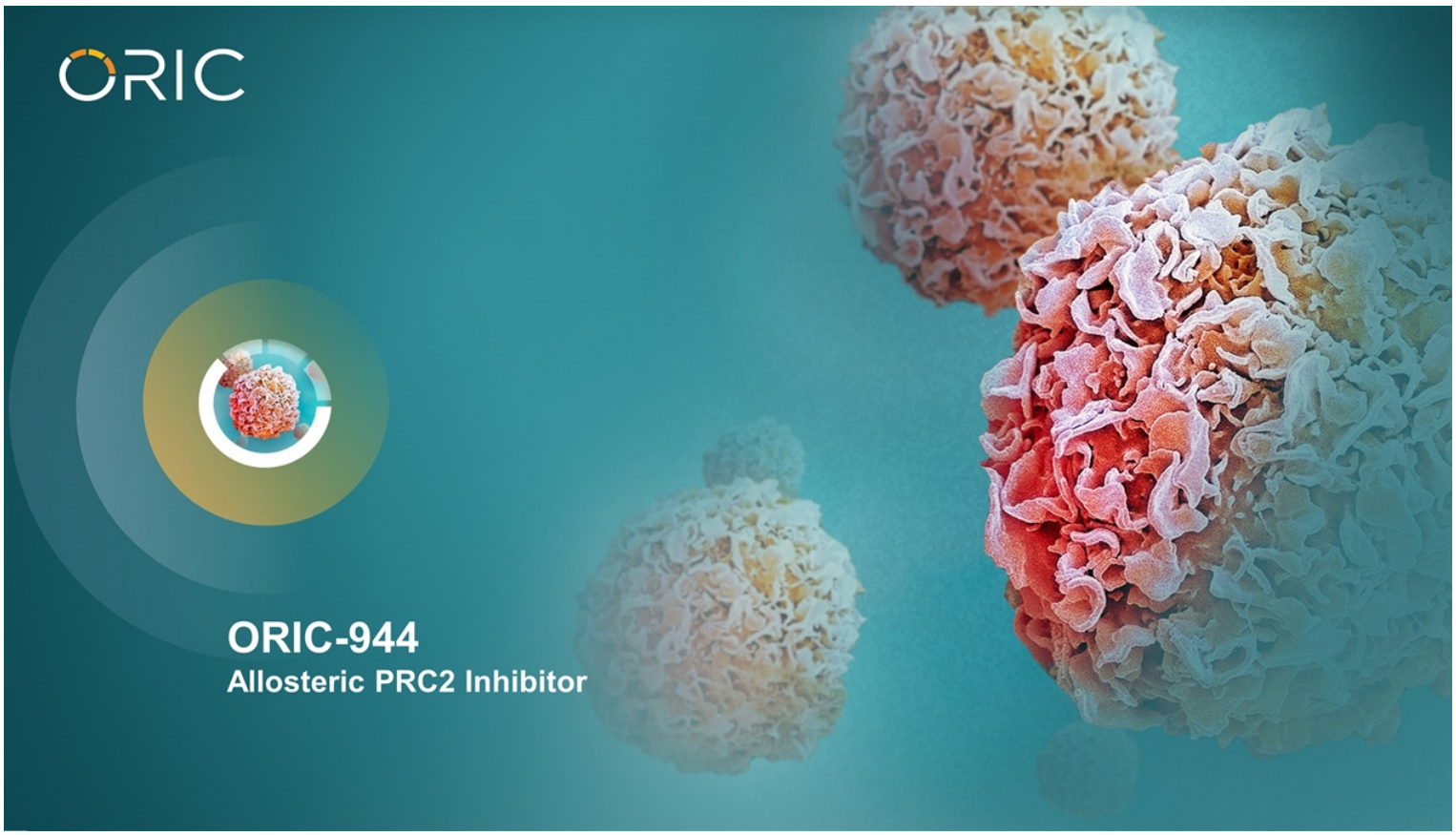


Tumor T Cell Abundance



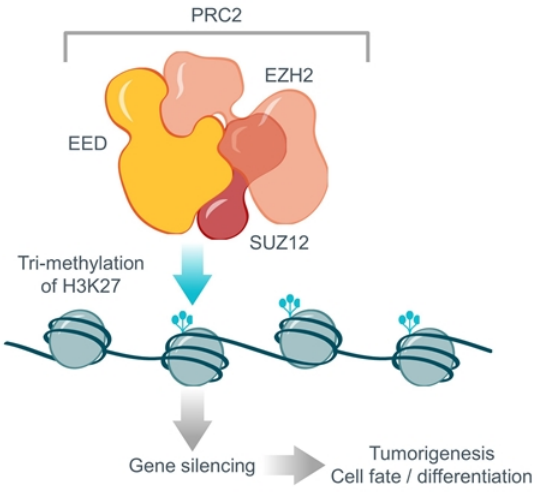
ORIC-533 IND filing expected in 1H 2021, after which a single agent clinical development path will be pursued in an undisclosed tumor type

Source: Chan et al. AACR Poster (2020).
Note: Syngeneic EG7 tumor model. *: p<0.05. **: p = 0.0006. ***: p < 0.0001.


ORIC
ORIC-944
Allosteric PRC2 Inhibitor

PRC2 Plays Pivotal Role in Transcriptional Regulation and Cancer

PRC2 Function



PRC2 Background

- Two druggable subunits:
  - EED: responsible for histone binding; target of ORIC-944
  - EZH2: responsible for histone methylation; target of first-generation inhibitors
- Dysregulation of PRC2 linked to several cancers
  - Decreased expression of target genes associated with poor prognosis in prostate cancer (1)
