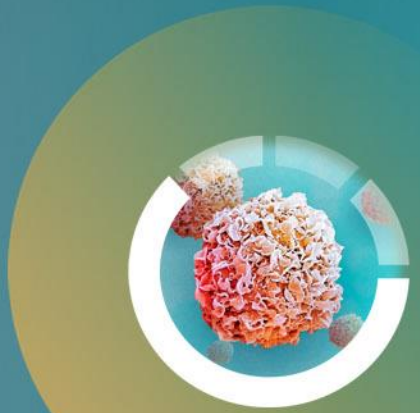
ORIC



Overcoming Resistance In Cancer

Company Overview

January 2025

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: our development plans and timelines; the potential advantages of our product candidates and programs; plans for the clinical trials and development of ORIC-114 and ORIC-944; ORIC-114 and ORIC-944 clinical outcomes, which may materially changes as patient enrollment continues or more patient data becomes available; the expected timing of reporting data from our clinical trials; our anticipated milestones and clinical updates; and the period over which we estimate our existing cash 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 health emergencies, economic instability or international conflicts on our operations, including clinical trials; the potential for current or future clinical trials of 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 or collaboration 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 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; regulatory developments in the United States and foreign countries; 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 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: Dedicated to **O**vercoming **R**esistance **I**n **C**ancer

Lead Programs Advancing toward Pivotal Studies

- Potential best-in-class TKI targeting NSCLC with EGFR exon 20, HER2 exon 20, and EGFR atypical mutations
- Potential best-in-class PRC2 inhibitor targeting mCRPC

Dual Engine for Pipeline Expansion

- Pipeline built from internal R&D and external business development
- Targeting one new IND candidate every 18 months

Experienced Management Team

- Heritage of discovering, developing, and commercializing oncology therapies at Ignyta, Medivation, Aragon, Pharmacyclics, and Genentech

Strong Financial Position

- Cash and investments of $282 million expected to fund company into late 2026 (1)

Anticipated Data Milestones

- ORIC-114 (NSCLC):
  - 1H25: 2L EGFR exon 20 and 2L+ HER2 exon 20
  - 2H25: 2L+ EGFR atypical
  - 1H26: 1L EGFR exon 20
  - Mid-2026: 1L EGFR exon 20 combination with SC amivantamab and 1L EGFR atypical
- ORIC-944 (mCRPC):
  - 4Q25 / 1H26: Combination with AR inhibitors

Two potential best-in-class programs expected to enter pivotal studies in 2H25 (ORIC-114) and early 2026 (ORIC-944)

(1) Unaudited balance as of September 30, 2024.

Executive Team with Expertise in Building Leading Oncology Companies

Jacob Chacko, MD Chief Executive Officer	• Previously CFO at Ignyta (acquired by Roche), raised >$500m in capital • TPG Capital (completed $10bn of aggregate acquisitions) and McKinsey & Company • Board member of 4D Molecular and Board Chair of Bright Peak; previously Turning Point, 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 >20 drug candidates into development • Director of Signal Transduction at Exelixis • Board member of NextRNA Therapeutics	Genentech EXELIXIS
Pratik Multani, MD Chief Medical Officer	• Previously CMO of Ignyta; led development and regulatory for ROZLYTREK (entrectinib) • CMO of Fate; previously at IDEC, Salmedix, 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 Business Development at Medivation (acquired by Pfizer) • Global Healthcare Investment Banking at Merrill Lynch	prothena Bank of America Merrill Lynch MEDIVATION
Dominic Piscitelli Chief Financial Officer	• Previously CFO at AnaptysBio, raised >$500m in capital • VP of Finance, Strategy and IR at Medivation and OSI Pharmaceuticals • Board member of Alterome Therapeutics and 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	synthorx ignyta Cooley
Edna Chow Maneval, PhD EVP Clinical Development	• Previously SVP at Ignyta; clinical lead for ROZLYTREK, led transition team through global filings • VP of Clinical Development at Seragon and Aragon, clinical lead for ERLEADA (apalutamide)	ignyta SERAGON PHARMACEUTICALS ARAGON PHARMACEUTICALS
Keith Lui SVP Commercial & Medical Affairs	• Previously SVP of Business Development, Commercial and Medical Affairs at DURECT • Led commercial strategy and launch-readiness at Pharmacyclics, Genentech, Prothena, and Oncopeptides	durect pharmacyclics An AbbVie Company Genentech

Clinical Pipeline Focused on Advancement of ORIC-114 and ORIC-944

Program	Indication	Discovery / IND Enabling	Phase 1/2	Pivotal / Phase 3	Clinical Collaboration	Anticipated Data Milestones
PRODUCT CANDIDATES						
ORIC-114 *EGFR/HER2 inhibitor*	EGFR exon 20 NSCLC (1)	• 1L combination with SC amivantamab • 1L monotherapy • 2L monotherapy			Johnson&Johnson	Mid-2026 1H26 1H25
	Atypical EGFR NSCLC	• 1L monotherapy • 2L+ monotherapy				Mid-2026 2H25
	HER2 exon 20 NSCLC	• 2L+ monotherapy				1H25
ORIC-944 *PRC2 inhibitor*	Prostate Cancer	• Combination with apalutamide			Johnson&Johnson	4Q25 / 1H26
		• Combination with darolutamide			BAYER	4Q25 / 1H26
DISCOVERY RESEARCH PROGRAMS						
Multiple programs targeting resistance mechanisms	Solid tumors					

(1) Clinical collaboration with Johnson & Johnson to evaluate ORIC-114 plus subcutaneous (SC) amivantamab in patients with first-line NSCLC with EGFR exon 20 insertion mutations.

Substantial Progress in 2024: Well Positioned to Build Value in 2025 and Beyond

2024 Accomplishments and Next Steps

ORIC-114
EGFR/HER2 inhibitor

- ✓ Completed dose escalation, selected provisional RP2Ds, and initiated multiple dose expansion cohorts
- ✓ Executed clinical supply agreement with JNJ to evaluate ORIC-114 in combination with SC amivantamab in 1L NSCLC EGFR exon 20
- ✓ Presented data further supporting potential best-in-class profile of ORIC-114 versus competitors

