



OVERCOMING RESISTANCE IN CANCER

**Business Update
ASCO 2021**

June 2, 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. Forward-looking statements contained in this presentation also include, but are not limited to, statements regarding: the continued clinical development of ORIC-101 in combination with nab-paclitaxel; clinical outcomes, which may materially change as patient enrollment continues or more patient data become available; the potential impact of competitor data on our programs; the expected timing of reporting updated data from the ORIC-101 clinical trial in combination with nab-paclitaxel and initial data from the ORIC-101 clinical trial in combination with enzalutamide; the expected timing and ability to initiate clinical trials for ORIC-533, ORIC-944 and ORIC-114; the potential benefits of ORIC-101 or our other product candidates; the planned IND filings for ORIC-533 and ORIC-944 and CTA filing for ORIC-114; our anticipated milestones and clinical updates; and the period over which we estimate our existing cash, cash equivalents and investments will be sufficient to fund our current operating plan.

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 results of our preclinical studies and clinical trials; risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use in humans 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, initial, interim, 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; changes in our plans to develop and commercialize our product candidates; 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 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 our 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 investments 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.

This presentation also contains interim results based on initial data from the ORIC-101 clinical trial in combination with nab-paclitaxel, including an initial safety analysis and initial antitumor activity analysis, as of the database cutoff date of 21 April 2021. The clinical trial is ongoing, and we have received additional data subsequent to such cutoff date. This presentation does not speak to, and you should make no assumptions about, such additional data. In addition, the information we have chosen to publicly disclose regarding ORIC-101 has been selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise. If the initial data that we report differ from updated, late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, ORIC-101 or any other product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

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.

Except as required by law, we undertake no obligation to update any statements in this presentation for any reason after the date of this presentation.

We have filed 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 preclinical 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 Business Update ASCO 2021

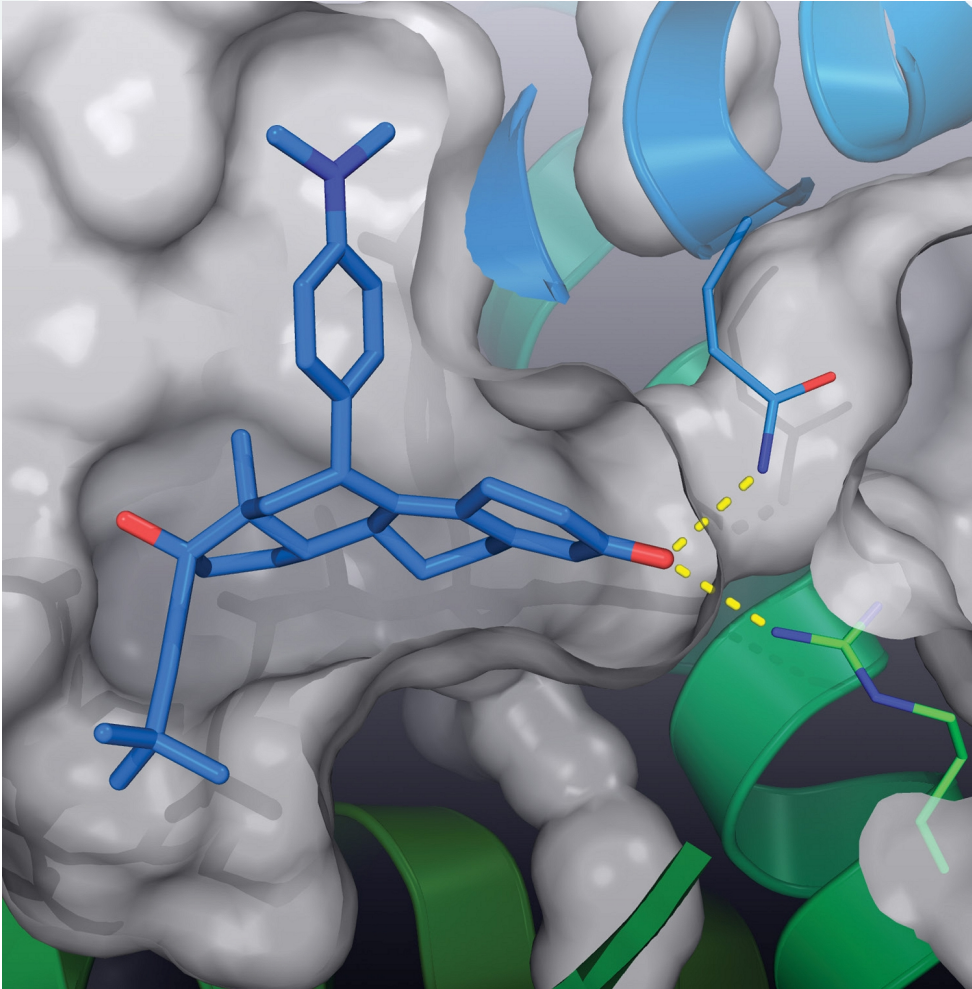
Agenda

- Executive Summary
 - Background on Glucocorticoid Receptor and ORIC-101
 - Initial Data from ORIC-101 Plus Nab-Paclitaxel Phase 1b Trial
 - ORIC-101 Plus Nab-Paclitaxel in Patients with Advanced PDAC
 - Summary and Pipeline Update
-

Participants

- Jacob Chacko, Chief Executive Officer
- Lori Friedman, Chief Scientific Officer
- Pratik Multani, Chief Medical Officer
- Dominic Piscitelli, Chief Financial Officer
- Pamela Munster, Trial Investigator and Senior Author
 - Professor, Department of Medicine (Hematology/Oncology), UCSF

Key Takeaways from the Initial Phase 1b Data of ORIC-101 in Combination with Nab-Paclitaxel in Advanced Solid Tumors



Well Tolerated with Nab-Paclitaxel at RP2D

- TRAEs primarily Grade 1-2; no treatment-related discontinuations
- No requirement for prophylactic G-CSF

PK Demonstrates Excellent Target Coverage and No DDI

- Plasma exposures at RP2D exceed threshold for GR inhibition
- No evidence of drug-drug interaction with nab-paclitaxel

Translational Data Show PD Modulation & High GR Prevalence

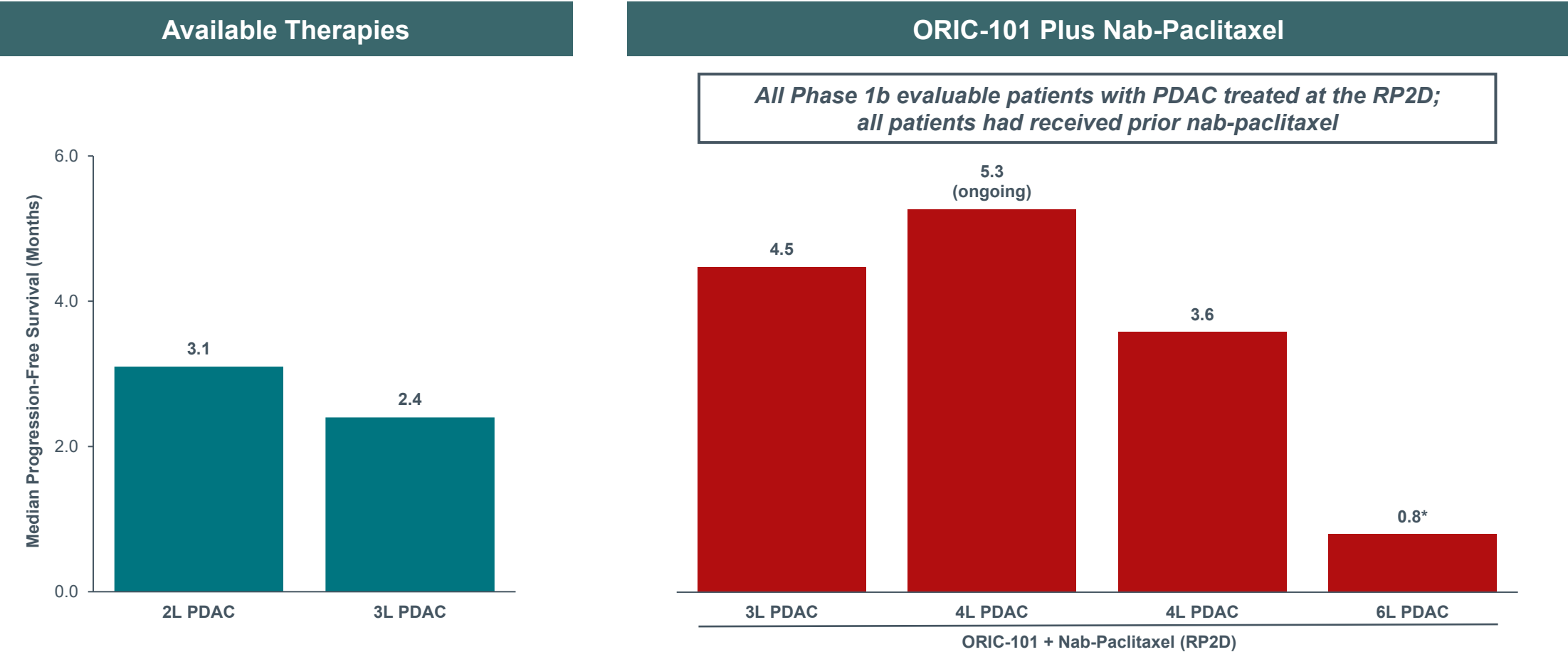
- Achieved consistent suppression of key GR biomarkers
- High rates of GR expression seen in tumor types of interest

Evidence of Antitumor Activity Across Multiple Solid Tumors

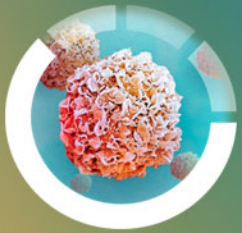
- Tumor regression and prolonged stable disease in heavily pretreated patients, including those previously treated with a taxane-based therapy
- Extended PFS in patients with late-line relapsed pancreatic cancer who had previously progressed on or after nab-paclitaxel

ORIC-101 Plus Nab-Paclitaxel Demonstrated Prolonged PFS in Patients with Late-Line Relapsed Pancreatic Cancer

Progression-Free Survival in Patients with Advanced PDAC



ORIC-101 plus nab-paclitaxel demonstrated longer PFS in patients with late-line relapsed PDAC (all of whom had received prior nab-paclitaxel) than is typically observed with earlier line therapies



Background on Glucocorticoid Receptor and ORIC-101

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

- 1 GR Implicated in Anti-Androgen Resistance in Prostate Cancer
- 2 GR Implicated in Chemotherapy Resistance in Solid Tumors

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

Russell Z. Szmulewitz^{1,*}, Elizabeth Chung¹, Hikmat Al-Ahmadie², Silver Daniel¹, Masha Kocherginsky¹, Aria Razmaria¹, Gregory P. Zagaja¹, Charles B. Brendler³, Walter M. Stadler¹, and Suzanne D. Conzen¹

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,*}

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

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

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

Erica M. Stringer-Reasor^a, Gabrielle M. Baker^c, Maxwell N. Skor^a, Masha Kocherginsky^d, Ernst Lengyel^b, Gini F. Fleming^{a,*}, Suzanne D. Conzen^{a,e,*}

^a Department of Medicine, The University of Chicago, Chicago, IL, United States
^b Obstetrics and Gynecology, The University of Chicago, Chicago, IL, United States
^c Pathology, The University of Chicago, Chicago, IL, United States
^d Health Studies, The University of Chicago, Chicago, IL, United States
^e Ben May Department for Cancer Research, The University of Chicago, Chicago, IL, United States

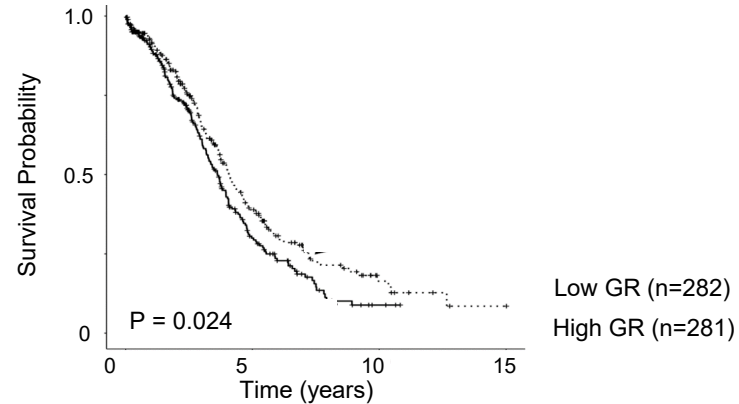
	Therapeutic Area	US Patient Population ⁽¹⁾	Anti-Cancer Treatment	Resistance Mechanism	Potential Solution
1	Prostate cancer	~175,000	AR modulators (e.g., Xtandi, Erleada)	GR bypasses AR signaling	GR Antagonist
2	Solid tumors	~180,000	Chemotherapy (e.g., Abraxane)	GR drives tumor survival and proliferation	

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

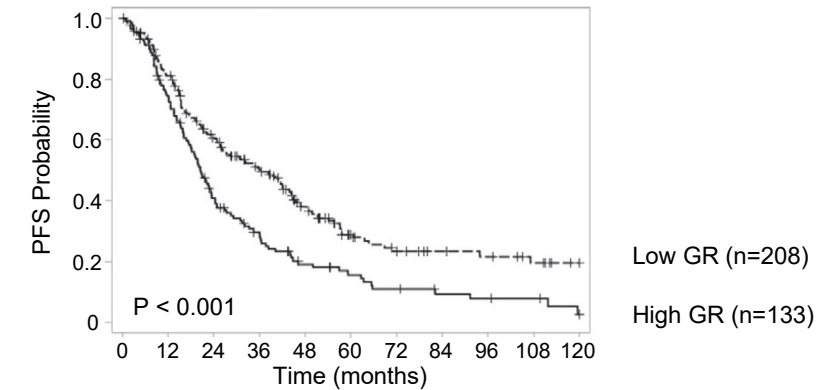
Glucocorticoid Receptor Expression Has Been Associated with Poor Clinical Outcomes in Patients with Solid Tumors

GR Expression Levels in Cancer Patients

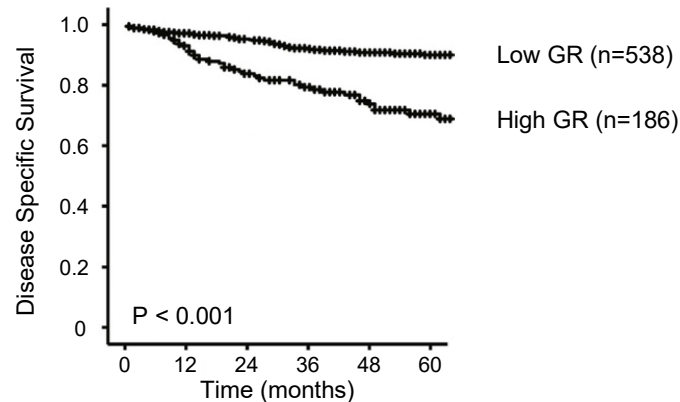
Overall Survival in Ovarian Cancer ⁽¹⁾



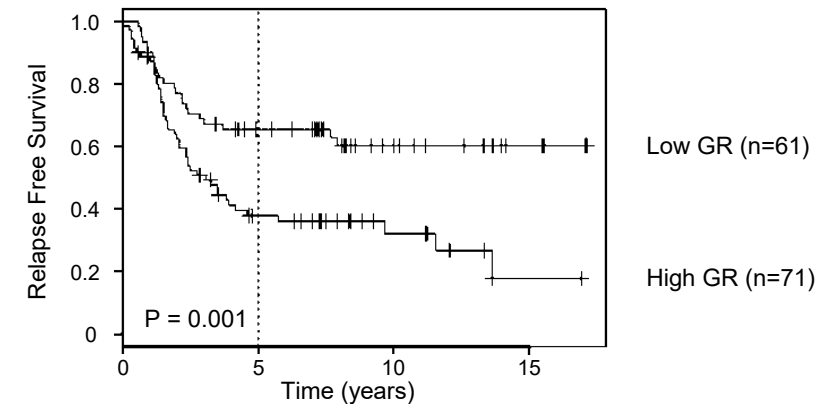
Progression-Free Survival in Ovarian Cancer ⁽²⁾