- First-generation inhibitors, designed to inhibit EZH2, have demonstrated promising clinical activity
  - Approved for epithelioid sarcoma and follicular lymphoma
  - Limited progress made for treatment of prostate cancer

PRC2 is a validated oncogenic target across several cancers with promising therapeutic potential in prostate cancer, among other indications

ORIC

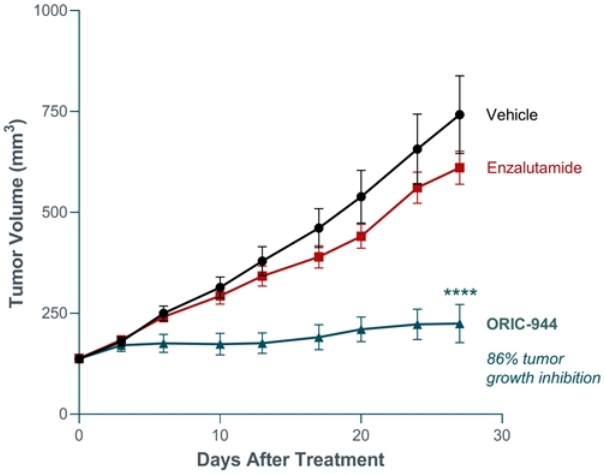
Note: EZH1, enhance of zeste homolog 1. EZH2, enhance of zeste homolog 2. EED, embryonic ectoderm development. SUZ12, suppressor of zeste 12. H3K27, histone H3 at lysine 27.
(1) Yu et al. Cancer Res. (2007).

ORIC-944 Targets the EED Subunit and Has Demonstrated Strong Single-Agent Activity in Enzalutamide-Resistant Prostate Cancer Models