ORIC-944
PRC2 inhibitor

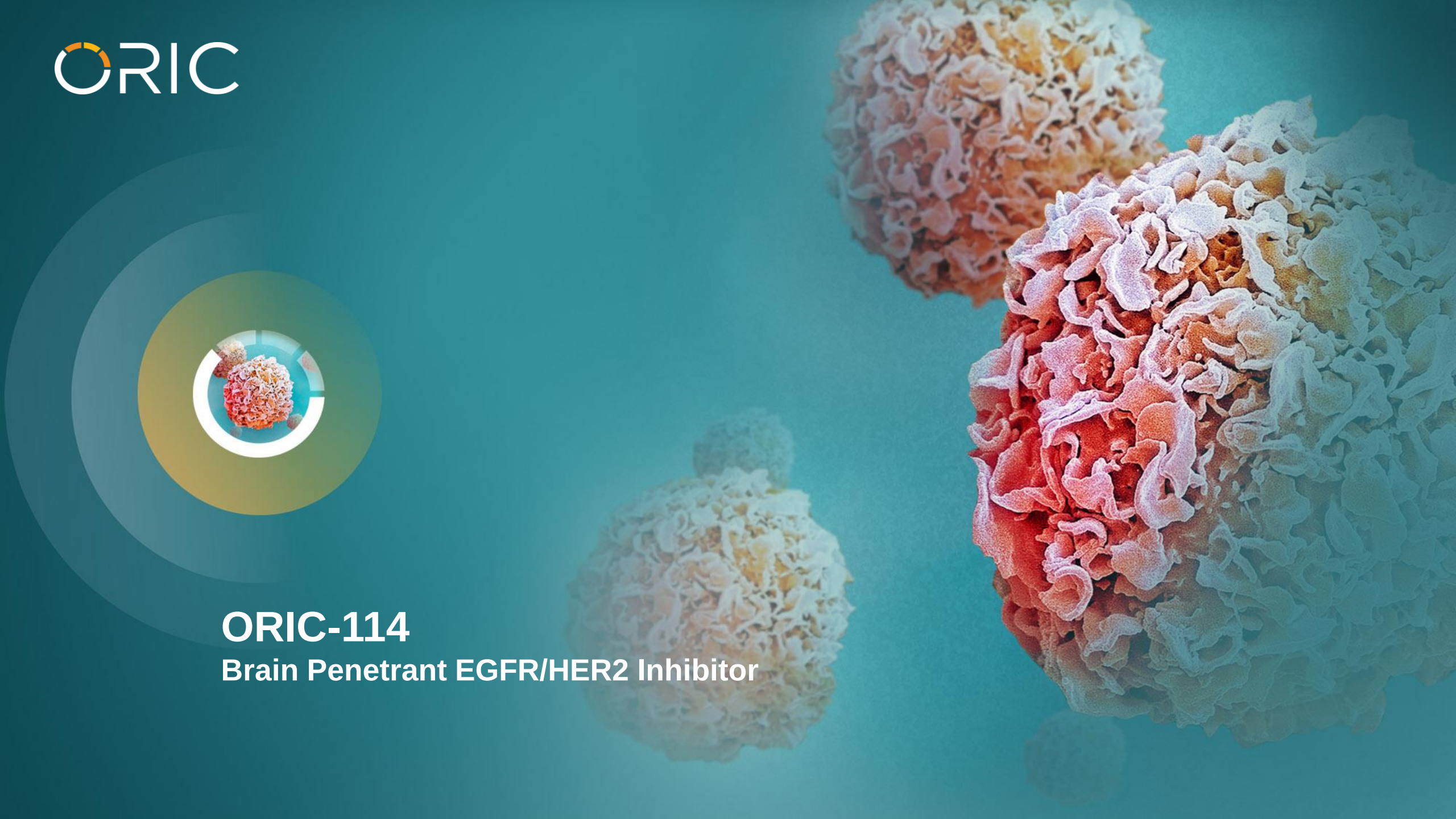
- ✓ Phase 1b single agent data demonstrated potential best-in-class drug properties and favorable safety, supporting advancement into combination development in prostate cancer
- ✓ Executed clinical supply agreements with JNJ and Bayer to evaluate ORIC-944 in combination with apalutamide and darolutamide in mCRPC and initiated combination cohorts mid-2024
- ✓ Presented data demonstrating potential best-in-class drug properties and data supporting mechanistic rationale for combination with AR inhibitors

Corporate

- ✓ Raised $125 million from healthcare specialist funds, extending cash runway into late 2026
- ✓ Expanded leadership team with appointment of SVP of Commercial and Medical Affairs

Two potential best-in-class programs expected to enter pivotal studies in 2H25 (ORIC-114) and early 2026 (ORIC-944)

ORIC



ORIC-114

Brain Penetrant EGFR/HER2 Inhibitor

ORIC-114: Potential Best-in-Class TKI to Overcome Limitations of Approved and Investigational Agents for EGFR and HER2 Mutated NSCLC

KEY LIMITATIONS of approved and investigational agents

- **Lack of CNS activity** in populations with high rate of CNS metastases leads to suboptimal clinical outcomes
- **Tolerability issues** with high rates of treatment discontinuations due to on- and off-target toxicity

ORIC-114 may address these limitations

- **Selectively targets EGFR and HER2** with high potency against exon 20 insertion and atypical mutations
- **Multiple confirmed responses** observed in heavily pretreated NSCLC patients with EGFR and HER2 exon 20
- **Demonstrated CNS activity** including first ever confirmed CNS complete response in an EGFR exon 20 patient with untreated brain metastases
- **Well-tolerated** with mostly Grade 1–2 TRAEs, low rates and severity of on-target rash and diarrhea, and minimal off-target toxicities

STATUS of development

- **Enrolling three cohorts in 2L NSCLC:** EGFR exon 20, HER2 exon 20, and EGFR atypical mutations
- **Initiating three cohorts in 1L NSCLC:** EGFR atypical, EGFR exon 20 monotherapy and in combination with SC amivantamab (in collaboration with Johnson & Johnson) (1)
- **Six Phase 1b data readouts expected through mid-2026**

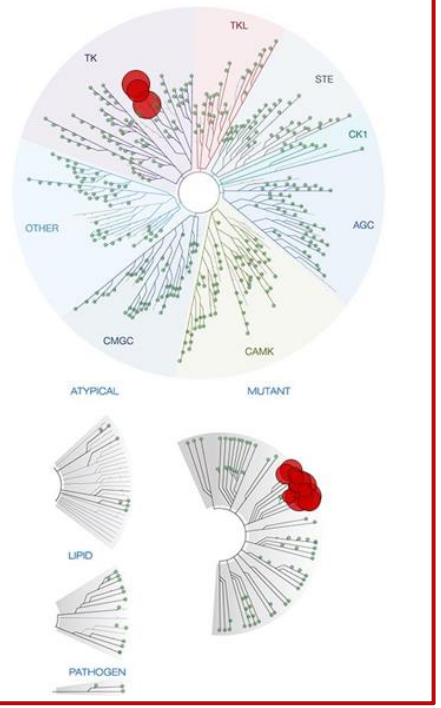
ORIC-114 is a potential best-in-class therapy for NSCLC with excellent selectivity and brain penetrance that has demonstrated promising clinical proof-of-concept in heavily pretreated patients with active CNS metastases

(1) Clinical collaboration with Johnson & Johnson to evaluate ORIC-114 plus subcutaneous (SC) amivantamab in 1L NSCLC patients with EGFR exon 20.

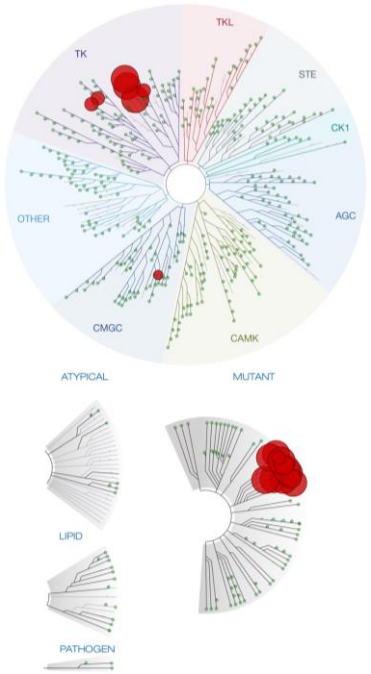
ORIC-114 Selectively Targets EGFR and HER2 with High Potency Against EGFR Exon 20 Insertion, HER2 Exon 20 Insertion and EGFR Atypical Mutations