Disease Specific Survival in Endometrial Cancer ⁽³⁾



Relapse-Free Survival in ER- Breast Cancer ⁽⁴⁾

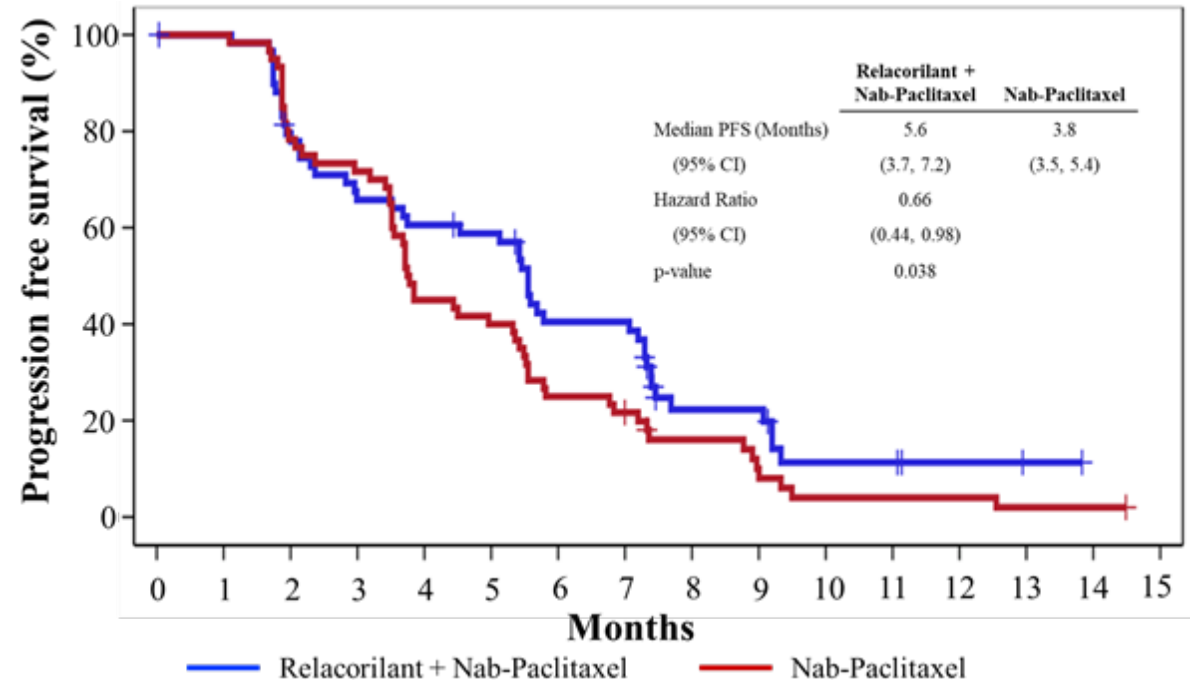


A GR antagonist has the potential to replicate the improved clinical outcomes observed in solid tumor patients with low GR expression

Competitor GR Antagonist Improved Progression-Free Survival in Heavily Pretreated Ovarian Cancer Patients in a Randomized Controlled Phase 2 Trial

Relacorilant Phase 2 Results in Ovarian Cancer

- 3-arm 1:1:1 randomized trial (n=178)
- Primary endpoint: PFS
 - Intermittent: 5.6 months (p=0.038*)
 - Continuous: 5.3 months
 - Control: 3.8 months

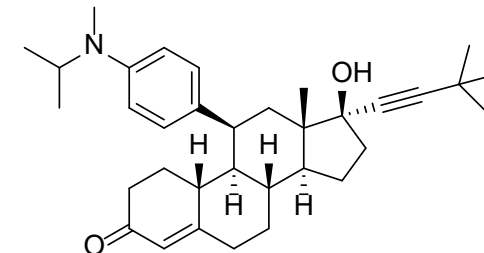


Relacorilant in combination with nab-paclitaxel demonstrated improved progression-free survival in patients with platinum-resistant ovarian cancer

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

In Vitro Profile

	Relacorilant	ORIC-101
GR antagonism IC ₅₀ (nM)	16	7.3
AR agonism IC ₅₀ (nM)	>2500	>2500
PR antagonism IC ₅₀ (nM)	>2500	22
CYP2C8 / 2C9 / 3A4 inhibition IC ₅₀ (nM)	210 / 2,000 / 1,300	>10,000 / >10,000 / 1,600



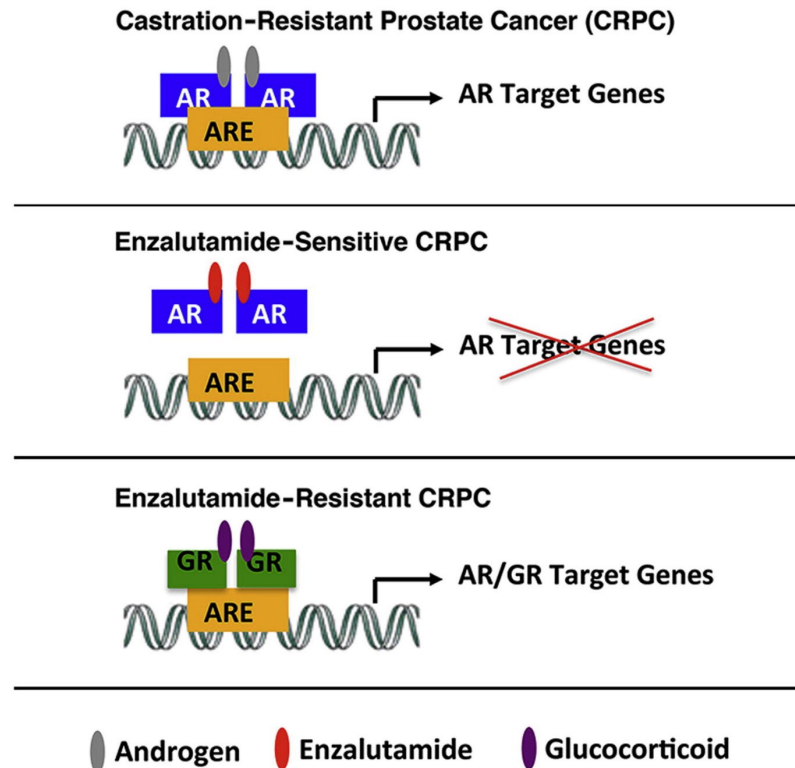
ORIC-101 Potential Advantages

- ✓ More potent GR inhibition
- ✓ PR activity: potential to treat PR+ breast cancers
- ✓ Decreased CYP binding to diminish DDI risk

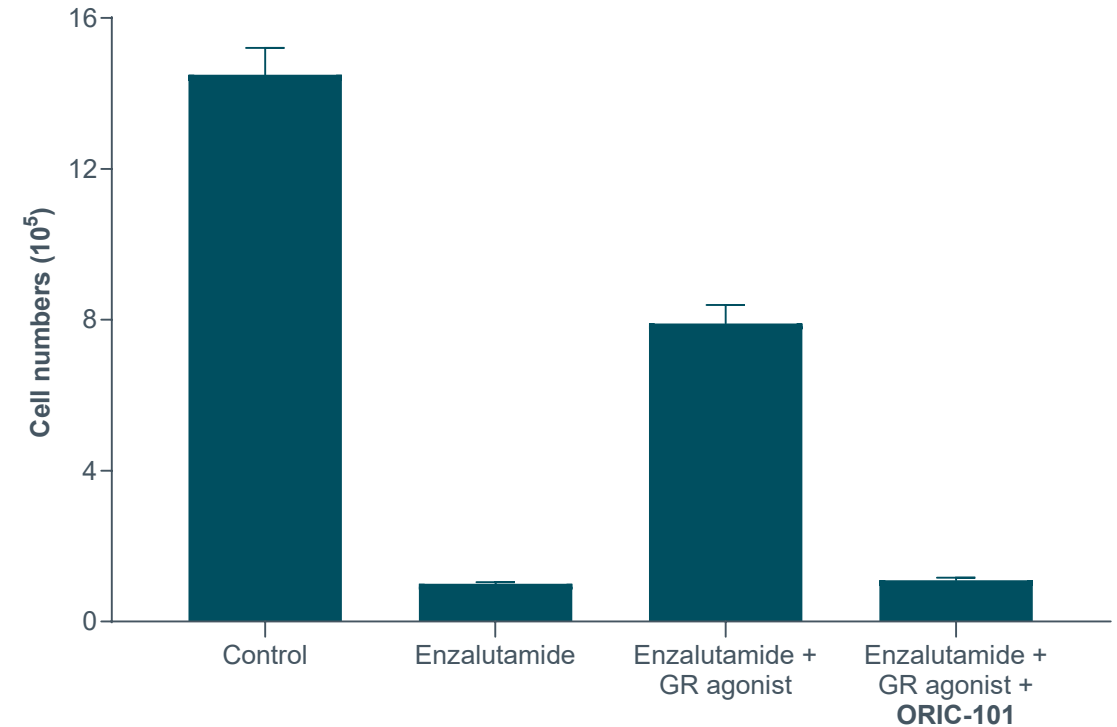
ORIC-101 is a potent and selective GR antagonist with reduced potential for drug-drug interaction versus other GR antagonists

ORIC-101 Overcomes GR-Mediated Resistance to Enzalutamide in Prostate Cancer Models

AR Inhibition Upregulates GR in Prostate Cancer Cells



ORIC-101 Reverses GR-Driven Enzalutamide Resistance

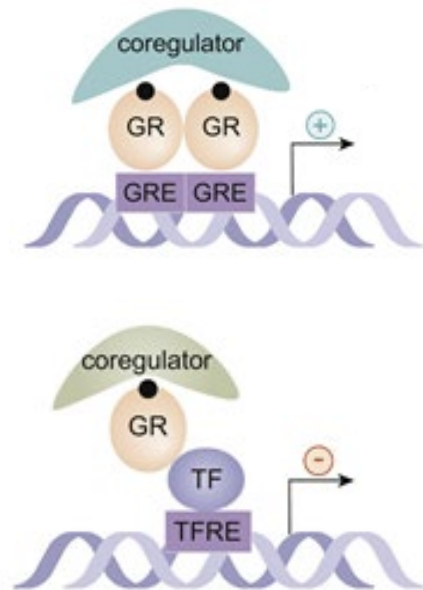


- ORIC-101 also reverses GR-driven resistance to AR PROTAC degraders in preclinical models

GR has been implicated as a bypass mechanism to anti-androgen treatment and a potential therapeutic target for prostate cancer

ORIC-101 Overcomes GR-Mediated Pro-Survival Mechanisms that Lead to Chemotherapy Resistance

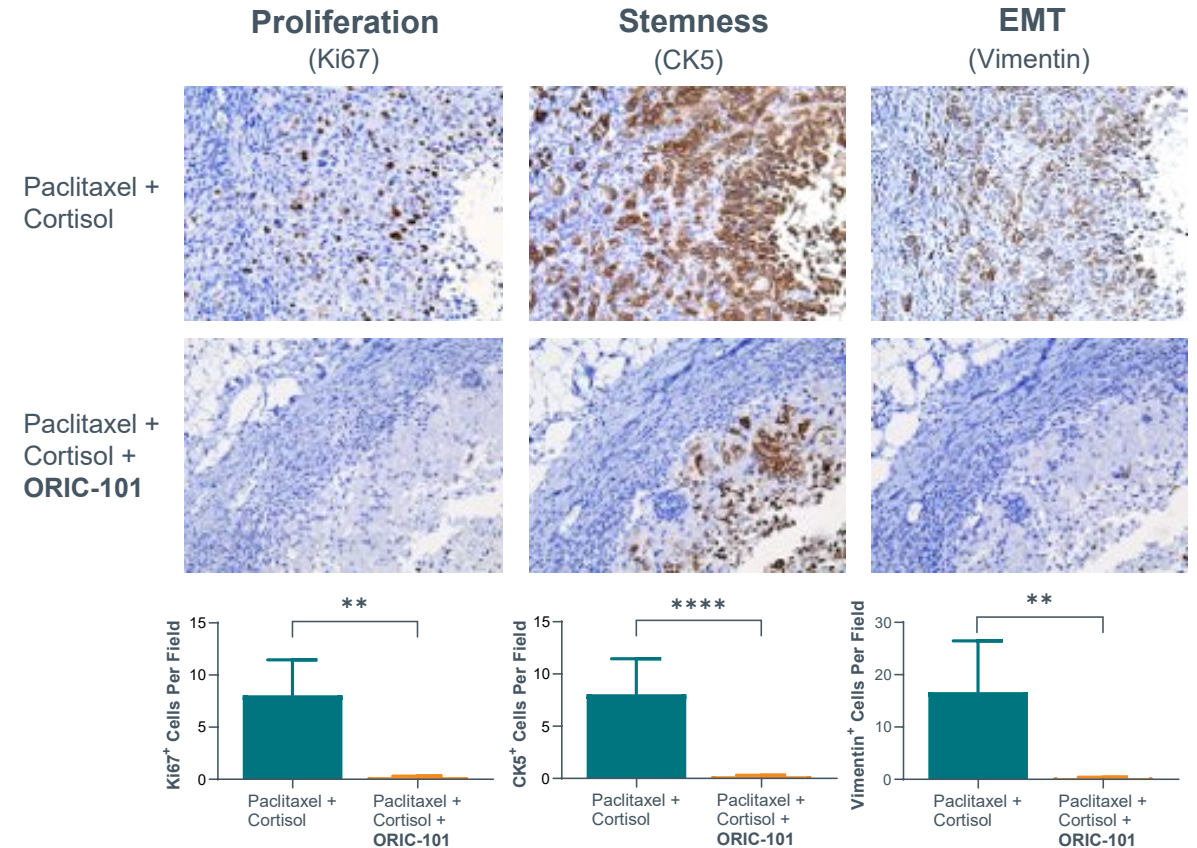
GR Acts as a Pro-Survival Mechanism in Tumors



Pro-Survival Mechanisms

- ↑ **Anti-apoptotic genes**
 - SGK1, DUSP1, BIRC3
- ↑ **Cell cycle promoting genes**
 - AKT, p38-MAPK, Ki67
- ↑ **Mesenchymal genes**
 - SNAI2, FN1
- ↑ **Stemness genes**
 - ALDH1A1, CK5
- ↓ **Pro-inflammatory genes**
 - ALDH1A1, CK5
- ↓ **Cell adhesion genes**
 - ICAM, VCAM

ORIC-101 Reversed EMT-Like Phenotype and Blocked Tumor Growth In Vivo

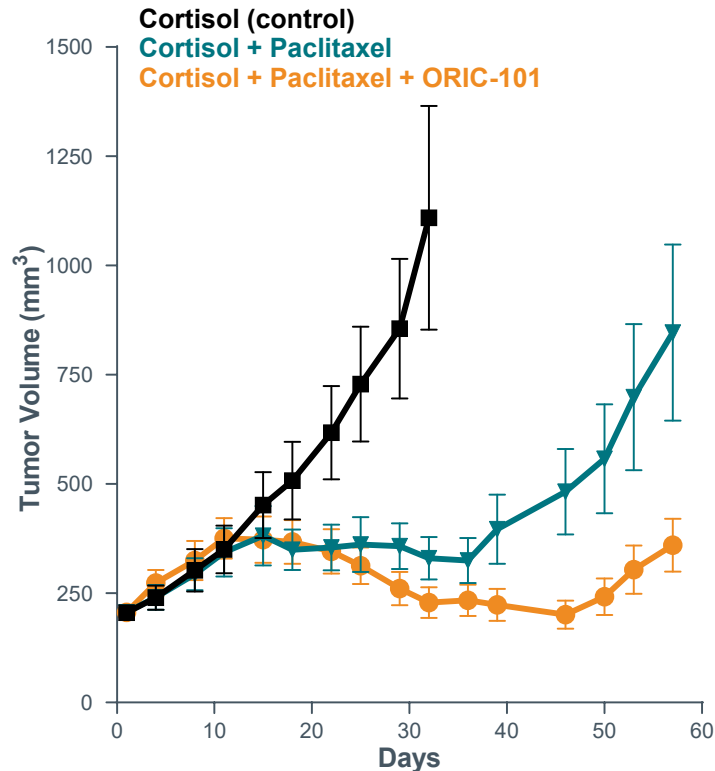


Counteracting GR is expected to block the transcriptional program driving tumor cell survival and therapeutic escape