Allosteric PRC2 Inhibition through EED May Improve Upon EZH2 Inhibitors

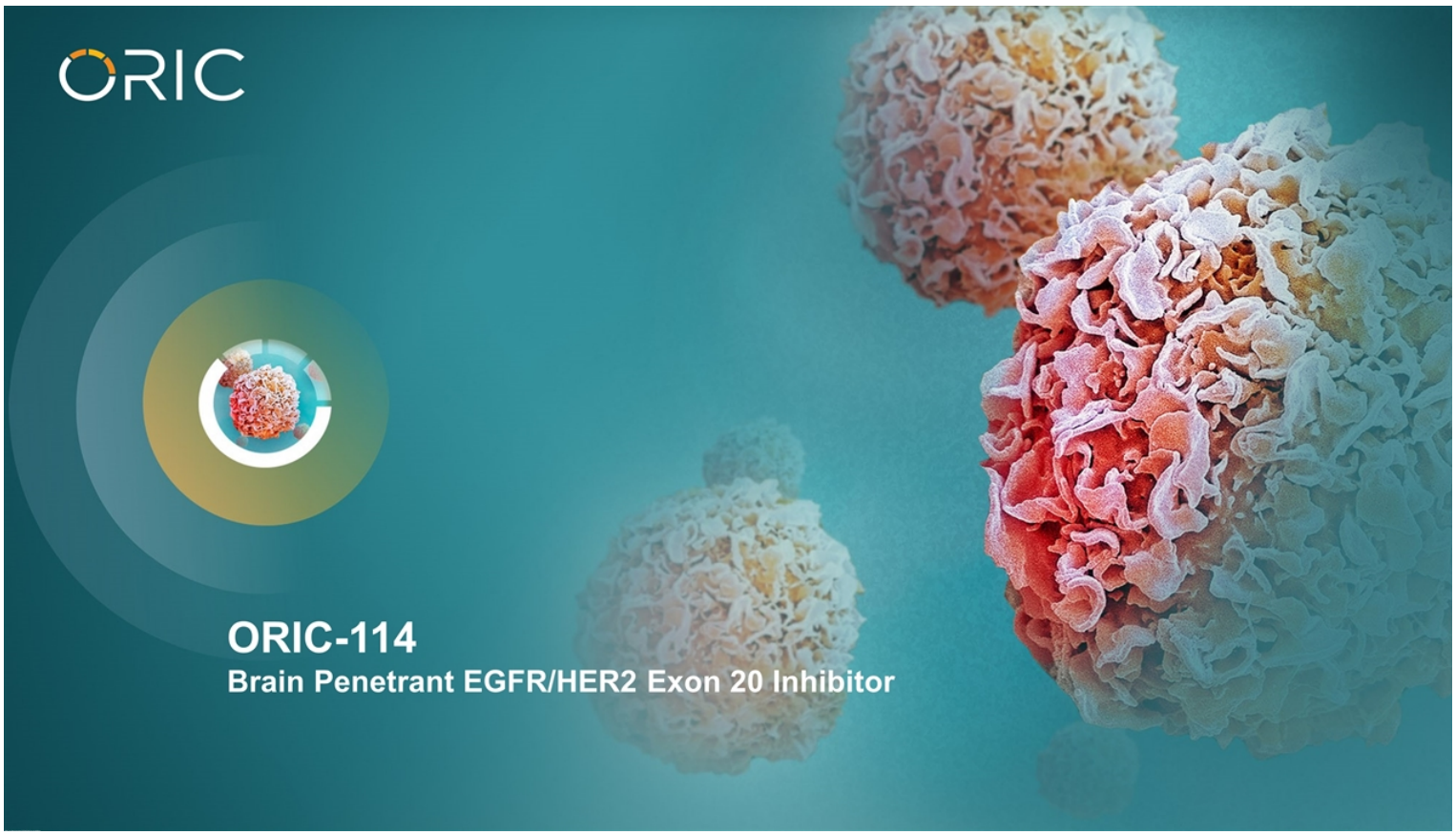
- ORIC-944 allosterically inhibits PRC2 by targeting EED
- Allosteric inhibition of PRC2 through EED may address limitations of EZH2 inhibitors
  - Active against EZH2 innate resistant PRC2 mutants (1)
  - Prevent acquired resistance through secondary mutations in EZH2 (2)
  - Inhibit compensatory bypass activity of EZH1 (3)
- ORIC-944 is associated with improved drug properties over other PRC2 inhibitors (4)
- ORIC-944 appears more effective than EZH2 inhibitors in prostate cancer models based on ORIC research

Demonstrated Strong Single-Agent Activity in Enzalutamide-Resistant Prostate Cancer Models



In vivo efficacy with ORIC-944 observed in multiple prostate cancer models; Along with improved drug properties, positions ORIC-944 as potential best-in-class PRC2 inhibitor for prostate cancer – IND filing expected 2H 2021

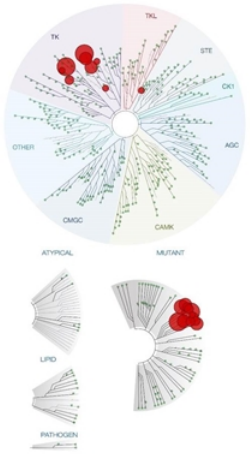
Source: ORIC data on file. Enzalutamide dose used was 30mg/kg QD. ****p < 0.0001. (1) Qi et al. Nat Chem Biol (2017). (2) Bisserier et al. Blood (2018). (3) Shen et al. Mol Cell (2008) and Honma et al. Cancer Sci (2017). (4) Italiano et al. Lancet Oncol (2018), Harb et al. TAT (2018) and Yap et al. Clin Cancer Res (2019).