Kinome Selectivity Comparison

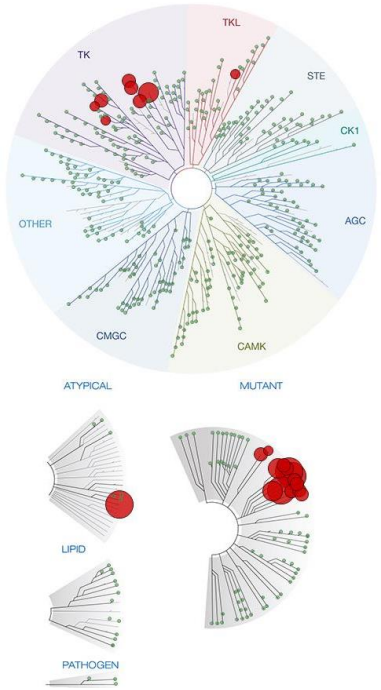
ORIC-114



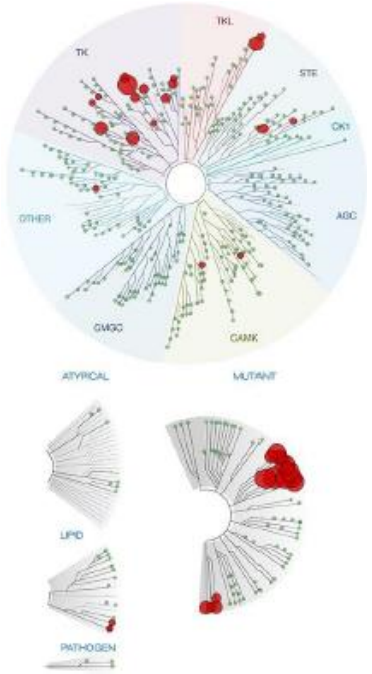
Firmonertinib



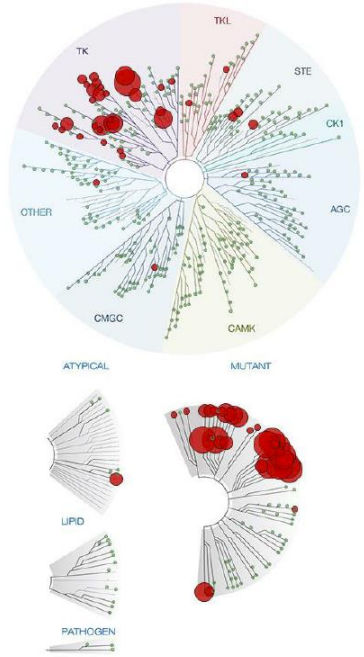
Zipalertinib



Lazertinib



BDTX-1535



Off-target Kinases Inhibited ≥80% at 1 μM				
ORIC-114	Firmonertinib	Zipalertinib	Lazertinib	BDTX-1535
0	4	7	14	25

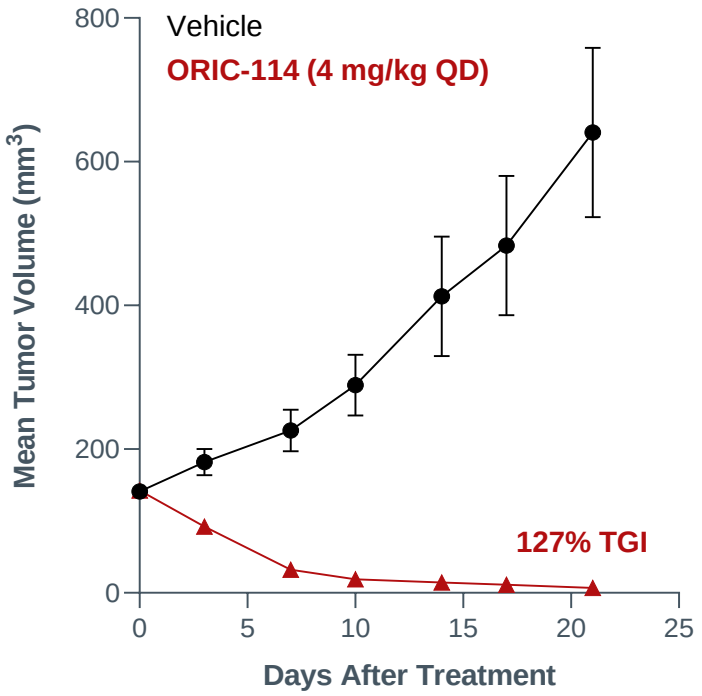
ORIC-114 has demonstrated an exquisitely clean kinome panel, mitigating the potential for off-target toxicities

Source: Junttila et al. ESMO (2023) and ORIC data on file.
Note: Kinase binding profiles across 468 kinases at 1 μM assessed using KINOMEscan. Red circles indicate kinases impacted within 10% of control. Table reports the number of off-target (non-EGFR/HER2) wildtype kinases inhibited 80% or more.

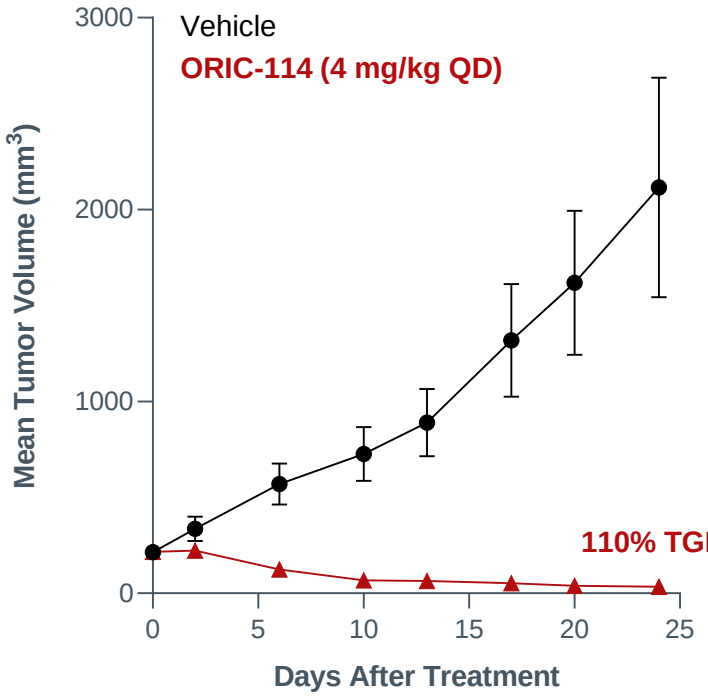
ORIC-114 Demonstrates Potent In Vivo Activity in EGFR Exon 20 Insertion Models