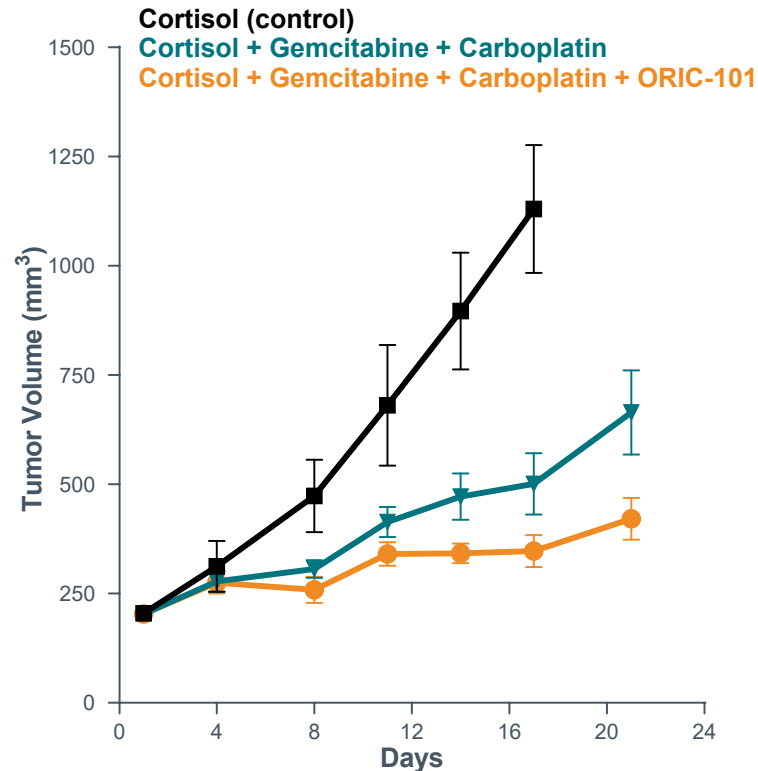
ORIC-101 Overcomes GR-Driven Resistance to Chemotherapy In Vivo

In Vivo Xenograft Models

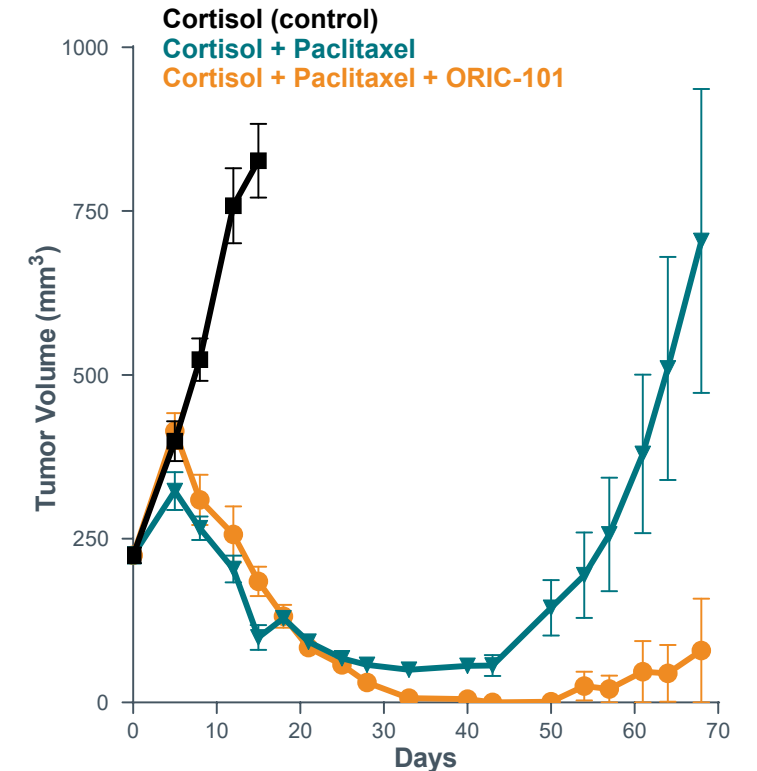
PDAC



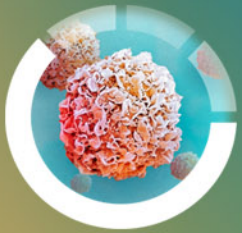
Ovarian Cancer



TNBC



Increased duration of antitumor activity demonstrated in xenograft models of PDAC, ovarian cancer, and TNBC and in combination with multiple classes of chemotherapy



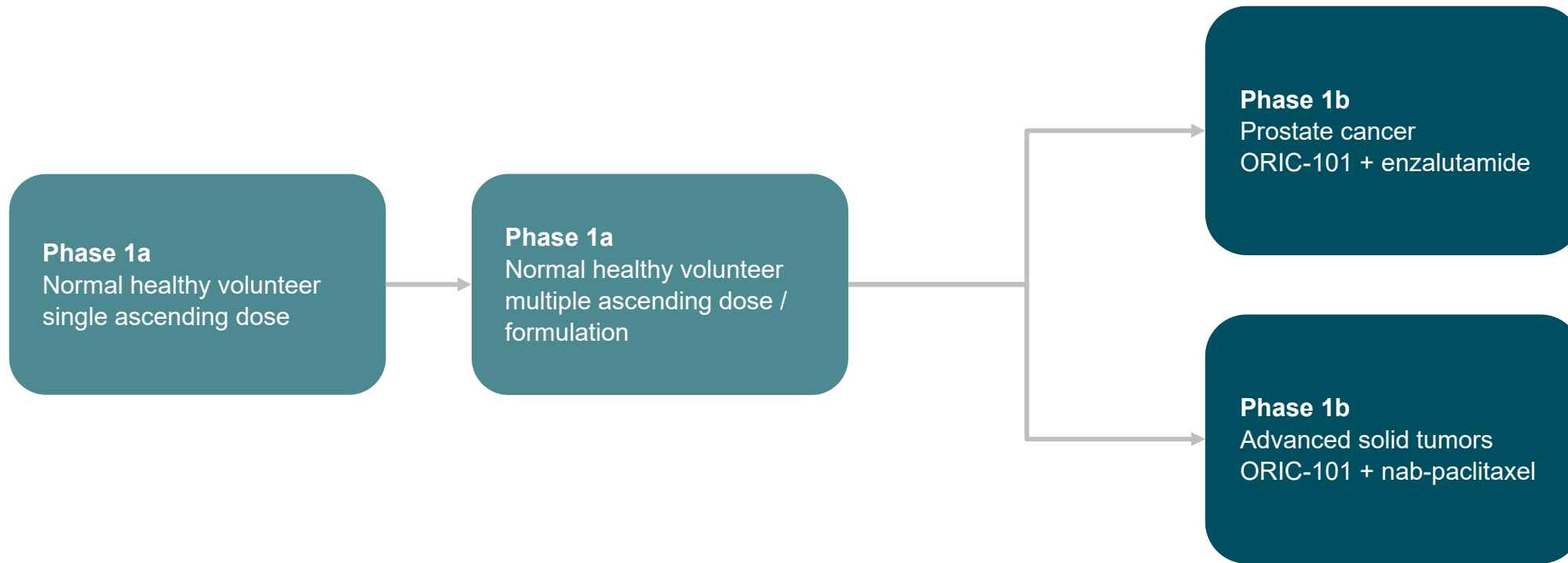
Initial Data from ORIC-101 Plus Nab-Paclitaxel Phase 1b Trial



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



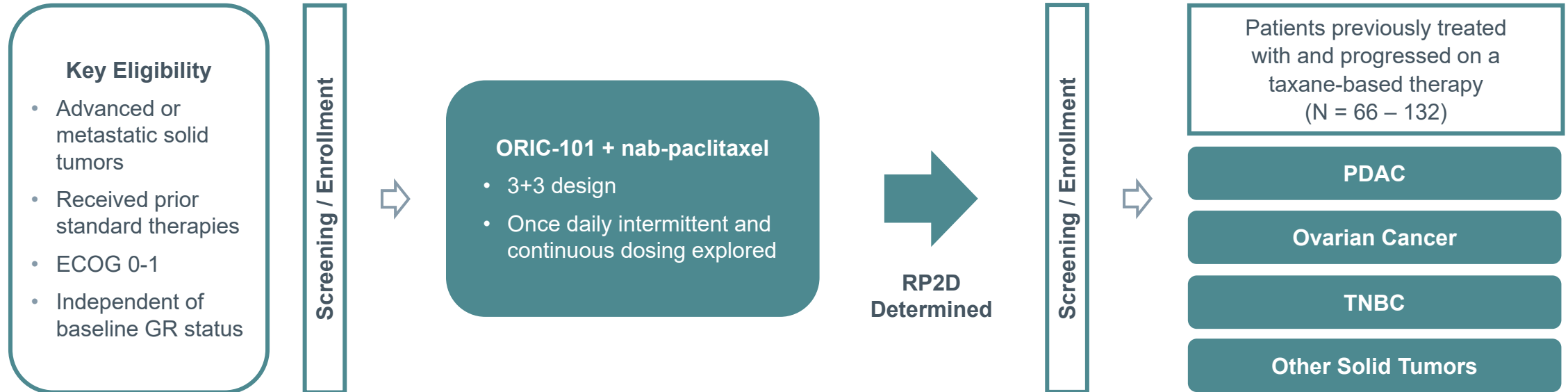
Each Phase 1b study is evaluating a distinct mechanism of action of GR inhibition through ORIC-101

ORIC Phase 1b Study of ORIC-101 Plus Nab-Paclitaxel in Advanced Solid Tumors

Phase 1b, Multicenter, Open-Label Study

Dose Escalation (Part I)

Dose Expansion (Part II)



Primary endpoints: Part I: recommended Phase 2 dose (RP2D); Part II: objective response rate by blinded independent central review

Key secondary endpoints: Part I: PK; Part II: safety, duration of response, progression-free survival, overall survival

Exploratory endpoints: GR / GR pathway by immunohistochemistry, disease- and GR-related molecular markers in tissue and blood

Selected RP2D as 160 mg ORIC-101 QD Continuous Dosing + 75 mg/m² Nab-Paclitaxel Based on Safety, PK, and PD

Doses and Regimens Explored – Selection of RP2D

Dose Level 1:

- Dose-limiting toxicities (DLTs) were reported in 2 patients: Grade 3 fatigue and Grade 4 neutropenia/thrombocytopenia

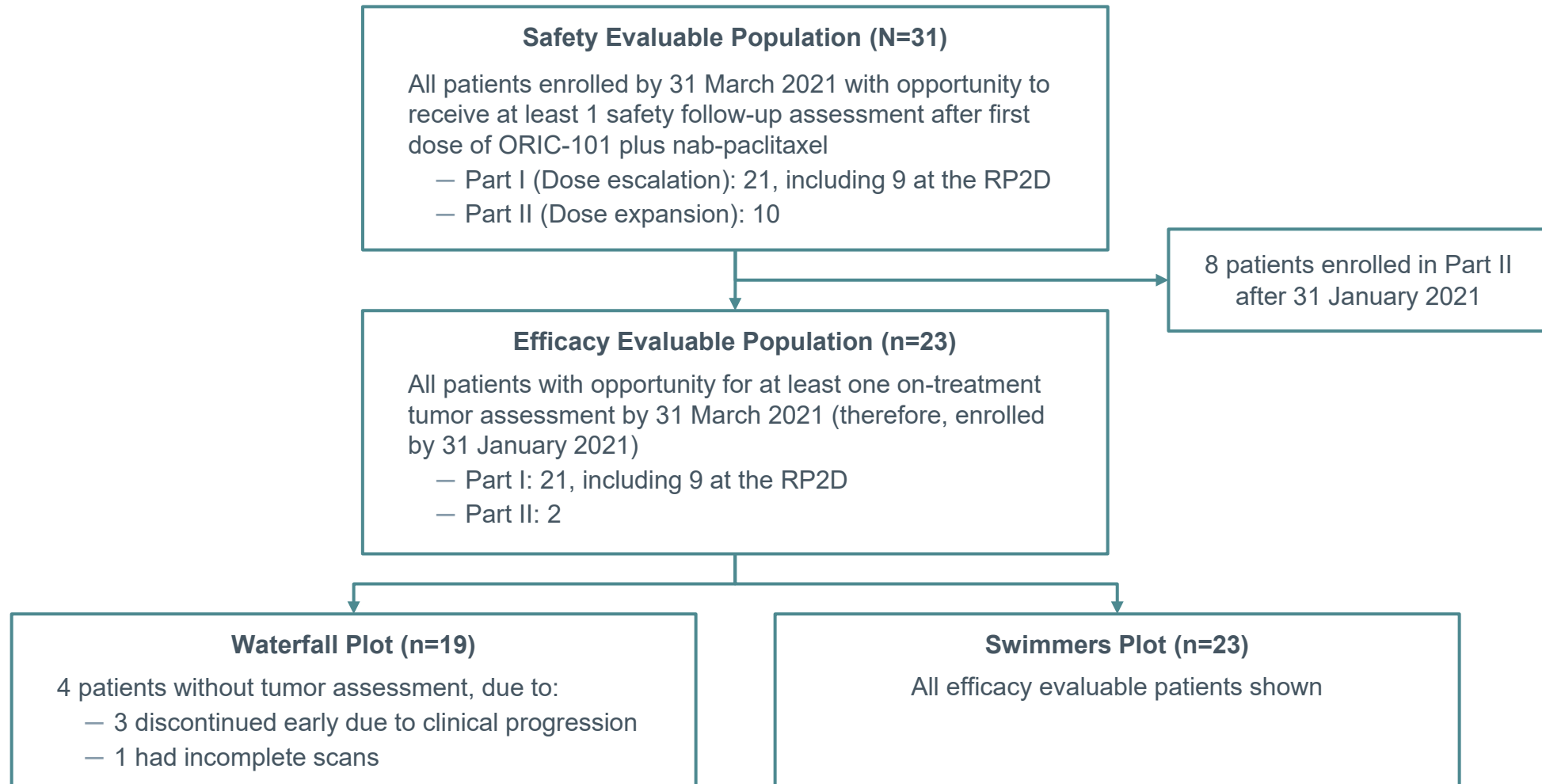
Dose Levels 1A – 2B (RP2D):

- No DLTs reported
- No prophylactic use of G-CSF
- ORIC-101 PK dose proportional, with no evidence of drug-drug interaction with nab-paclitaxel
- PBMC biomarker data indicated on-target PD modulation achieved
- Continuous dosing demonstrated sustained PD effect at the RP2D

Dose Level	n	ORIC-101 dose	ORIC-101 regimen	Nab-Paclitaxel dose
1	3	240 mg QD	Intermittent	100 mg/m ²
1A	3	80 mg QD	Intermittent	75 mg/m ²
2A	3	160 mg QD	Intermittent	75 mg/m ²
3A	3	240 mg QD	Intermittent	75 mg/m ²
2B (RP2D)	9	160 mg QD	Continuous	75 mg/m ²
Expansion (RP2D)	10	160 mg QD	Continuous	75 mg/m ²

As of 31 March 2021, Thirty-One Patients Were Enrolled of Which Twenty-Three Were Efficacy Evaluable