ORIC
ORIC-114
Brain Penetrant EGFR/HER2 Exon 20 Inhibitor

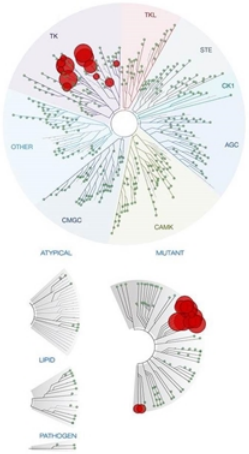
ORIC-114 Was Designed to Selectively Target EGFR and HER2 with High Potency Against Exon 20 Insertion Mutations

Head-to-Head Kinome Selectivity Profiling

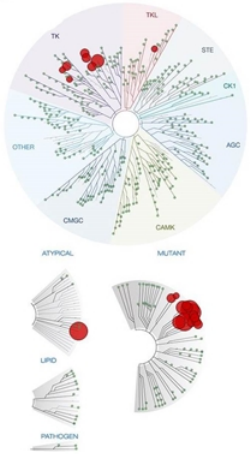
TAK-788



Poziotinib

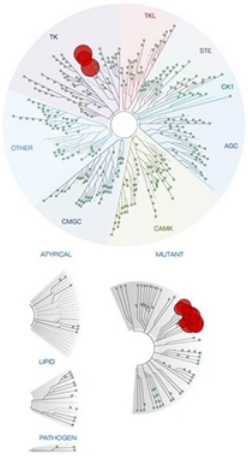


CLN-081



vs.

ORIC-114

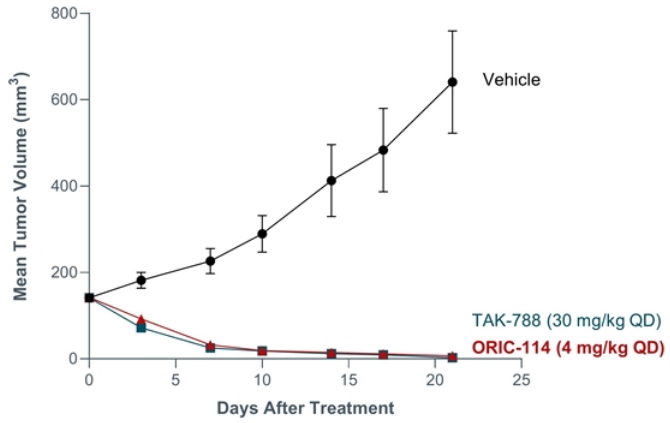


Source: Data on file. Note: All kinome selectivity screens conducted in 468 kinases at 1µM. Top 10% shown.

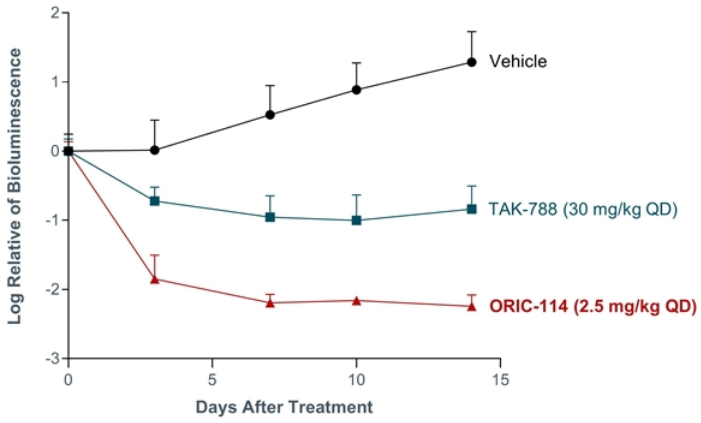
ORIC-114 Demonstrates Potent In Vivo Activity in an EGFR Exon 20 Insertion Model and Intracranial EGFR Mutant Model