In Vivo Efficacy – NSCLC EGFR Exon 20 Insertion Models

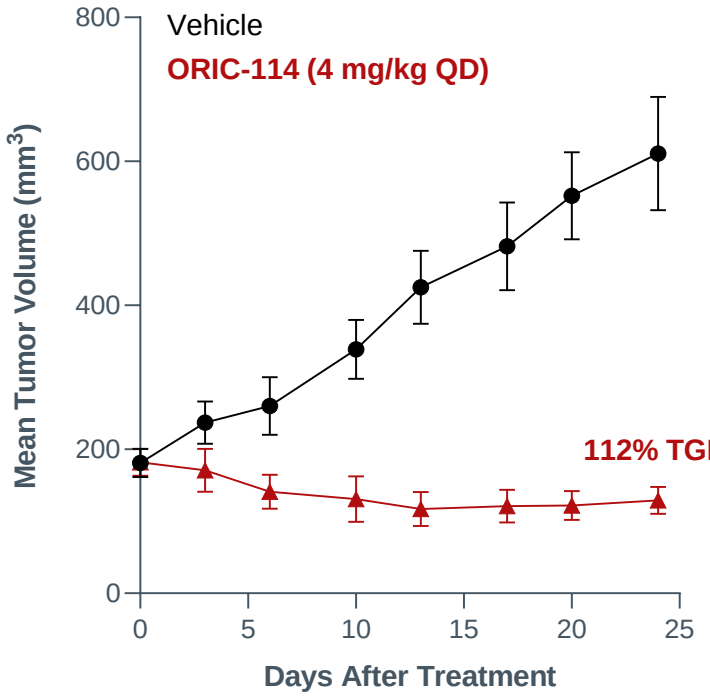
EGFR Exon 20 insNPH



EGFR Exon 20 insASV



EGFR Exon 20 insG



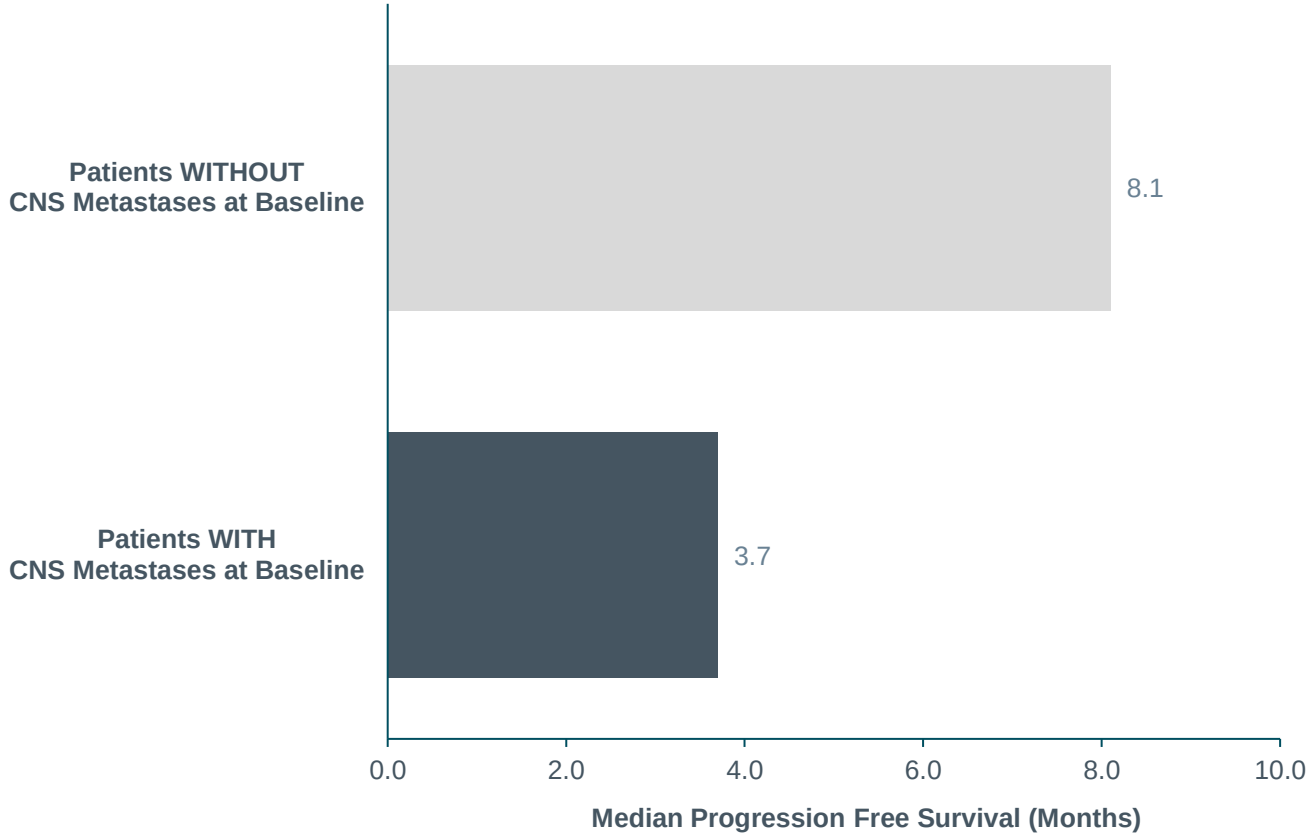
ORIC-114 demonstrates potent tumor regression in multiple NSCLC EGFR exon 20 insertion models without significant body weight loss

Source: Junttila et al. AACR (2021).

Drugs Lacking CNS Activity Often Have Worse Clinical Outcomes in NSCLC

Case Study on NSCLC Targeted Therapy without CNS Activity: Mobocertinib

- In mobocertinib's phase 1/2 trial, ~35% of patients had CNS metastases at baseline
- Patients with CNS metastases at baseline had markedly worse outcomes
  - Brain was the first site of progression in 68% of patients with CNS metastases at baseline and in 38% of all patients
  - ORR was 25% in patients with CNS metastases at baseline compared to 43% in all patients



Approximately 35% of EGFR exon 20 NSCLC patients have CNS metastases at baseline and the brain is a frequent site of progression in patients with and without CNS metastases at baseline, leading to shorter PFS with therapies lacking CNS activity

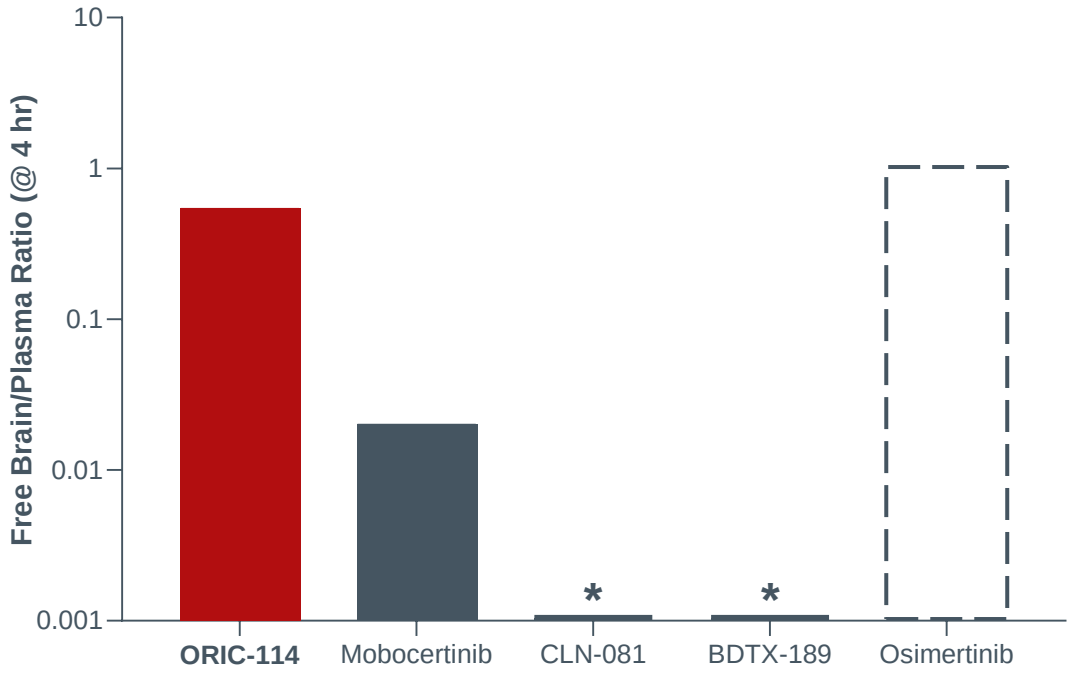
Source: Janne et al. ASCO (2019) and Ramalingam et al. ASCO (2021).

Superior Brain Penetration of ORIC-114 Differentiates from Comparator Exon 20 Targeted Agents

ORIC-114 Properties Allowed Optimization of Brain Exposure

- Minimal pump engagement
  - Key pumps that limit brain penetration, PGP and BCRP drug transporters, have minimal impact on ORIC-114 in cell assays
- Suitable physicochemical properties
  - LogP, LogD, TPSA, MW, HBD/HBA, pKa
- High free unbound exposure in brain tissue
  - Mouse Kp,uu 0.5
  - Dog Kp,uu 1.5