Safety and Efficacy Evaluable Populations



Heavily Pretreated Patients Were Enrolled Across Multiple Tumor Types

Patient Disposition and Baseline Characteristics

- As of 31 March 2021, a total of 31 patients were enrolled in Parts I and II of the Phase 1b study:
 - 12 at non-RP2D levels
 - 19 at the RP2D
- Diverse tumor types:
 - 13 different solid tumors
 - Majority were PDAC (35%), ovarian (13%), or TNBC (6%)
- Heavily pretreated patients; at the RP2D:
 - Patients had received a median of 4 prior therapies, ranging from 2 to 12
 - All patients had received taxane-based therapy

n (%), median (range)	Non-RP2D (n=12)	RP2D (n=19)	TOTAL (N=31)
Ongoing	0	7 (37)	7 (23)
Discontinued	12 (100)	12 (63)	24 (77)
Disease Progression	6 (50)	10 (53)	16 (52)
Adverse Event	5 (42)	1 (5)	6 (19)
Other	1 (8)	1 (5)	2 (6)
Age, years	54 (44, 80)	61 (24, 74)	60 (24, 80)
Sex			
Male	7 (58)	5 (26)	12 (39)
Female	5 (42)	14 (74)	19 (61)
ECOG			
0	4 (33)	5 (26)	9 (29)
1	8 (67)	14 (74)	22 (71)
Tumor Type			
PDAC	4 (33)	7 (37)	11 (35)
Ovarian	0	4 (21)	4 (13)
TNBC	0	2 (11)	2 (6)
Other Solid Tumor	8 (67)	6 (32)	14 (45)
Number of Prior Therapies	2 (1, 6)	4 (2, 12)	4 (1, 12)
Prior Taxane	2 (17)	19 (100)	21 (68)

ORIC-101 Plus Nab-Paclitaxel Was Well Tolerated at the RP2D, with No Requirement for Prophylactic G-CSF and No Treatment-Related Discontinuations

Safety and Tolerability Profile

At the RP2D:

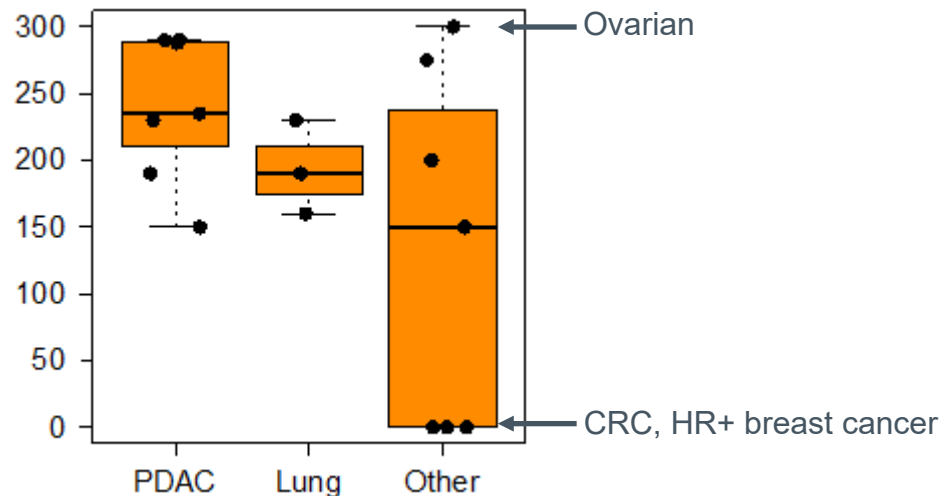
- Well tolerated
 - Tolerability profile consistent with single-agent nab-paclitaxel
- Treatment-related AEs were primarily Grade 1 or 2, with only three Grade 3:
 - Neutropenia (n=2)
 - Rash (n=1)
 - All resolved with dose interruption
- No treatment-related discontinuations
- No requirement for prophylactic G-CSF

Treatment-Related Adverse Events >10% or Grade ≥3, n (%)	Non-RP2D (n=12)		RP2D (n=19)		TOTAL (N=31)	
	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3
Nausea	5 (42)	1 (8)	7 (37)	-	12 (39)	1 (3)
Fatigue	5 (42)	1 (8)	4 (21)	-	9 (29)	1 (3)
Anemia	4 (33)	3 (25)	4 (21)	-	8 (26)	3 (10)
Diarrhea	7 (58)	-	1 (5)	-	8 (26)	-
Leukopenia	5 (42)	3 (25)	3 (16)	-	8 (26)	3 (10)
Neutropenia	4 (33)	2 (17)	3 (16)	2 (11)	7 (23)	4 (13)
Aspartate aminotransferase increased	5 (42)	1 (8)	1 (5)	-	6 (19)	1 (3)
Vomiting	3 (25)	-	3 (16)	-	6 (19)	-
Alopecia	3 (25)	-	2 (11)	-	5 (16)	-
Alanine aminotransferase increased	4 (33)	1 (8)	-	-	4 (13)	1 (3)
Hypotension	2 (17)	1 (8)	-	-	2 (6)	1 (3)
Thrombocytopenia	2 (17)	1 (8)	-	-	2 (6)	1 (3)
Hepatic failure (Grade 5)	1 (8)	1 (8)	-	-	1 (3)	1 (3)
Hyperbilirubinemia	1 (8)	1 (8)	-	-	1 (3)	1 (3)
Laryngeal inflammation	1 (8)	1 (8)	-	-	1 (3)	1 (3)
Liver injury	1 (8)	1 (8)	-	-	1 (3)	1 (3)
Rash maculo-papular	-	-	1 (5)	1 (5)	1 (3)	1 (3)
Syncope	1 (8)	1 (8)	-	-	1 (3)	1 (3)

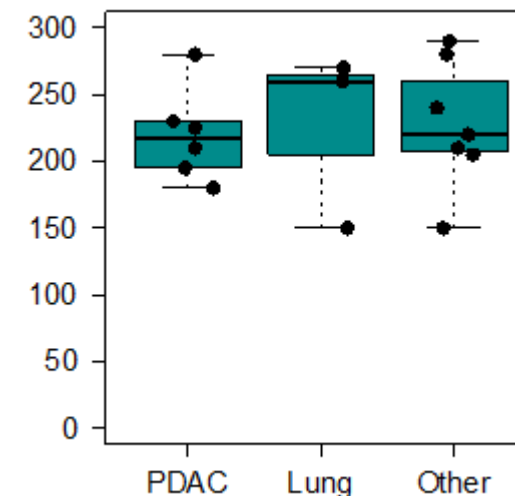
GR Positivity Is Prevalent in Tumor Tissues From Phase 1b Patients

Baseline GR Expression by IHC

GR H-score in Tumors



GR H-score in Stroma



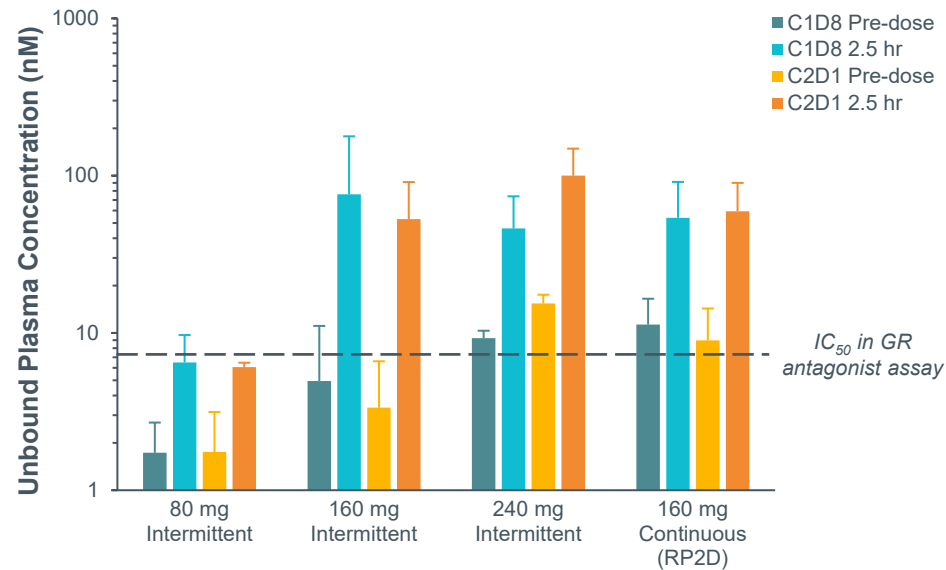
- Baseline GR levels quantified with ORIC's proprietary IHC assay; on-treatment and post-treatment GR quantified when available
- GR levels were high in PDAC and ovarian cancer, low in CRC; dose expansion cohorts do not include CRC
- 53% of tumors and 75% of stroma in Phase 1b have GR H-score ≥ 200 in pretreatment biopsies; exceptions with high stromal but no tumor GR staining were CRC and HR+ breast cancer

**Majority of tumors from Phase 1b patients express GR protein;
Data support tumor types selected for Phase 1b Part II (PDAC, ovarian cancer, TNBC)**

ORIC-101 Pharmacokinetic Data from Phase 1b Demonstrate Excellent Target Coverage and Lack of Drug-Drug Interaction with Nab-Paclitaxel

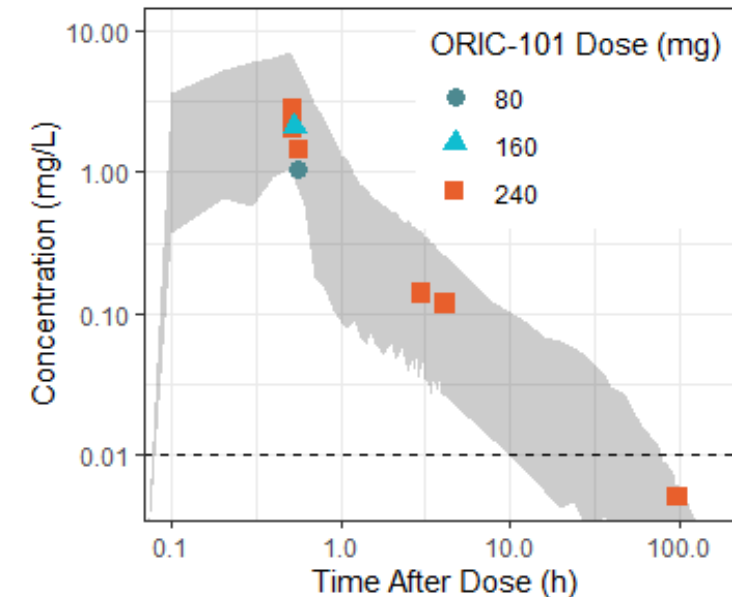
ORIC-101 Phase 1b Pharmacokinetic Data

ORIC-101 PK Demonstrates Excellent Target Coverage



- Target coverage achieved with ORIC-101 doses >80 mg ⁽¹⁾
- Pre-dose (trough) levels exceed target plasma concentrations within 1 week of dosing
- Continuous dosing provides more consistent plasma exposures and sustained target coverage

Nab-Paclitaxel PK Demonstrates No DDI

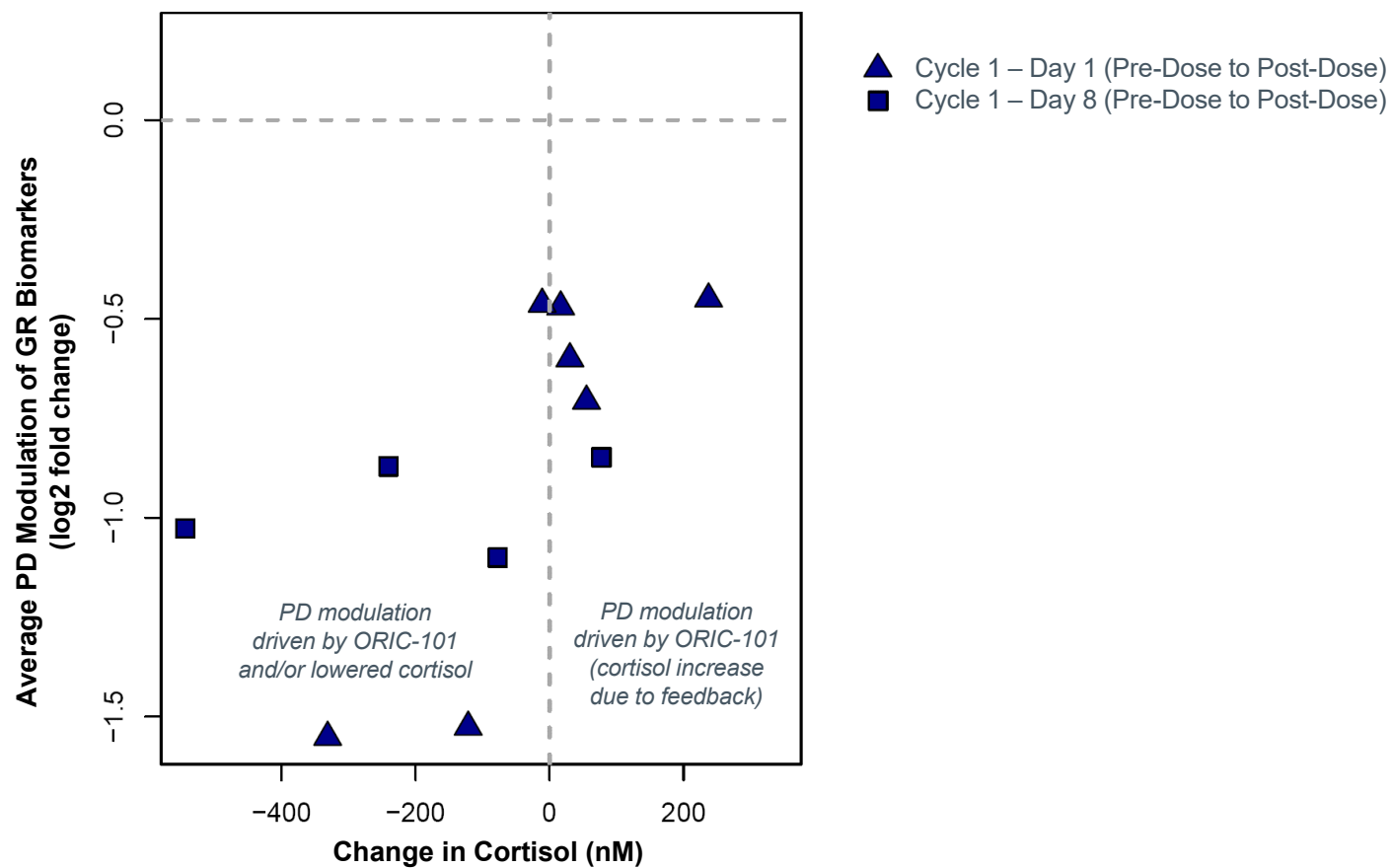


- No changes in nab-paclitaxel concentrations with varying doses of ORIC-101 based on a population PK simulation of nab-paclitaxel (gray shaded region)

ORIC-101 dosing at the RP2D achieves complete and continuous target coverage without drug-drug interaction with nab-paclitaxel