In Vivo Efficacy

NSCLC EGFR Exon 20 Insertion Model



Intracranial NSCLC EGFR Mutant Model

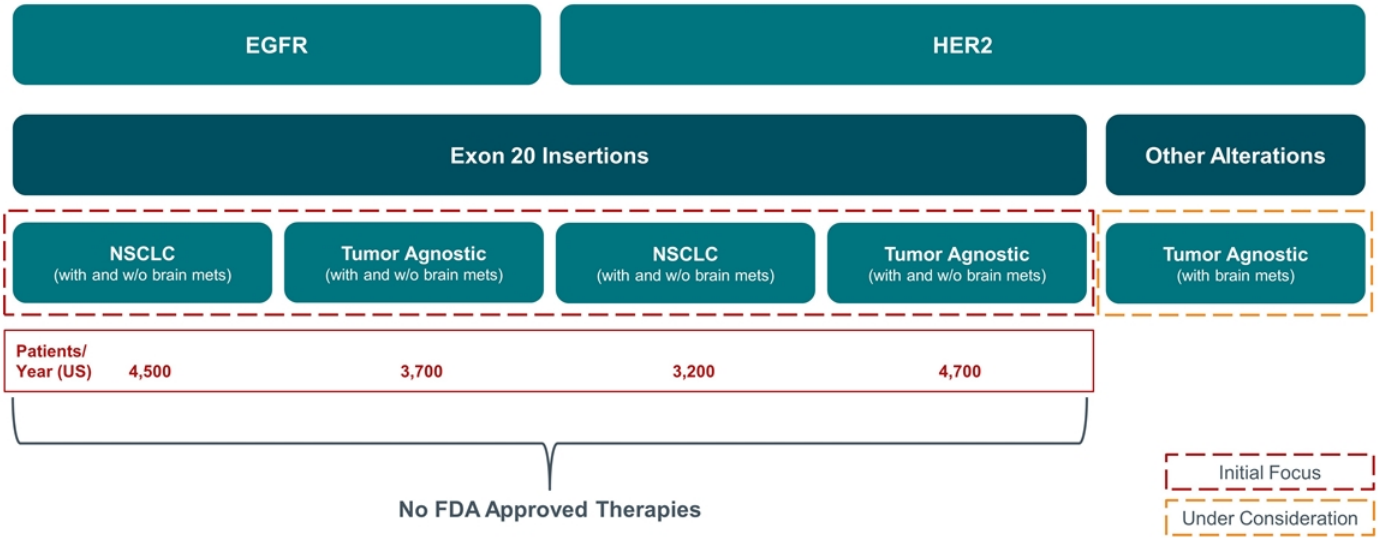


ORIC-114 demonstrates potent tumor regression in an exon 20 insertion model at lower doses than TAK-788 and has potential to treat patients with brain metastases, which may represent approximately one-third of the exon 20 insertion population – CTA filing expected 2H 2021

Source: Data on file. Patil et al. Clin Lung (2020). Note: Left graph shows a NSCLC EGFR exon 20 insertion in vivo model in NPH variant. Right graph shows an intracranial NSCLC EGFR exon 19 deletion mutation in vivo model. Quantification of the bioluminescence photon flux in mice with intracranial PC9-Luc tumors.