ORIC-114 Exhibits High Ratio of Free (Unbound) Brain/Plasma Exposure in Mice

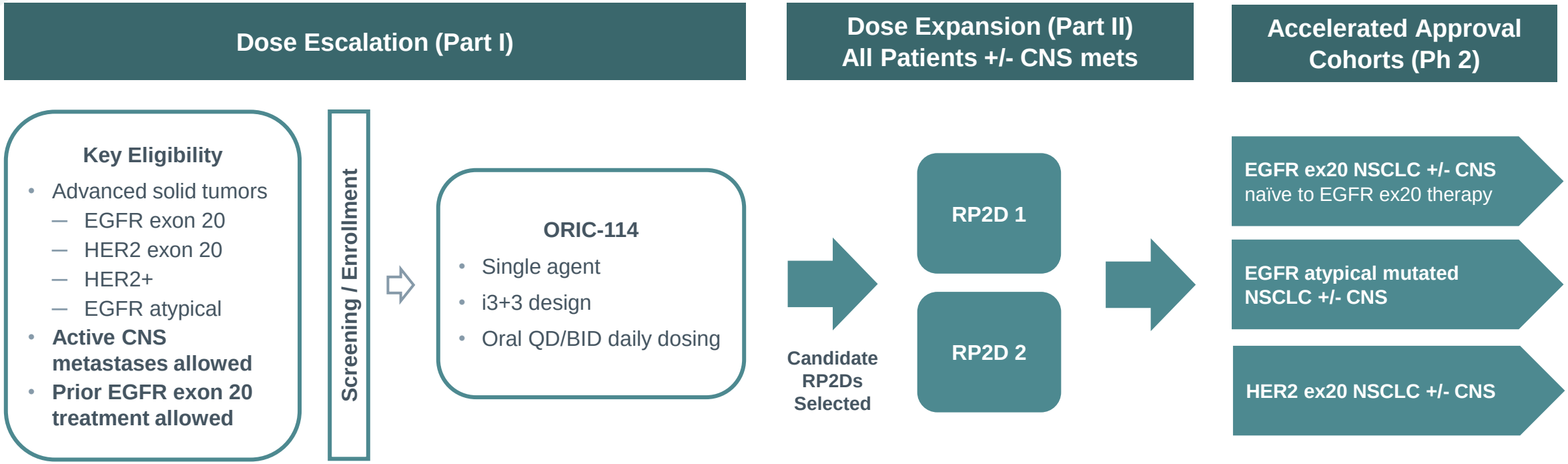


Extensive preclinical profiling demonstrates superior CNS properties of ORIC-114 versus competitors; Excellent free brain exposure across species for ORIC-114 as exhibited by Kp,uu

Source: Junttila et al. AACR (2021), Junttila et al. AACR-NCI-EORTC (2021) and ORIC data on file. * Brain exposures were below quantification limit.

First-In-Human Phase 1b Study of ORIC-114

Phase 1b, Multicenter, Open-Label Study



Primary endpoints: Part I: Safety and candidate RP2Ds; Part II: Dose expansion (RP2D selection) and ORR (per RECIST v1.1)

Key secondary endpoints: Part I: PK; Part II: Safety; DOR, CBR and PFS, including intracranial ORR/PFS

Initial safety, PK/PD, and preliminary antitumor data from dose escalation (part I) presented at ESMO 2023

Note: ClinicalTrials.gov identifier: NCT05315700. Dose expansion may include QD and BID dosing, fed/fasted dosing. RP2D, recommended Phase 2 dose

ORIC-114 Phase 1 Patient Disposition and Baseline Characteristics

Patient Disposition and Baseline Characteristics

- 50 patients were treated with increasing doses of ORIC-114
- Of the NSCLC patients with EGFR exon 20
  - ≥1 prior EGFR ex20: 81%
  - ≥2 prior EGFR ex20: 19%
  - CNS mets at baseline: 86%
- Of the NSCLC patients with HER2 exon 20
  - ≥1 prior HER2 agent: 30%
  - CNS mets at baseline: 38%

	EGFR Ex20 (n=21)	HER2 Ex20 (n=24)	HER2+ (n=5)	Total (N=50)
Age, years, median (range)	63 (31,80)	63 (25,86)	66 (48,68)	63 (25,86)
Females, n (%)	10 (48)	11 (46)	3 (60)	24 (48)
ECOG performance score, n (%)				
0	1 (5)	10 (42)	3 (60)	14 (28)
1	20 (95)	14 (58)	2 (40)	36 (72)
Non-smoker, n (%)	12 (57)	16 (68)	3 (60)	31 (62)
Prior lines of therapies, median (min, max)	2 (1,6)	2 (0,7)	4 (1,7)	2 (0,7)
Prior therapies, n (%)				
Chemotherapy	21 (100)	23 (96)	5 (100)	49 (98)
EGFR targeted agents	18 (86)	1 (4)	–	19 (38)
EGFR exon 20 targeted agents	17 (81)	–	–	17 (34)
Amivantamab	15 (71)	–	–	15 (30)
Mobocertinib	4 (19)	–	–	4 (8)
Other (CLN-081, BLU-451)	2 (10)	–	–	2 (4)
HER2 targeted agents	–	7 (30)	3 (60)	10 (20)
CNS metastases at baseline, n (%)	18 (86)	9 (38)	1 (20)	28 (56)

Phase 1b enrolled heavily pretreated patients with exceptionally high rates of prior exon 20 targeted therapy and CNS metastases at baseline

Note: All data as of the data cut-off on September 26, 2023.

ORIC-114 Has Been Generally Well Tolerated Despite More Heavily-Pretreated Patients and Less Stringent Enrollment Criteria for Prior Therapy and CNS Disease

Treatment Related Adverse Events Occurring in ≥10% of Patients

- Well tolerated safety profile with mostly Grade 1-2 TRAEs
- Minimal EGFR-wt related or other toxicities
- Low rates and severity of rash and diarrhea
  - No Grade ≥3 rash
  - Low rate of Grade 3 diarrhea (6%)
- Infrequent dose reduction and discontinuations

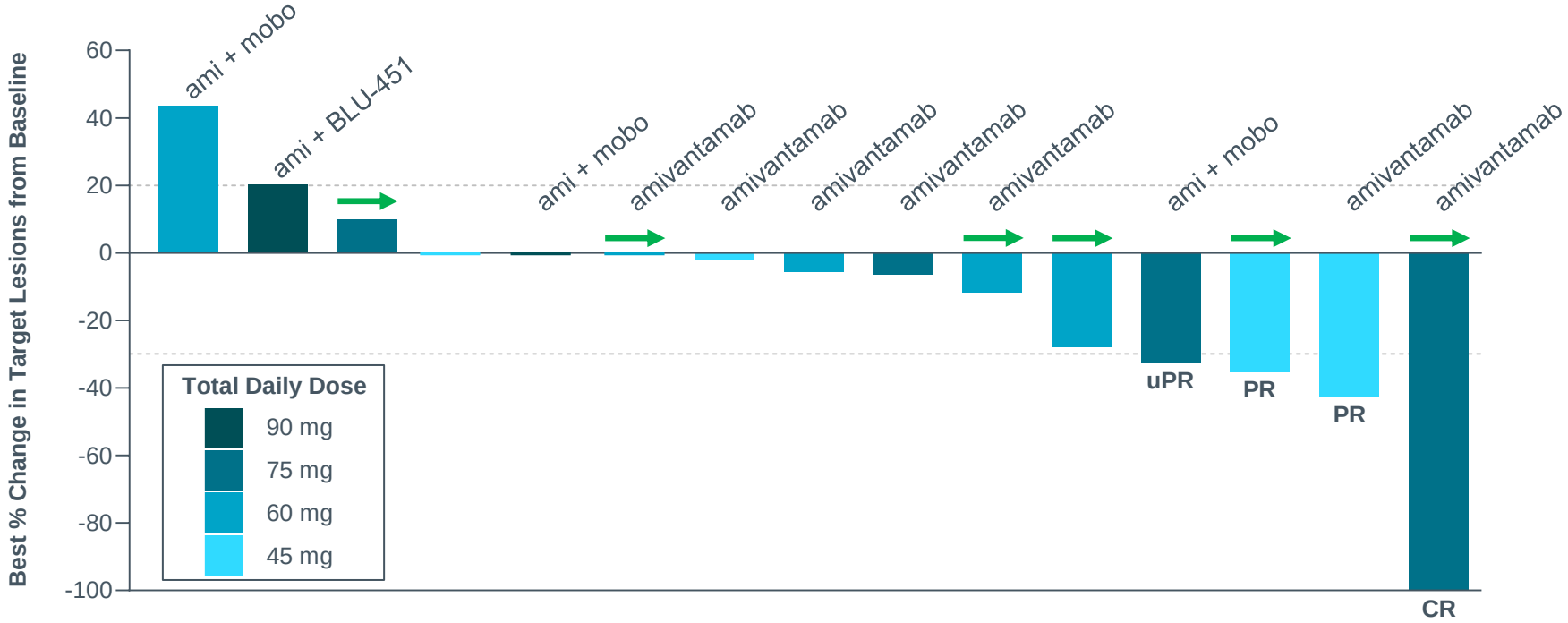
	<45 mg TDD (n=18)				45 – 60 mg TDD (n=23)				≥75 mg TDD (n=9)				Total (N=50)
Preferred Term, n (%)	**Gr1**	**Gr2**	**Gr3**	**≥Gr4**	**Gr1**	**Gr2**	**Gr3**	**≥Gr4**	**Gr1**	**Gr2**	**Gr3**	**≥Gr4**	**All Grades**
Rash*	6 (33)	4 (22)	–	–	6 (26)	6 (26)	–	–	4 (44)	1 (11)	–	–	27 (54)
Diarrhea	2 (11)	2 (11)	–	–	7 (30)	2 (9)	2 (9)	–	2 (22)	2 (22)	1 (11)	–	20 (40)
Stomatitis	4 (22)	2 (11)	–	–	2 (9)	2 (9)	1 (4)	–	2 (22)	2 (22)	–	–	15 (30)
Paronychia	1 (6)	2 (11)	–	–	4 (17)	4 (17)	–	–	2 (22)	1 (11)	–	–	14 (28)
Pruritis	2 (11)	–	–	–	4 (17)	2 (9)	1 (4)	–	1 (11)	1 (11)	–	–	11 (22)
Nausea	1 (6)	–	–	–	2 (9)	2 (9)	–	–	1 (11)	1 (11)	1 (11)	–	8 (16)
Decreased appetite	–	1 (6)	–	–	5 (22)	1 (4)	–	–	–	–	–	–	7 (14)
Vomiting	2 (11)	–	–	–	2 (9)	–	–	–	1 (11)	1 (11)	1 (11)	–	7 (14)
Dose Reductions		2 (18)				3 (13)				3 (33)			8 (16)
Dose Discontinuations		1 (9)				1 (4)				–			2 (4)