ORIC-101 Achieved Consistent Suppression of Key GR Biomarkers

Change in GR Biomarkers: Pre-Dose to Post-Dose at the RP2D in PBMCs

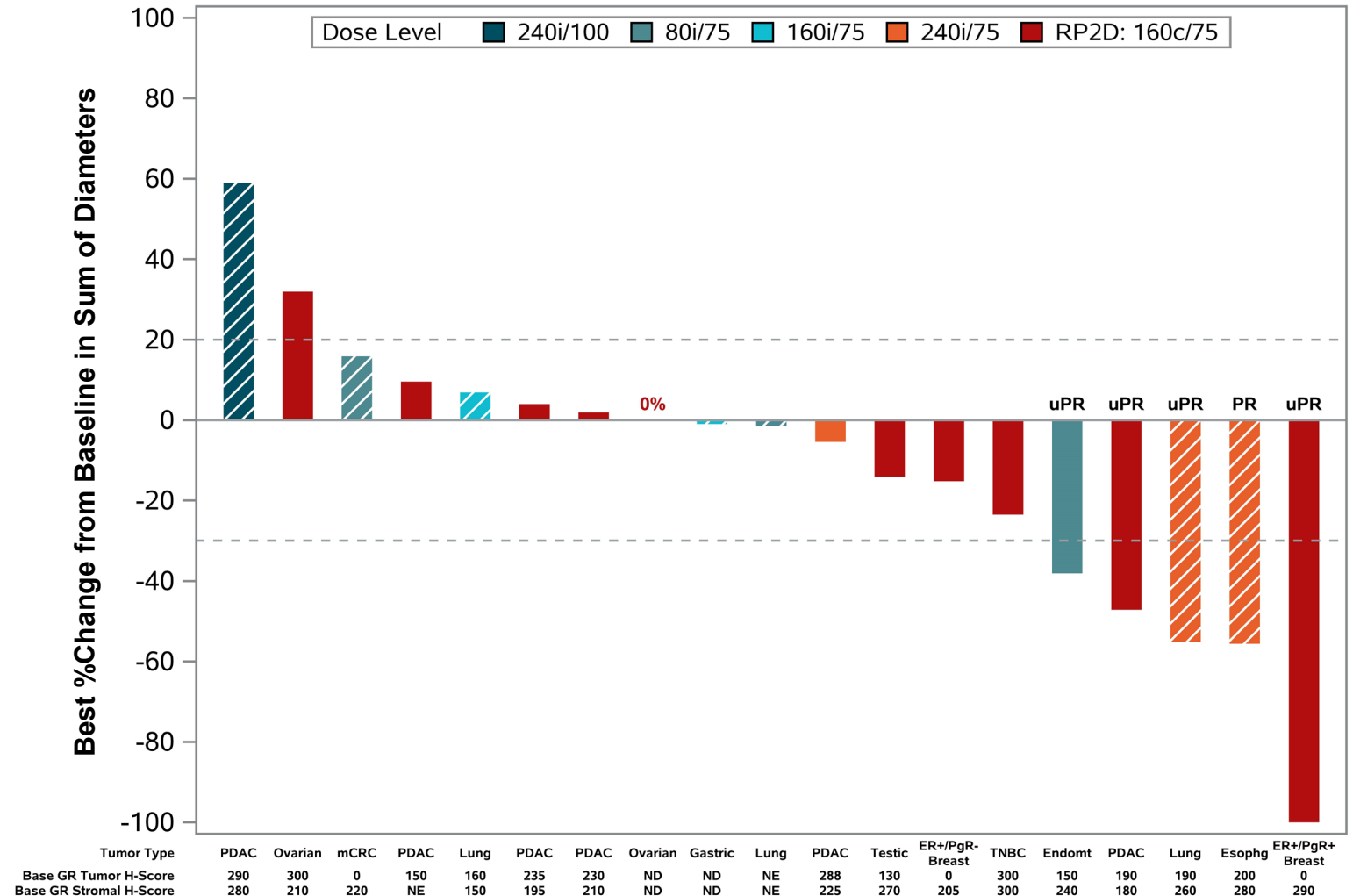


PD modulation of key GR biomarkers achieved with continuous dosing, even in the presence of high physiologic cortisol levels

Preliminary Antitumor Activity Observed in Evaluable Patients

Best %Change in Target Lesions

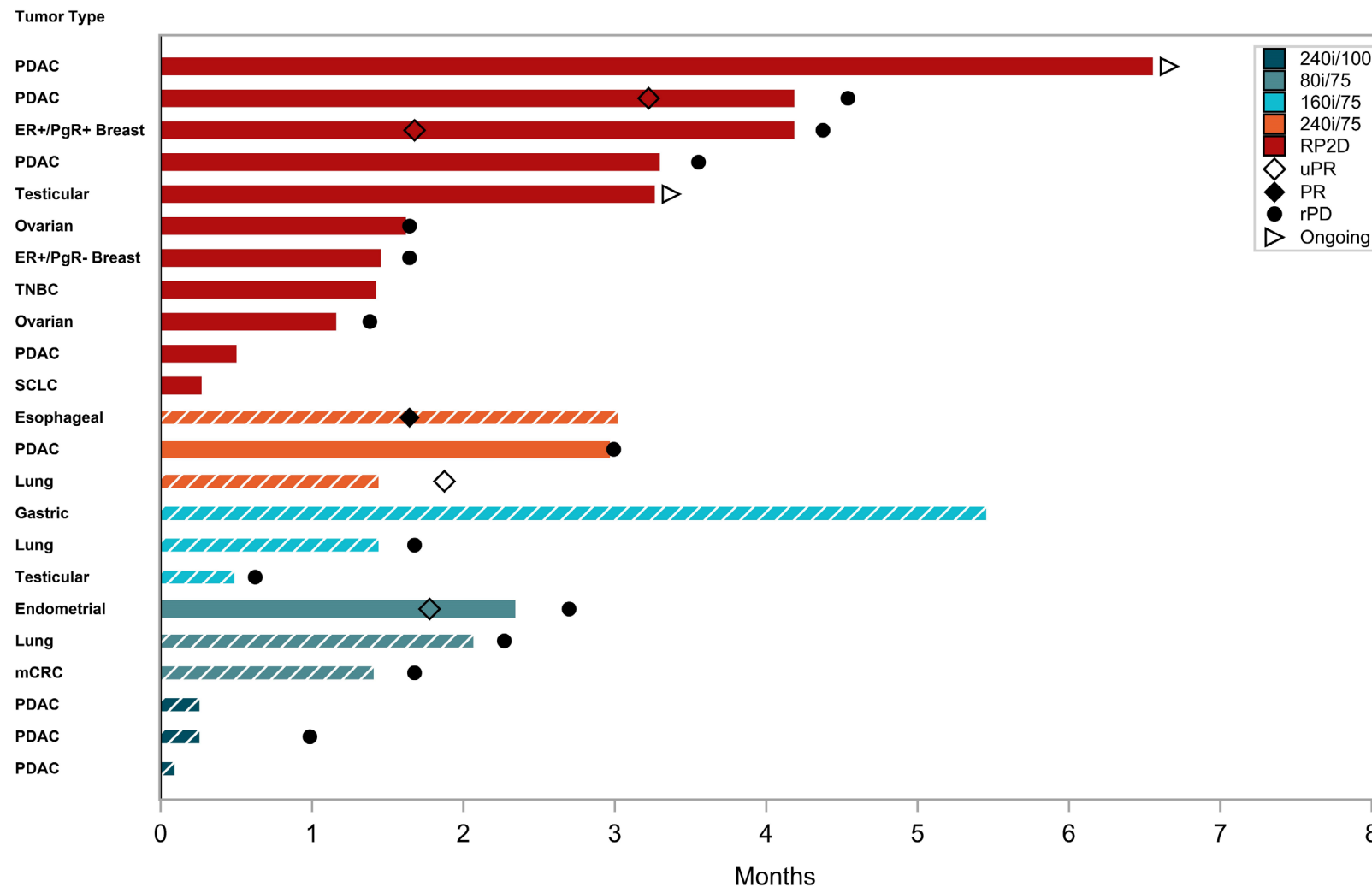
- Evidence of antitumor activity based upon tumor regression observed across multiple solid tumors
 - All had previously progressed on or after a taxane-based therapy
- Tumor regression seen in heavily pretreated patients with PDAC, endometrial and breast cancers
 - 5 partial responses
 - 1 confirmed
 - 4 unconfirmed



Preliminary Antitumor Activity Observed in Evaluable Patients (Cont'd)

Time on Treatment

- Further evidence of antitumor activity based upon prolonged disease stabilization (>3 months) across multiple solid tumors
 - PDAC, breast, gastric, esophageal, and testicular cancers
- Extended progression-free survival in patients with late-line relapsed PDAC who had previously progressed on or after nab-paclitaxel



Preliminary Clinical Benefit Observed with ORIC-101 Plus Nab-Paclitaxel in Multiple Patients with Advanced Solid Tumors

Endometrial	Breast (ER+/PR+)	PDAC	PDAC	Gastric	Esophageal	Large Cell Neuroendocrine Lung
Partial Response (Unconfirmed)	Partial Response (Unconfirmed)	Partial Response (Unconfirmed)	Stable Disease	Stable Disease	Partial Response (Confirmed)	Partial Response (Unconfirmed)
38% decrease in target lesions	100% decrease in target lesions	47% decrease in target lesions	2% increase in target lesions	1% decrease in target lesions	56% decrease in target lesions	55% decrease in target lesions
PFS 2.7 months	PFS 4.4 months	PFS 4.5 months	PFS 5.3 months (ongoing)	PFS 4.4 months	PFS 3.8 months	PFS 1.9 months
80 mg ORIC-101 int + 75 mg/m ² nab-pac	160 mg ORIC-101 cont + 75 mg/m ² nab-pac	160 mg ORIC-101 cont + 75 mg/m ² nab-pac	160 mg ORIC-101 cont + 75 mg/m ² nab-pac	160 mg ORIC-101 int + 75 mg/m ² nab-pac	240 mg ORIC-101 int + 75 mg/m ² nab-pac	240 mg ORIC-101 int + 75 mg/m ² nab-pac
Prior Therapies 1. megestrol 2. carboplatin+ paclitaxel 3. investigational agent 4. investigational agent	Prior Therapies 1. palbociclib+fulvestrant 2. capecitabine+ nab-pac 3. doxorubicin 4. everolimus+ exemestane 5. eribulin 6. gemcitabine 7. cyclophosphamide 8. cyclophosphamide+ methotrexate+5-FU	Prior Therapies 1. FOLFIRINOX 2. gemcitabine+ nab-pac	Prior Therapies 1. gemcitabine+ nab-pac 2. 5-FU+irinotecan 3. FOLFOX	Prior Therapies 1. FOLFOX 2. investigational agent	Prior Therapies 1. cisplatin+5-FU 2. carboplatin+etoposide 3. epirubicin+cisplatin+ 5-FU 4. investigational agent 5. investigational agent 6. investigational agent	Prior Therapies 1. cisplatin+etoposide 2. durvalumab 3. durvalumab+ carboplatin+etoposide
Baseline GR H-scores • Tumor: 150 • Stromal: 240	Baseline GR H-scores • Tumor: 0 • Stromal: 290	Baseline GR H-scores • Tumor: 190 • Stromal: 180	Baseline GR H-scores • Tumor: 230 • Stromal: 210	Baseline GR H-scores • Tumor: Not done • Stromal: Not done	Baseline GR H-scores • Tumor: 200 • Stromal: 280	Baseline GR H-scores • Tumor: 190 • Stromal: 260

38% Decrease in Target Lesions in Taxane-Refractory Endometrial Cancer

Demographics

54F with heavily pretreated endometrial cancer, metastatic to lung, liver and peritoneum

Treatment History

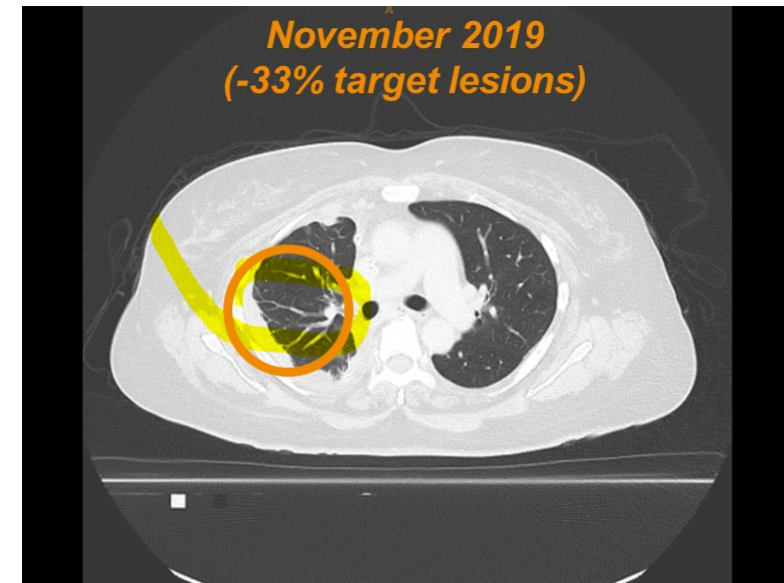
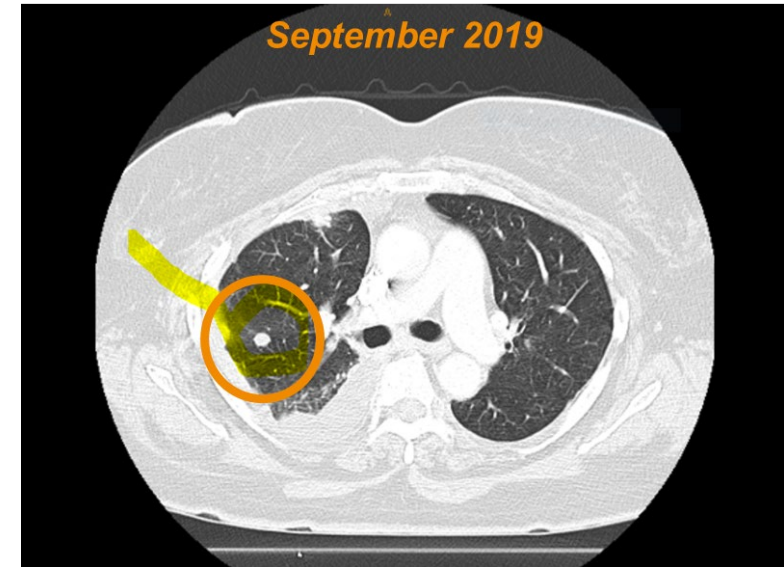
- 1L metastatic: **paclitaxel** + carboplatin
- 2L and 3L metastatic: investigational agents

ORIC-101 Dosing Regimen

- 80 mg ORIC-101 QD intermittent + 75 mg/m² nab-paclitaxel

Best Response

- Response assessment at end of Cycle 2
 - **Target lesions: -33% (uPR)**
 - CA-125 reduced from 686 to 525
- Restaging at end of Cycle 3:
 - **Target lesions: -38%**
 - Progressed with new pleural lesions
 - **PFS of 11.7 weeks (2.7 months)**



100% Decrease in Target Lesions in Taxane-Refractory ER+/PR+ Breast Cancer

Demographics

54F with heavily pretreated ER+/PR+ breast cancer, metastatic to bone, CNS, lung, lymph nodes, and liver