There Are Multiple Potential Areas for Development with ORIC-114

Potential Development Opportunities for ORIC-114

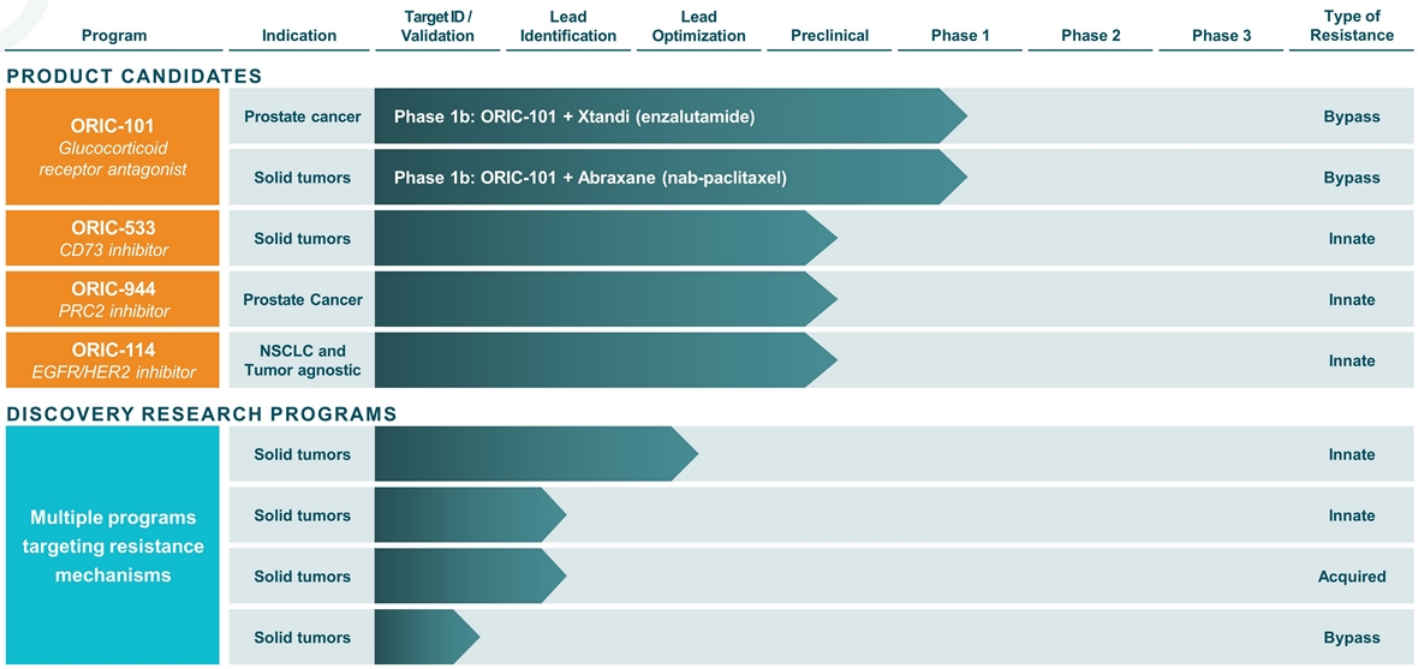


ORIC-114 is expected to be studied as a single agent across multiple areas of unmet need using a tumor agnostic approach; Exon 20 insertions in NSCLC may represent over 7,500 patients in the US annually plus an additional 8,500 patients across other cancers

ORIC

Source: Heymach et al. WCLC Presentation (2018).

Broad Pipeline Targeting Multiple Resistance Mechanisms



ORIC Vision: Become a Leading Oncology Company at the Forefront of Overcoming Resistance In Cancer

Experienced Leadership	• Heritage of discovering and developing multiple approved oncology medicines at Ignyta, Medivation, Aragon and Genentech
Lead Program Targeting Multiple Large Indications	• Two clinical trials focused on resistance to anti-androgen treatment in prostate cancer and resistance to chemotherapy in solid tumors • Preliminary POC by competitor compound not optimized for oncology
Broad Pipeline	• Fully integrated discovery and development team advancing internally-discovered and externally-sourced pipeline beyond lead program
Multiple Upcoming Catalysts	• Data from multiple clinical trials evaluating distinct mechanisms of resistance expected in 2021 • Three IND/CTAs expected in 2021
Strong Financial Foundation	• Existing cash, cash equivalents and marketable securities expected to fund current operating plan into 2H 2023
Anticipated Milestones and Clinical Updates	• **ORIC-101**: Phase 1b with Xtandi in metastatic prostate cancer — Interim safety, efficacy and translational data: 2H 2021 • **ORIC-101**: Phase 1b with Abraxane in solid tumors — Interim safety, efficacy and translational data: 1H 2021 • **ORIC-533**: IND filing: 1H 2021 • **ORIC-944**: IND filing: 2H 2021 • **ORIC-114**: CTA filing: 2H 2021

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