ORIC-114 was well tolerated with mainly Grade 1 and 2 adverse events and little evidence of off-target toxicities

Note: All data as of the data cut-off on September 26, 2023. * Rash includes the following terms: acne, dermatitis, dermatitis acneiform, eczema, hand dermatitis, and rash. TDD, total daily dose. TRAE, treatment related adverse event.

EGFR Exon 20: Tumor Regressions Across Multiple Active ORIC-114 Doses

Preliminary Activity (NSCLC patients with EGFR exon 20 and treated at ≥45 mg TDD)



Prior EGFR exon 20 therapy	+	+	-	-	+	+	+	+	+	+	-	+	-	+	+
CNS Metastases at Baseline	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+
Best CNS Response	ND	PD	PD	SD/PR	PD	PD	—	SD/PR	—	SD/PR	SD/PR	SD/PR	SD/PR	SD/PR	**CR**

2 of 3 CNS lesions resolved

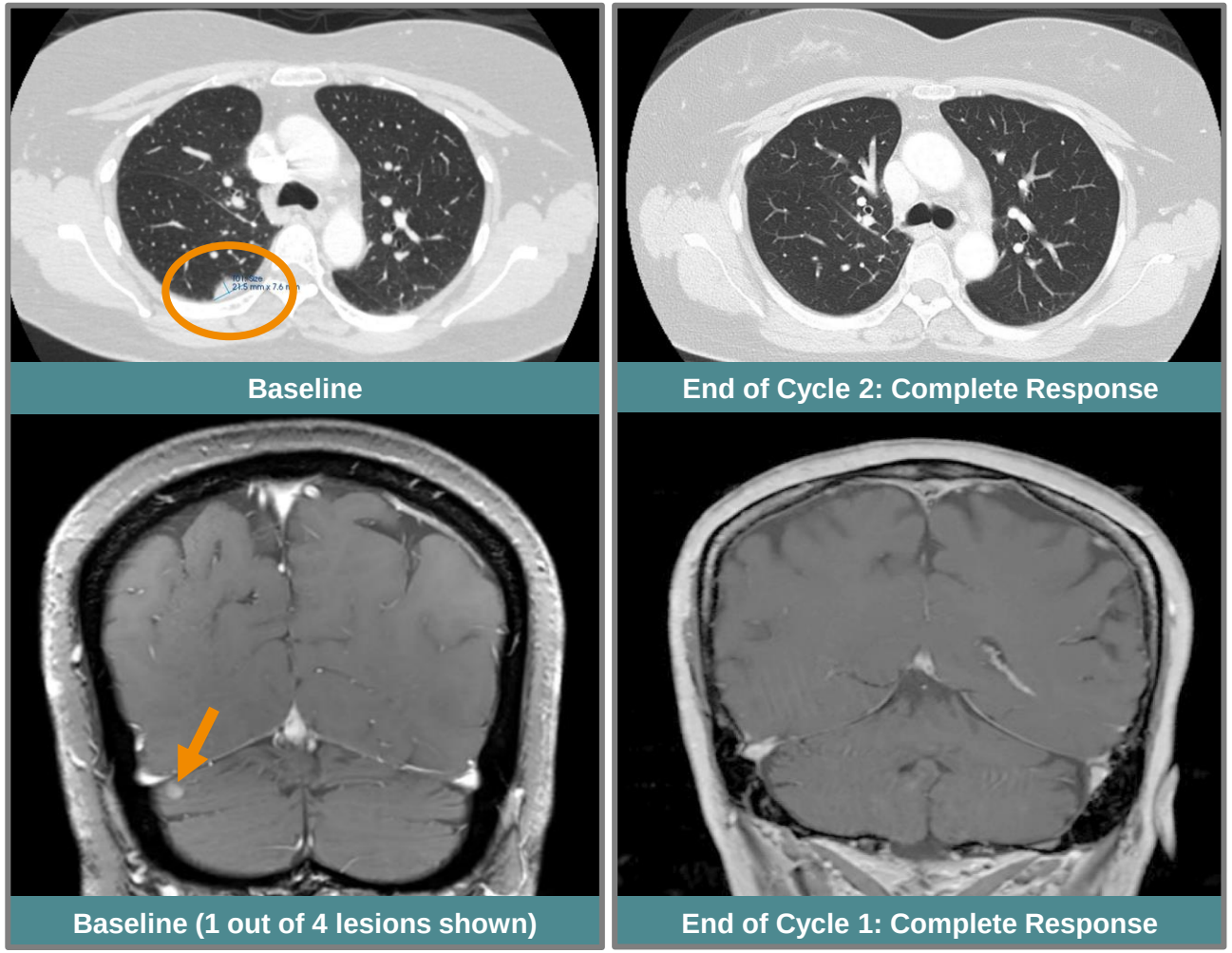
4 of 4 CNS lesions resolved

Systemic and CNS activity observed in heavily pretreated patients, including prior EGFR exon 20 therapy & active brain metastases

Note: All data as of the data cut-off on September 26, 2023. ND: not done, SD/PR: Non-CR/Non-PD (RECIST 1.1), Response-evaluable: Dose level ≥45 mg TDD and at least one post-baseline tumor assessment.

Confirmed Complete Intracranial and Systemic Response in Patient with EGFR Exon 20 Mutated NSCLC and Active CNS Metastases Progressed on Prior EGFR Exon 20 Targeted Therapy

- **Patient:** 55F with EGFR exon 20 mutated NSCLC
- **Prior therapy:** Pemetrexed/cisplatin and amivantamab
- **Metastases at baseline:** Four active CNS non-target lesions
  - Previously untreated
  - No prior surgery
  - No prior radiation
- **ORIC-114 dose:** 75 mg QD
- **Systemic response:** Partial response after Cycle 1 (60% reduction in all target and non-target lesions) followed by complete response at the end of Cycle 2 (100% reduction of all target and non-target lesions), subsequently confirmed
- **CNS response:** Complete response after Cycle 1 (100% reduction of all 4 CNS lesions) confirmed after Cycle 2
- **Grade ≥2 treatment-related AEs:** Grade 2 mucositis and paronychia
- **Duration of treatment:** Cycle 9 (ongoing)



ORIC-114 demonstrated single agent clinical activity in a key cancer and molecular subtype (i.e., NSCLC and EGFR exon 20) in a patient typically excluded from clinical trials (i.e., active brain metastases) and previously treated with EGFR exon 20 therapy

Note: All data as of the data cut-off on September 26, 2023.