Treatment History

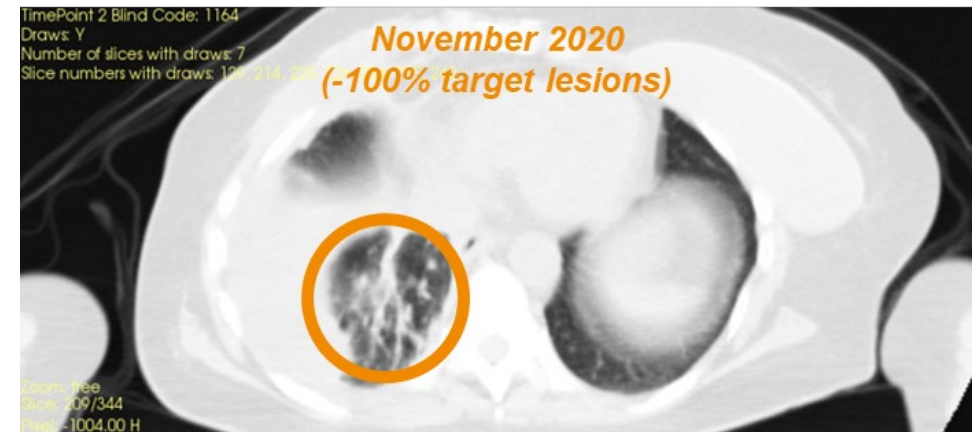
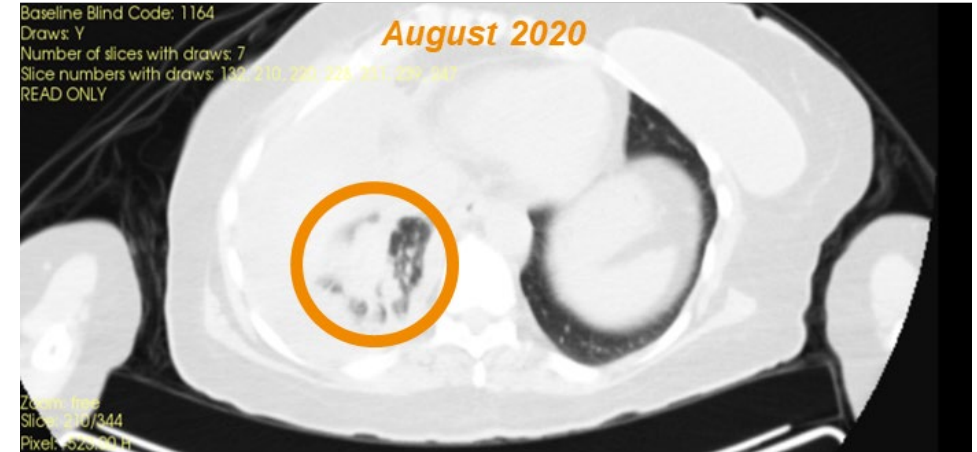
- Initial surgery and adjuvant chemo/RT
- 1L metastatic: palbociclib + fulvestrant
- 2L metastatic: **nab-paclitaxel** + capecitabine
- 3L – 8L metastatic therapies: additional cytotoxic chemotherapy, targeted agents, and anti-estrogen agents

ORIC-101 Dosing Regimen

- 160 mg ORIC-101 QD continuous + 75 mg/m² nab-paclitaxel

Best Response

- Response assessment at end of Cycle 2
 - **Target lesions: -100% (uPR)**
- Restaging at end of Cycle 4
 - **Target lesion: -100%** (no systemic progression)
 - New lesions in the CNS
 - **PFS of 19.3 weeks (4.4 months)**



47% Decrease in Target Lesions in Taxane-Refractory PDAC

Demographics

66M with heavily pretreated PDAC, metastatic to the liver

Treatment History

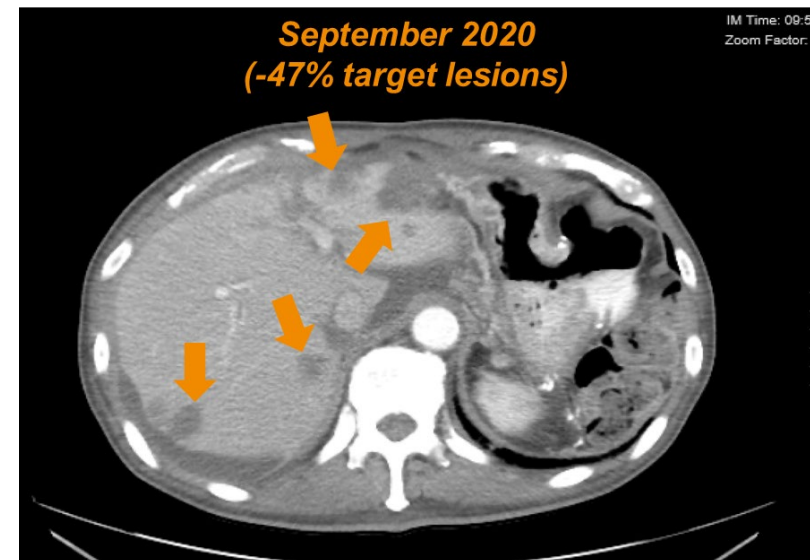
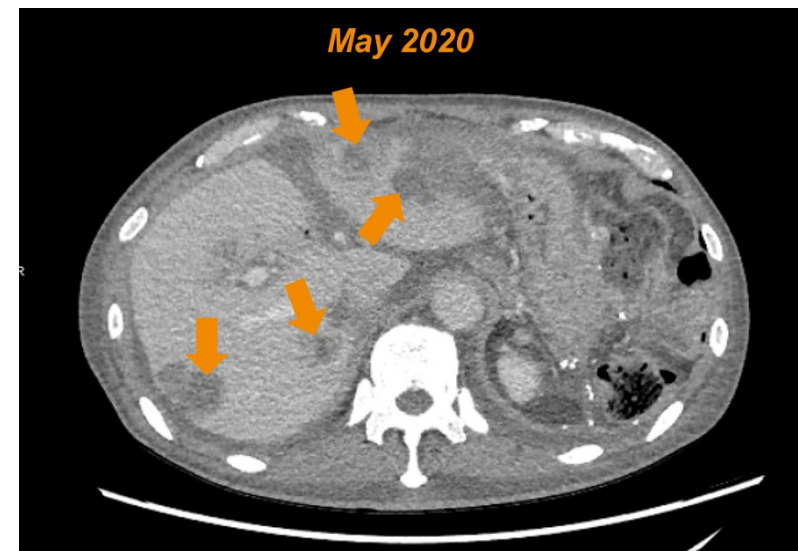
- Neoadjuvant: FOLFIRINOX
- Partial pancreatectomy
- 1L metastatic: gemcitabine + **nab-paclitaxel**

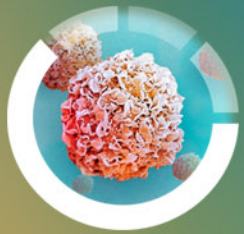
ORIC-101 Dosing Regimen

- 160 mg ORIC-101 QD continuous + 75 mg/m² nab-paclitaxel

Best Response

- Response assessment at end of Cycle 2
 - **Target lesions: stable**
- Restaging at end of Cycle 3
 - **Target lesions: -47% (uPR)**
- Restaging at end of Cycle 5
 - Progressed with growth of target lesions and development of a new liver lesion
 - **PFS of 19.7 weeks (4.5 months)**



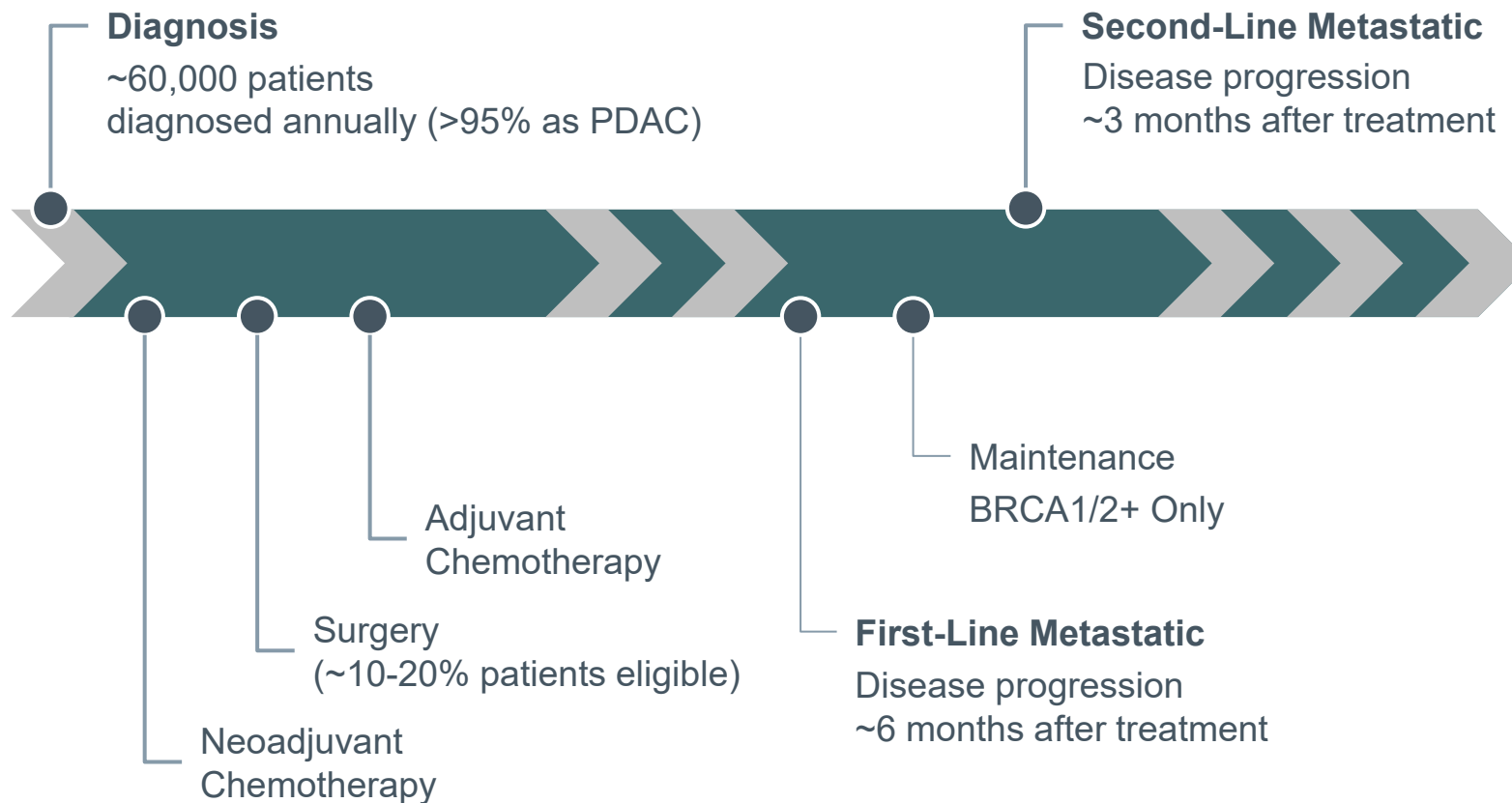


ORIC-101 Plus Nab-Paclitaxel in Patients with Advanced PDAC



Significant Unmet Medical Need Exists for Patients with Pancreatic Cancer

>48,000 Patients Die Annually from Pancreatic Cancer in the US



Pancreatic Cancer

Limited Treatment Options
and Poor Outcomes

- Short PFS in 1L and 2L with current standards of care
- Low response rates in 2L
- No taxane retreatment effect
- Significant toxicities associated with current treatments

~80% of pancreatic cancer patients are diagnosed when the disease has metastasized, at which point average survival is less than one year

Very Few Treatment Options Are Available for Patients with Pancreatic Cancer

Pancreatic Cancer Treatment Overview

	Good Performance Status		Poor Performance Status	BRCA1/2 or PALB2
First-Line	FOLFIRINOX	gemcitabine + nab-paclitaxel*	single agent chemotherapy	gemcitabine + cisplatin
Second-Line	gemcitabine + nab-paclitaxel	liposomal irinotecan + 5-FU + leucovorin* or FOLFIRINOX	single agent chemotherapy	gemcitabine + cisplatin
Third-Line	Investigational Therapies			

Chemotherapy remains the standard of care for 1L and 2L pancreatic cancer; preferred regimens primarily dependent on patient performance status

Treatments for Pancreatic Cancer are Associated with Limited Progression-Free Survival and Severe Adverse Events

Selected Treatment Options for Pancreatic Cancer

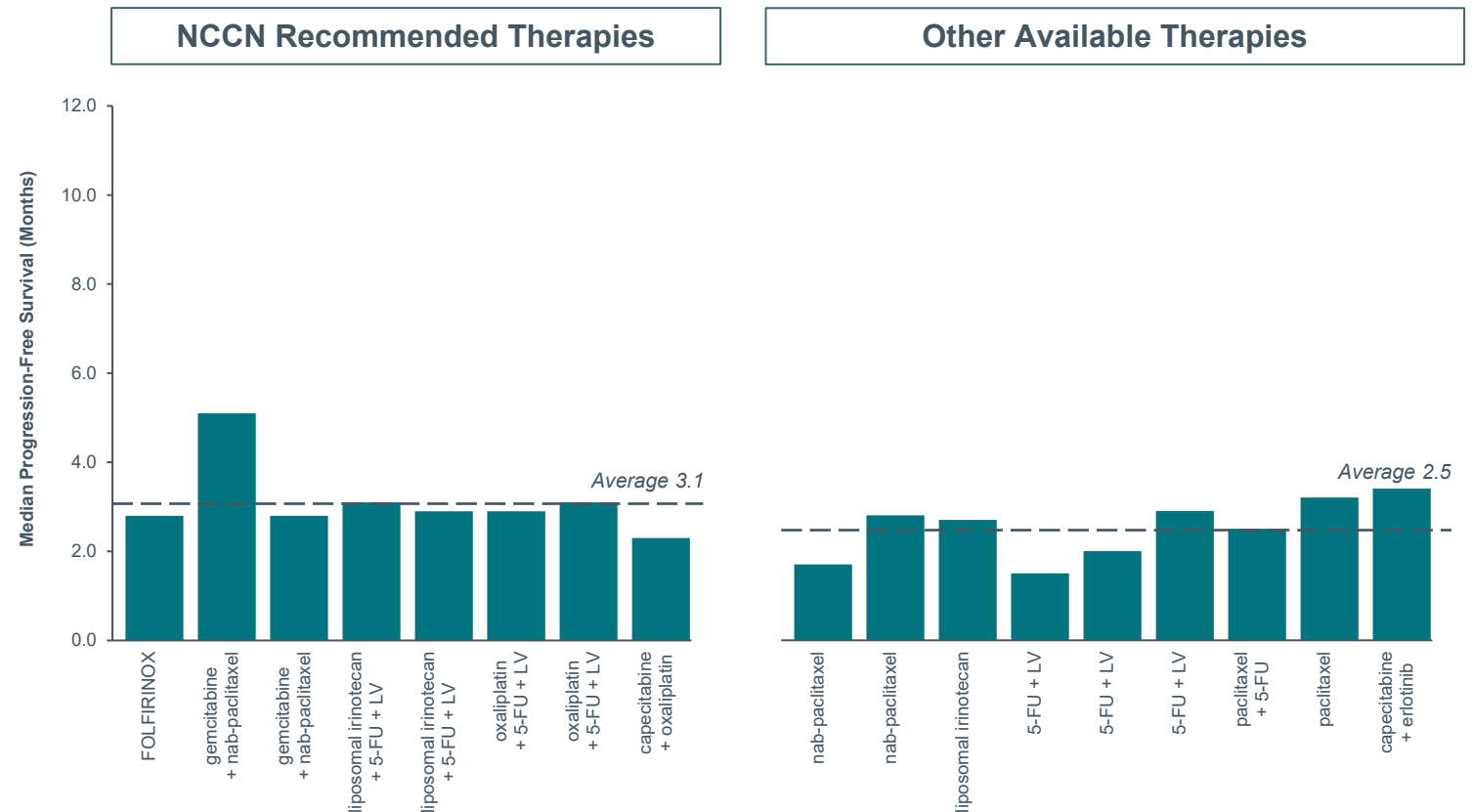
	Regimen	MOA	Approval	Patients	Key Efficacy Data	Notable Grade ≥3 Adverse Events
First-Line	FOLFIRINOX	Chemotherapy	Not approved	First-Line	PFS: 6.4 months OS: 11.1 months	Neutropenia (46%) Fatigue (24%) Vomiting (15%) Diarrhea (13%) Febrile neutropenia (5%)
	nab-paclitaxel + gemcitabine	Chemotherapy	2013	First-Line	PFS: 5.5 months OS: 8.5 months	Neutropenia (38%) Leukopenia (31%) Fatigue (17%) Peripheral neuropathy (17%)
Second-Line	liposomal irinotecan + 5-FU + leucovorin	Chemotherapy	2015	Second-Line (post-gemcitabine)	PFS: 3.1 months OS: 6.1 months	Neutropenia (39%) Fatigue (14%) Diarrhea (13%) Vomiting (11%)

Treatments for pancreatic cancer are associated with significant tolerability challenges and limited progression-free survival of only 6 months for first line regimens and 3 months for second line regimens