ORIC-114 Is the Only EGFR Exon 20 Inhibitor to Demonstrate a Systemic Complete Response and CNS Complete Response, Despite More Challenging Patients

Comparison of Selected Eligibility Criteria, Baseline Characteristics, and Clinical Activity

- EGFR exon 20 inhibitor clinical studies typically EXCLUDE:
  - Prior EGFR exon 20 treatment
  - Untreated CNS metastases
- ORIC-114 trial enrolled significantly higher percentage of patients with prior EGFR exon 20 treatment and baseline CNS metastases
- Despite more challenging patients, ORIC-114 demonstrated:
  - Systemic complete response
  - CNS complete response in untreated CNS metastases
  - Responses post-amivantamab

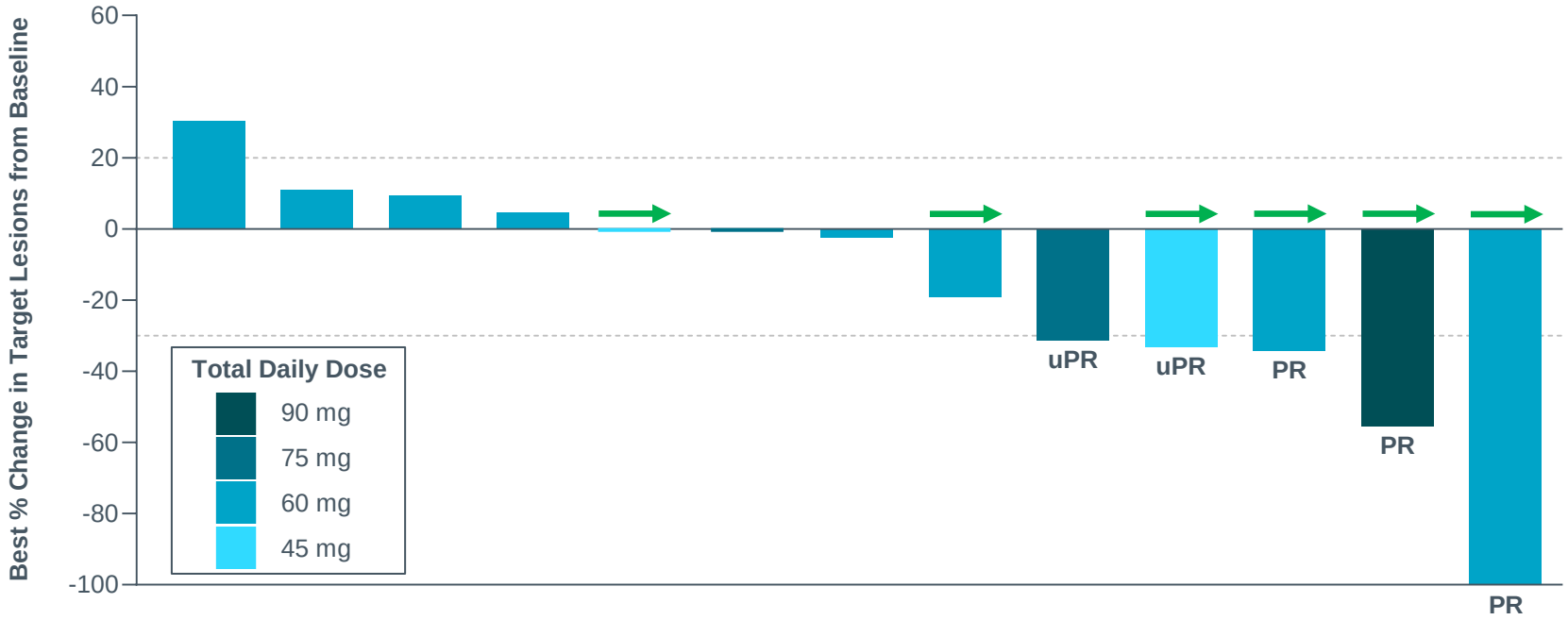
	Amivantamab	CLN-081	Sunvozertinib	Furmonertinib	BLU-451	ORIC-114
Trial	Phase 1	Phase 1	Phase 2	Phase 1	Phase 1	Phase 1
ENROLLMENT						
Prior EGFR ex20i Allowed (1)	No	No	No	No	Yes	**Yes**
% Prior EGFR ex20i	1%	4%	3%	NR	75%	**81%**
Untreated CNS Mets Allowed	No	No	No	No	Yes	**Yes**
% Baseline CNS Mets	22%	38%	32%	34%	58%	**86%**
CLINICAL ACTIVITY						
Systemic Complete Response	Yes	No	No	No	No	**Yes**
CNS Complete Response in Untreated CNS Mets (2)	No	No	No	No	No	**Yes**
ORR in EGFR ex20i Naive	~40%	~41%	~61%	42%	TBD	**TBD**
Post-Amivantamab Response	NA	No	Yes	No	No	**33% confirmed ORR (at 75 mg)**

Even while allowing patients with prior exon 20 treatment and untreated brain metastases, ORIC-114 is the only EGFR exon 20 inhibitor to demonstrate a confirmed complete systemic response and confirmed complete CNS response

Note: All data as of the data cut-off on September 26, 2023. Source: Park et al. J Clin Oncol (2021), Zhou et al. JAMA Oncology (2021), Piotrowska et al. J Clin Oncol (2023), Han et al. WCLC (2023), Wang et al. ASCO (2023), and Nguyen et al. ASCO (2023). (1) Amivantamab prohibited prior EGFR exon 20 treatment in dose expansion. CLN-081 allowed prior EGFR exon 20 treatment selectively during accelerated titration dose escalation only. (2) Treatment history for brain metastases not disclosed for BLU-451.

HER2 Exon 20: Tumor Regressions Across Multiple Active ORIC-114 Doses

Preliminary Activity (NSCLC patients with HER2 exon 20 and treated at ≥45 mg TDD)



Prior HER2 therapy	-	+	-	-	-	-	+	-	-	-	-	+	-
CNS Metastases at Baseline	+	-	-	+	-	-	-	-	-	+	+	-	-
Best CNS Response	SD/PR	—	—	ND	—	—	—	—	—	SD/PR	SD/PR	—	—

Shrinkage of CNS lesions

ORIC-114 demonstrated clinical activity in patients with HER2 exon 20 NSCLC, including in patients with baseline brain metastases

Note: All data as of the data cut-off on September 26, 2023. ND: not done, SD/PR: Non-CR/Non-PD (RECIST 1.1), Response-evaluable: Dose level ≥45 mg TDD and at least one post-baseline tumor assessment.