Disease Progression of 2L Pancreatic Cancer Is Approximately 3 Months or Less

Progression-Free Survival in 2L Pancreatic Cancer

- Treatment typically includes available chemotherapy or investigational agent
- PFS and OS are outcomes of interest
 - ORR typically 0% to <5% for single agent chemotherapy
 - ORR typically 0% to <15% for combination regimens
- Recommended therapies associated with PFS of ~3 months
- Retreatment is rare in relapsed PDAC
 - No evidence of nab-paclitaxel retreatment effect after prior taxane-based regimen



Various chemotherapy regimens are utilized for 2L pancreatic cancer with minimal success; objective response rates for combination regimens typically 0% to <15% and progression-free survival less than 3 months

Preliminary Clinical Benefit with ORIC-101 Plus Nab-Paclitaxel at the RP2D in Heavily Pretreated Patients with PDAC that Received Prior Nab-Paclitaxel

Efficacy Evaluable Patients with PDAC Enrolled at RP2D

3L PDAC	4L PDAC	4L PDAC	6L PDAC
Partial Response (Unconfirmed)	Stable Disease	Stable Disease	Stable Disease
66 year-old male	74 year-old male	67 year-old female	66 year-old male
PFS 4.5 months	PFS 5.3 months (ongoing)	PFS 3.6 months	PFS 0.8 months (censored**)
160 mg ORIC-101 continuous + 75 mg/m ² nab-paclitaxel	160 mg ORIC-101 continuous + 75 mg/m ² nab-paclitaxel	160 mg ORIC-101 continuous + 75 mg/m ² nab-paclitaxel	160 mg ORIC-101 continuous + 75 mg/m ² nab-paclitaxel
Prior Therapies 1. FOLFIRINOX 2. gemcitabine + nab-paclitaxel	Prior Therapies 1. gemcitabine + nab-paclitaxel 2. 5-FU + irinotecan 3. FOLFOX	Prior Therapies 1. FOLFIRINOX 2. gemcitabine + nab-paclitaxel 3. 5-FU + irinotecan	Prior Therapies 1. gemcitabine + capecitabine 2. FOLFIRINOX 3. gemcitabine + nab-paclitaxel 4. FOLFIRI 5. gemcitabine + capecitabine + docetaxel
Time on Treatment of Last Prior Therapy • 2.8 months	Time on Treatment of Last Prior Therapy • 2.0 months	Time on Treatment of Last Prior Therapy • 2.9 – 3.9 months*	Time on Treatment of Last Prior Therapy • 0.9 months
Baseline GR H-score • Tumor: 190 • Stromal: 180	Baseline GR H-score • Tumor: 230 • Stromal: 210	Baseline GR H-score • Tumor: 150 • Stromal: Non-Evaluable	Baseline GR H-score • Tumor: 235 • Stromal: 195

ORIC-101 plus nab-paclitaxel demonstrated longer PFS in patients with late-line relapsed PDAC (all of whom had received prior nab-paclitaxel) than is typically observed with earlier line therapies; additionally, PFS compares favorably to time on treatment of last prior therapy

Discussion with Professor Pamela Munster, M.D., UCSF

Trial Investigator and Senior Author

Guest KOL



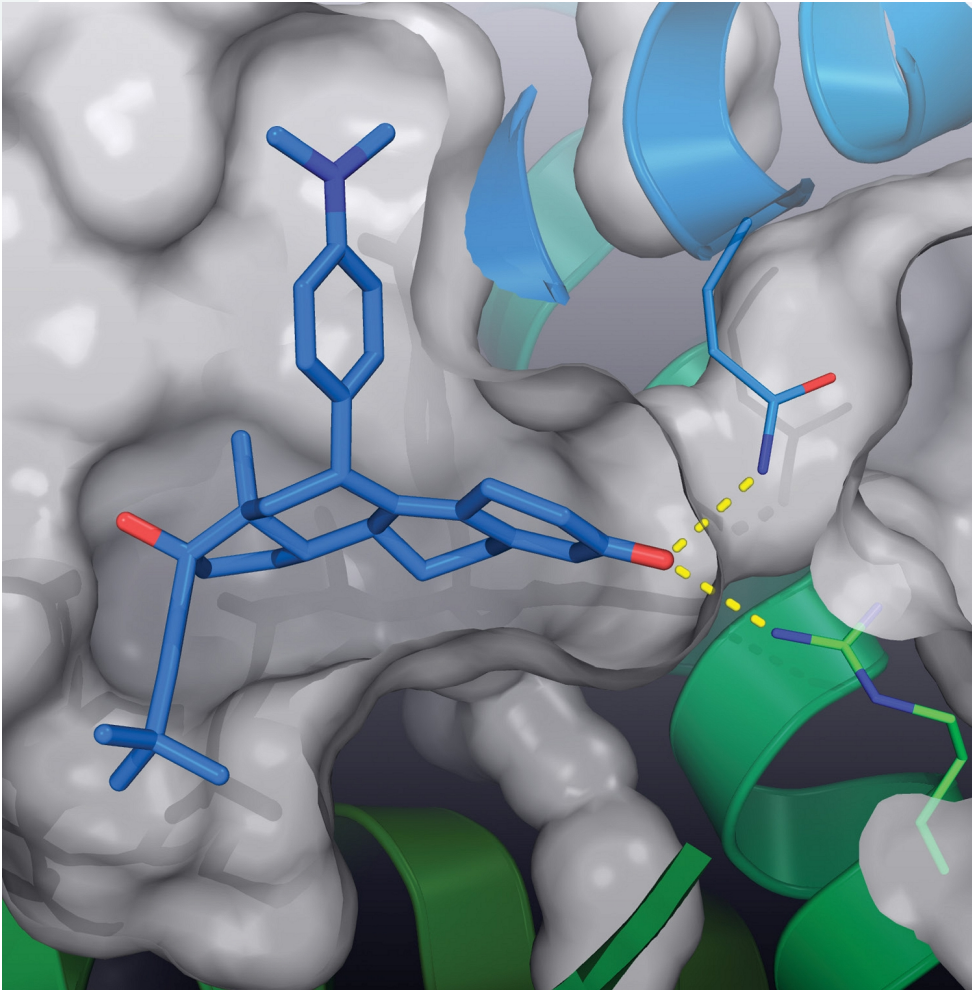
Pamela Munster, M.D.

- Professor, Department of Medicine (Hematology/Oncology), UCSF
- Director, Early Phase Clinical Trials Unit
- Co-leader of the Center for BRCA Research
- Co-Leader, Molecular Oncology Program, UCSF Helen Diller Family Comprehensive Cancer Center

Topics of Discussion

- Views on GR as a chemotherapy resistance mechanism and the therapeutic potential of GR antagonism
- Experience with and commentary on ORIC-101 in combination with nab-paclitaxel
- Observations on patients enrolled in the Phase 1b trial with focus on PDAC
- Placing this experience in the context of the current therapeutic landscape of PDAC
- Views on the next steps of ORIC-101 development

Key Takeaways from the Initial Phase 1b Data of ORIC-101 in Combination with Nab-Paclitaxel in Advanced Solid Tumors



Well Tolerated with Nab-Paclitaxel at RP2D

- TRAEs primarily Grade 1-2; no treatment-related discontinuations
- No requirement for prophylactic G-CSF

PK Demonstrates Excellent Target Coverage and No DDI

- Plasma exposures at RP2D exceed threshold for GR inhibition
- No evidence of drug-drug interaction with nab-paclitaxel

Translational Data Show PD Modulation & High GR Prevalence

- Achieved consistent suppression of key GR biomarkers
- High rates of GR expression seen in tumor types of interest

Evidence of Antitumor Activity Across Multiple Solid Tumors

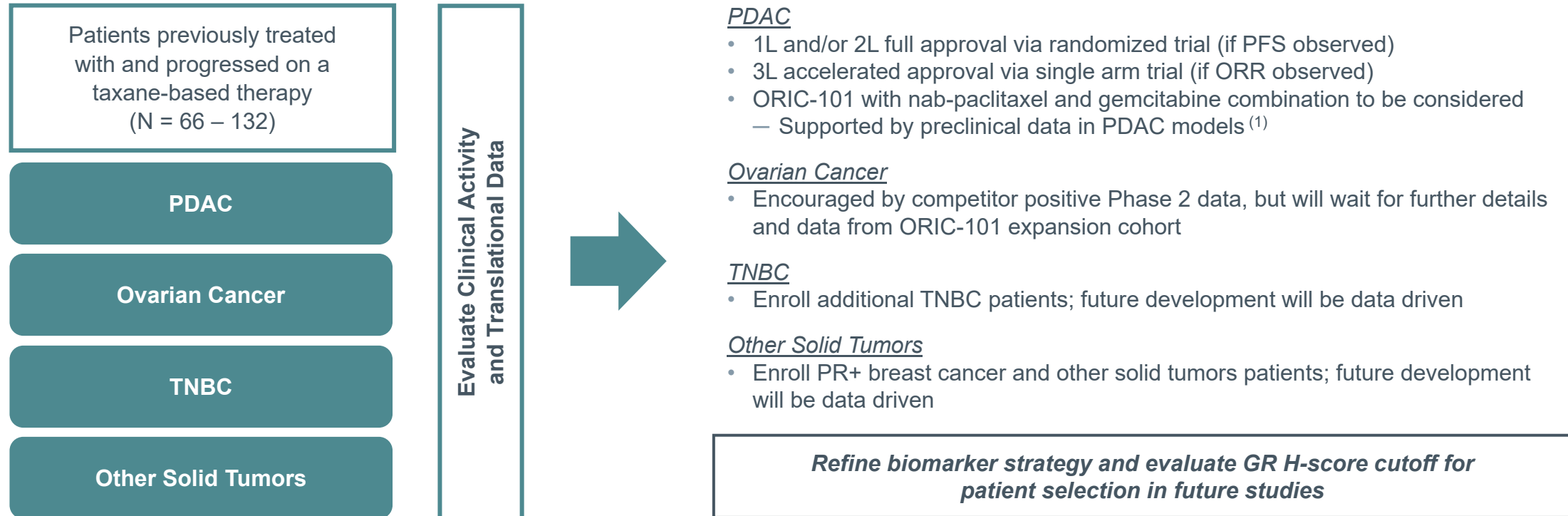
- Tumor regression and prolonged stable disease in heavily pretreated patients, including those previously treated with a taxane-based therapy
- Extended PFS in patients with late-line relapsed pancreatic cancer who had previously progressed on or after nab-paclitaxel

Next Steps for Development of ORIC-101 in Combination with Nab-Paclitaxel

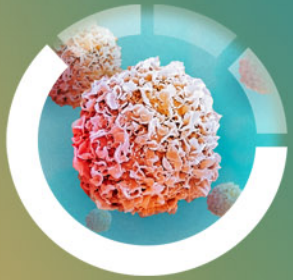
ORIC-101 Clinical Development Considerations

Dose Expansion (Part II) – Ongoing

Potential Paths Forward Will Depend on Nature of Efficacy Signal



Clinical activity and translational data from ongoing expansion cohorts will guide next steps for ORIC-101 development; updated Phase 1b expansion cohort data expected to be reported in 2022



Summary and Pipeline Update

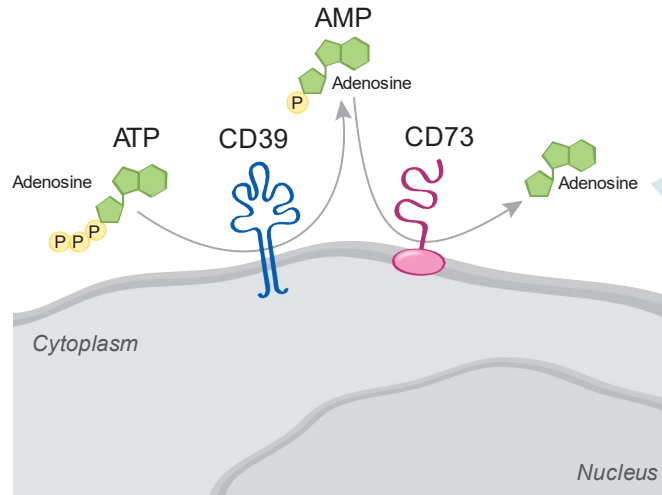


Broad Pipeline Targeting Multiple Resistance Mechanisms

Program	Indication	Target ID / Validation	Lead Identification	Lead Optimization	Preclinical	Phase 1	Phase 2	Phase 3	Type of Resistance
PRODUCT CANDIDATES									
ORIC-101 <i>Glucocorticoid receptor antagonist</i>	Prostate cancer	Phase 1b: ORIC-101 + Xtandi (enzalutamide)						Bypass	
	Solid tumors	Phase 1b: ORIC-101 + Abraxane (nab-paclitaxel)						Bypass	
ORIC-533 <i>CD73 inhibitor</i>	Undisclosed					Innate			
ORIC-944 <i>PRC2 inhibitor</i>	Prostate Cancer					Innate			
ORIC-114 <i>EGFR/HER2 inhibitor</i>	NSCLC and Tumor agnostic					Innate			
DISCOVERY RESEARCH PROGRAMS									
Multiple programs targeting resistance mechanisms	Solid tumors					Innate			
	Solid tumors					Innate			
	Solid tumors					Acquired			
	Solid tumors					Bypass			

ORIC-533 Is an Oral Small Molecule CD73 Inhibitor Targeting Single Agent Clinical Development Path in Undisclosed Indication – IND Filing in 2Q 2021

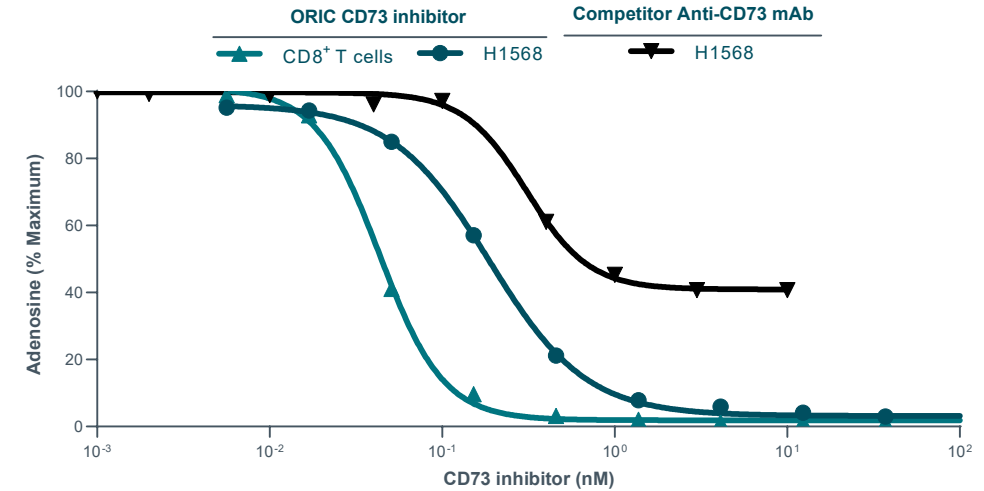
Adenosine Has Been Linked to Cancer Therapy Resistance



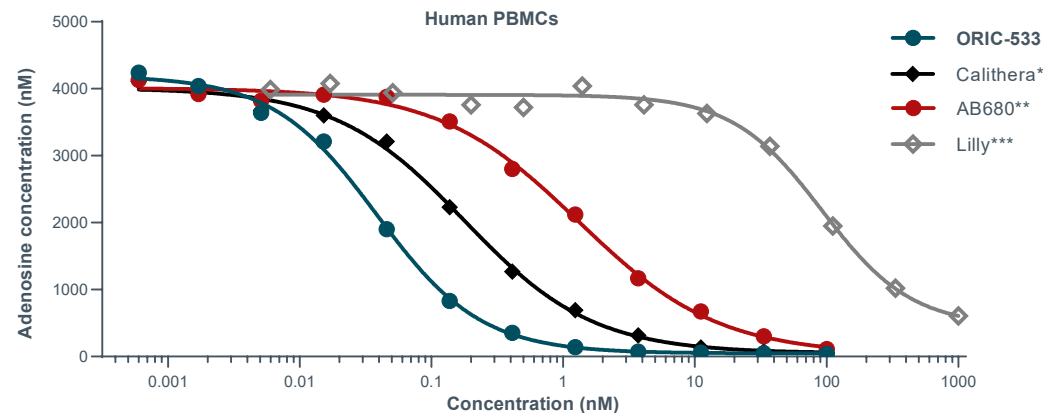
Increased Adenosine Inhibits:

- T cell priming
- T cell activation / cytolytic activity
- NK degranulation
- Macrophage M1 polarization
- DC maturation / activation

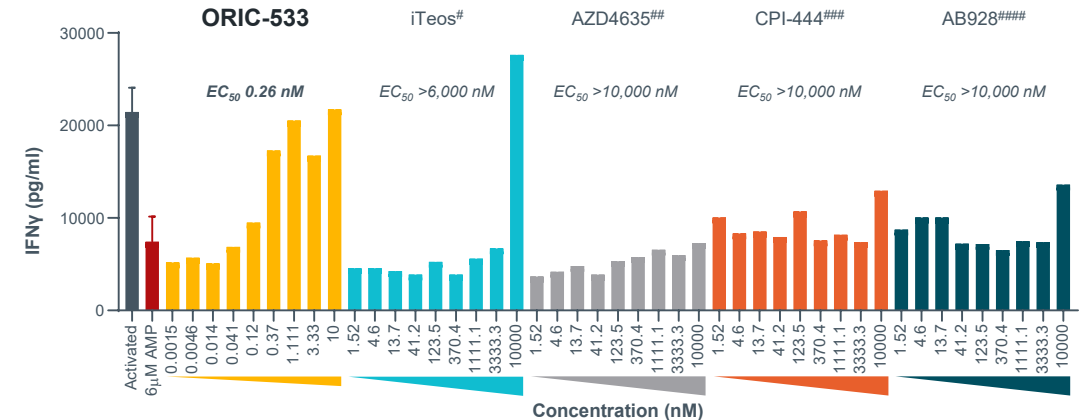
ORIC Oral CD73 Inhibitors Demonstrate Potent Adenosine Inhibition with Enhanced Activity Over an Antibody-Based Approach



ORIC-533 More Potently Blocks Adenosine than Competitor Small Molecule CD73 Inhibitors

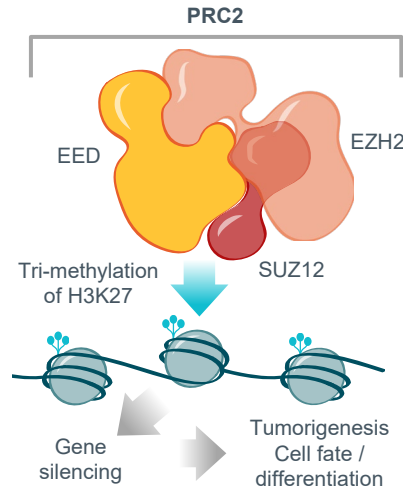


ORIC-533 Restores T Cell Function More Potently than A_{2A}/A_{2B} Receptor Antagonists in Moderate/High AMP



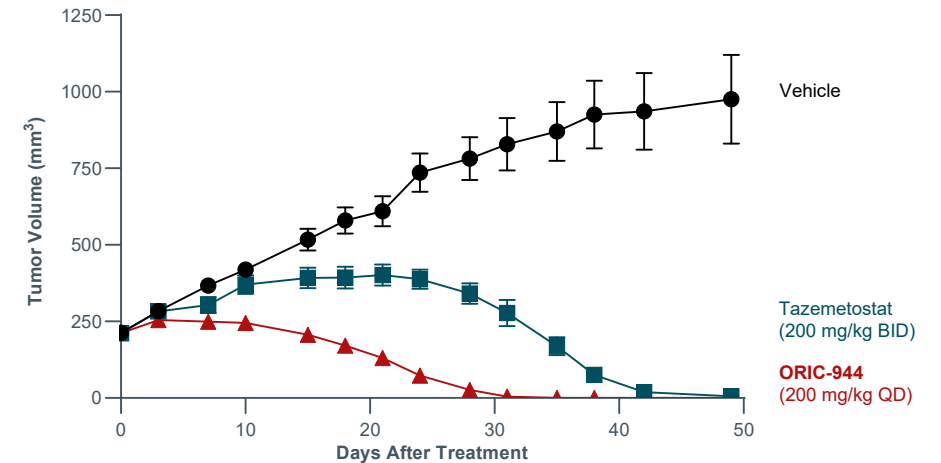
ORIC-944 Is an Allosteric PRC2 Inhibitor Targeting Treatment Resistant Prostate Cancer – IND Filing Expected in 2H 2021

PRC2 Plays Pivotal Role in Transcriptional Regulation and Cancer

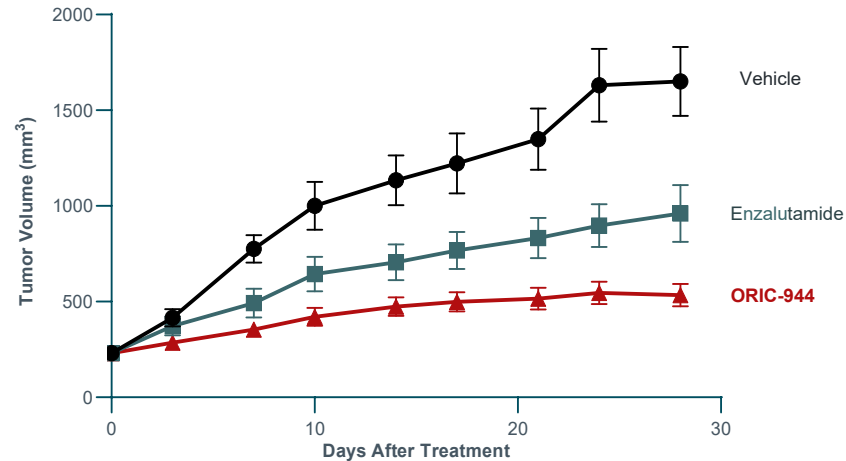


- Two druggable subunits:
 - EED: directs histone binding
 - EZH2: directs histone methylation
- PRC2 dysregulated in several cancers
- First-generation PRC2 inhibitors, inhibiting EZH2, demonstrated promising clinical activity
 - Approved for epithelioid sarcoma and follicular lymphoma
 - Limited progress for treatment of prostate cancer

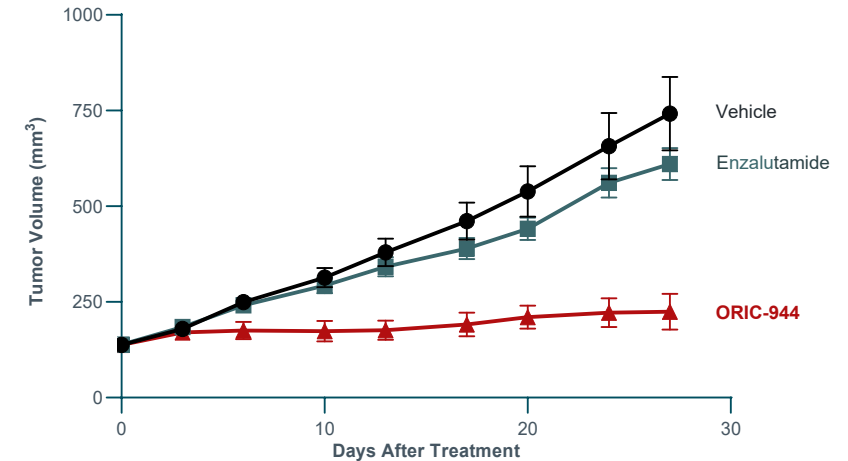
Allosteric PRC2 Inhibition May Improve Upon EZH2 Inhibitors



Single-Agent Activity in Prostate Cancer Model

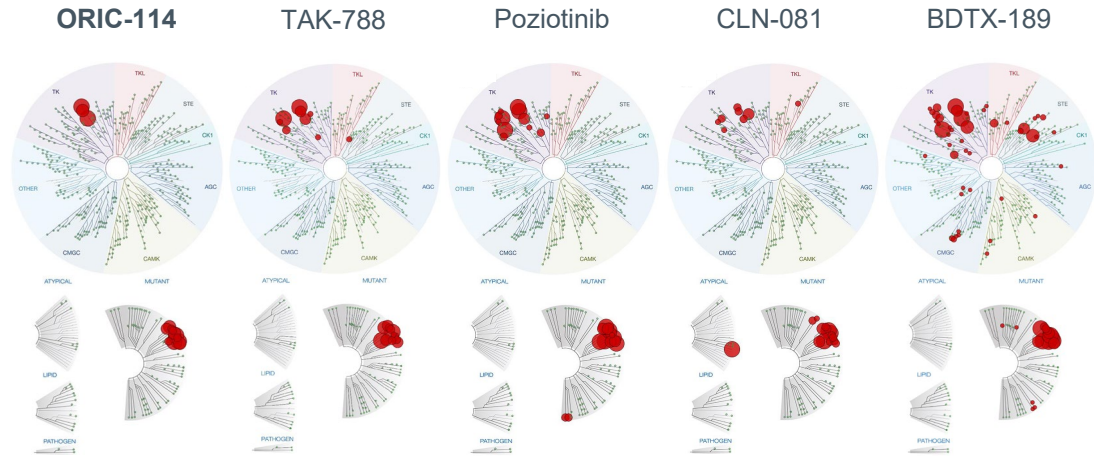


Single-Agent Activity in AR-v7+ Prostate Cancer Model

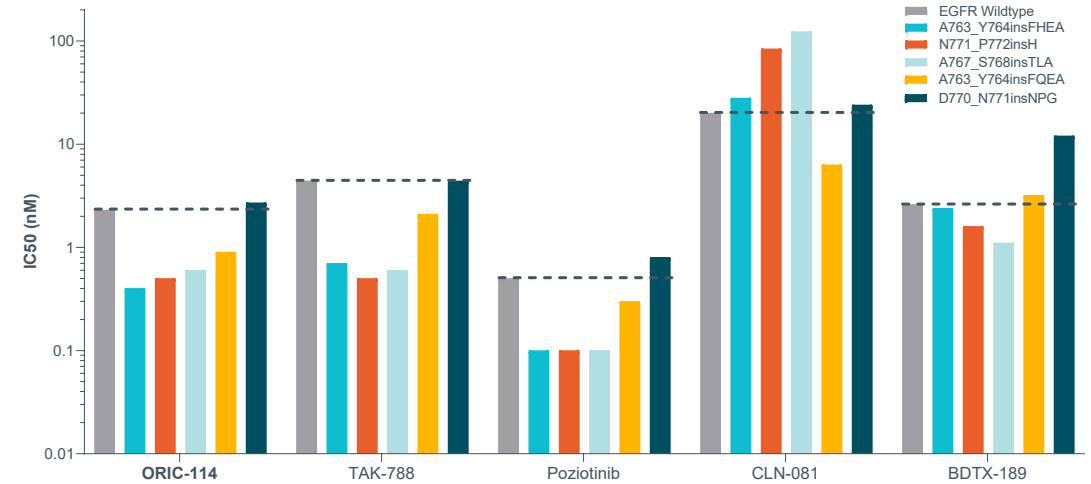


ORIC-114 Is a Brain Penetrant, Orally Bioavailable, Irreversible Inhibitor Targeting EGFR and HER2 Exon 20 Mutations – CTA Filing Expected in 2H 2021

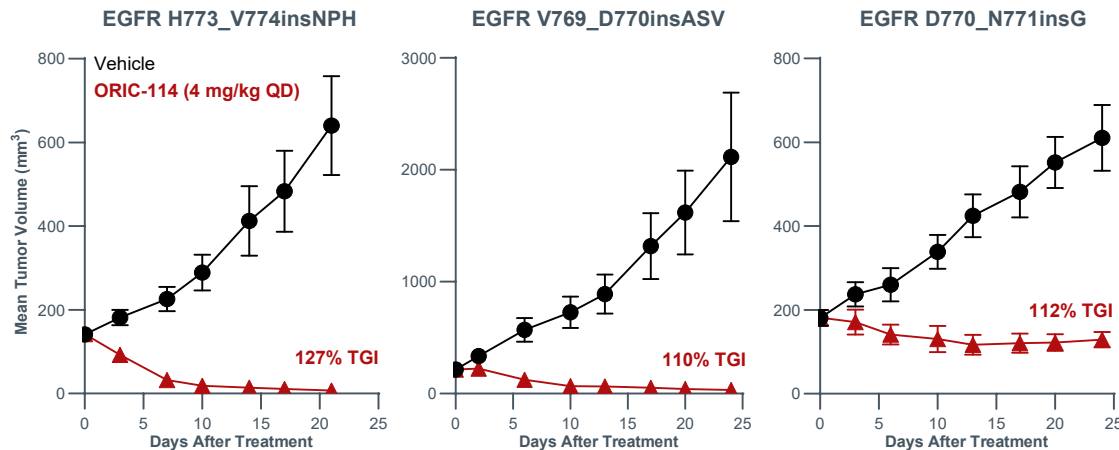
Excellent Selectivity for EGFR and HER2



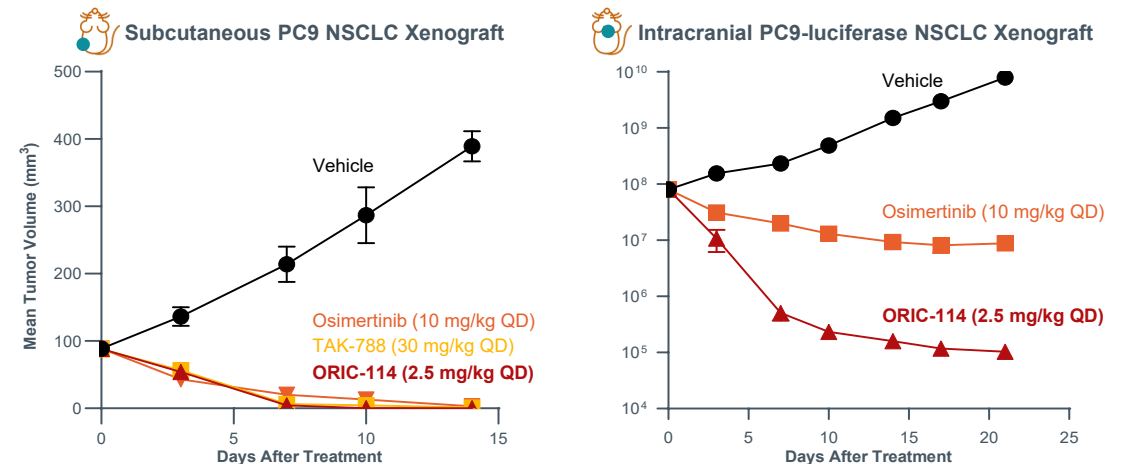
High In Vitro Potency Against EGFR Exon 20 Mutations



Potent In Vivo Activity in EGFR Exon 20 Insertion Models



Superior Efficacy in an Intracranial EGFR Mutant Model



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 (1) anti-androgen resistance in prostate cancer and (2) chemotherapy resistance in solid tumors
- Clinical data from ORIC and competitor support chemotherapy resistance hypothesis

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 2021-2022
- Three IND/CTAs expected in 2021

Strong Financial Foundation

- Existing cash, cash equivalents & investments expected to fund company into 2H 2023

Anticipated Milestones and Clinical Updates

- **ORIC-101:** Initial Phase 1b with Xtandi in metastatic prostate cancer: 2H 2021
- **ORIC-101:** Updated Phase 1b with Abraxane in solid tumors: 2022
- **ORIC-533:** IND filing: 2Q 2021
- **ORIC-944:** IND filing: 2H 2021
- **ORIC-114:** CTA filing: 2H 2021