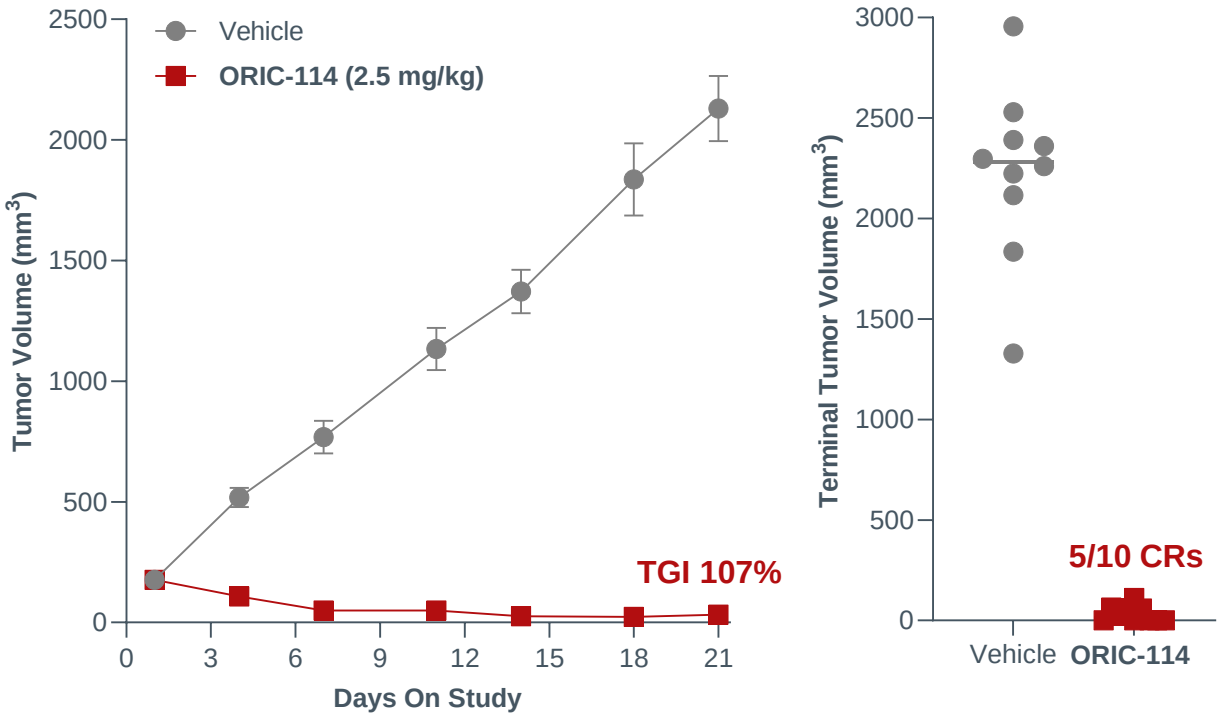
In Addition to EGFR Exon 20, ORIC-114 Also Demonstrates Excellent Preclinical Activity Against Atypical Mutations in EGFR, Revealing an Additional Opportunity

ORIC-114 In Vitro and In Vivo Activity in Atypical EGFR Mutations

ORIC-114 Demonstrates Superior In Vitro Potency

Type	Atypical Mutations	BaF3 Cell EC50 Ratio EGFR WT / Mutant		
		ORIC-114	Afatinib	Firmonertinib
primary	G719C	**8x**	4x	2x
	G719S	**9x**	4x	1x
	L747S	**1x**	1x	1x
	L747P	**2x**	1x	2x
acquired	L858R L718V	**31x**	13x	1x
	L858R L718Q	**7x**	1x	0.1x
	del19 G796S	**5x**	5x	0.5x
	del19 L792H	**3x**	1x	0.09x

ORIC-114 Induces Complete Tumor Regressions In Vivo



ORIC-114 is a promising therapy for NSCLC patients with atypical mutations in EGFR, based on promising preclinical activity and the emerging clinical profile in patients with EGFR and HER2 exon 20 insertion mutations

Source: Junttila et al. ESMO (2023). Note: Left graph, Ba/F3 cells stably expressing EGFR wild-type or EGFR carrying classical or atypical mutations. Middle graph, EGFR G719S atypical mutant xenograft model. Right graph: Individual terminal tumor volumes at day 21. Mean is indicated by a line. No body weight loss observed. Complete response, CR, defined as tumor of undetectable size.

ORIC Entered into a Clinical Collaboration with Johnson & Johnson to Evaluate ORIC-114 Plus Amivantamab in 1L NSCLC Patients with EGFR Exon 20

ORIC Johnson & Johnson

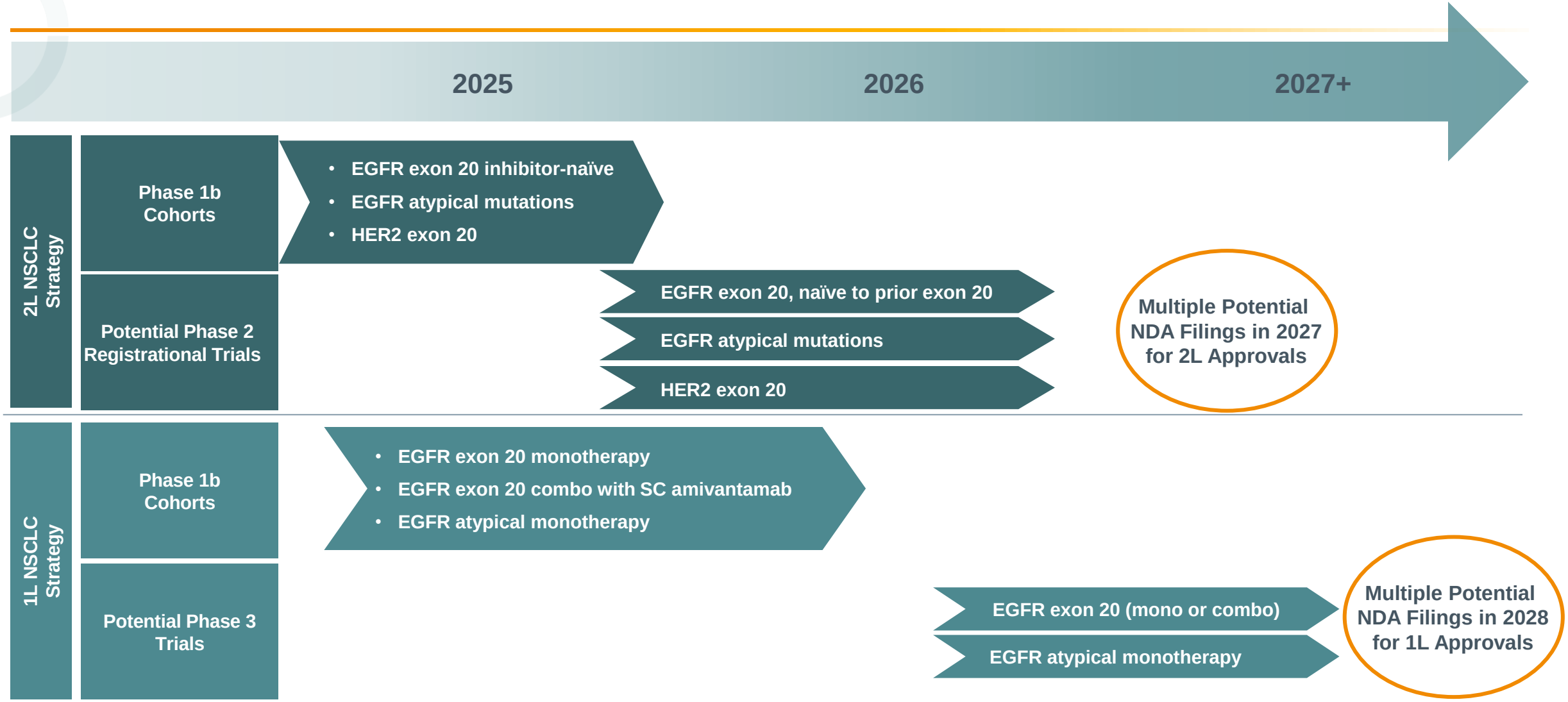
Collaboration Overview	• ORIC-114 plus SC amivantamab to be evaluated in 1L NSCLC with EGFR exon 20 insertions — Phase 1b combination study initiation expected in 1Q25 • ORIC to conduct the initial study and Johnson & Johnson to provide SC amivantamab • ORIC retains development and commercialization rights to ORIC-114
Combination Rationale	✓ Potential for deeper and more durable clinical activity than either agent alone — ORIC-114 provides CNS exposure to treat and/or prevent brain metastases — Amivantamab provides activity against potential TKI resistance mechanisms (e.g., cMET, C797S) — Combination may provide more potent and comprehensive coverage across exon 20 insertions ✓ Proof of concept established with lazertinib plus amivantamab in classical EGFR mutations (1) ✓ Chemotherapy free regimen

ORIC and Johnson & Johnson are evaluating the potential of ORIC-114 plus SC amivantamab in 1L NSCLC with EGFR exon 20; initial data from the combination trial expected in mid-2026

ORIC

(1) Cho et al. N Engl J Med (2024).

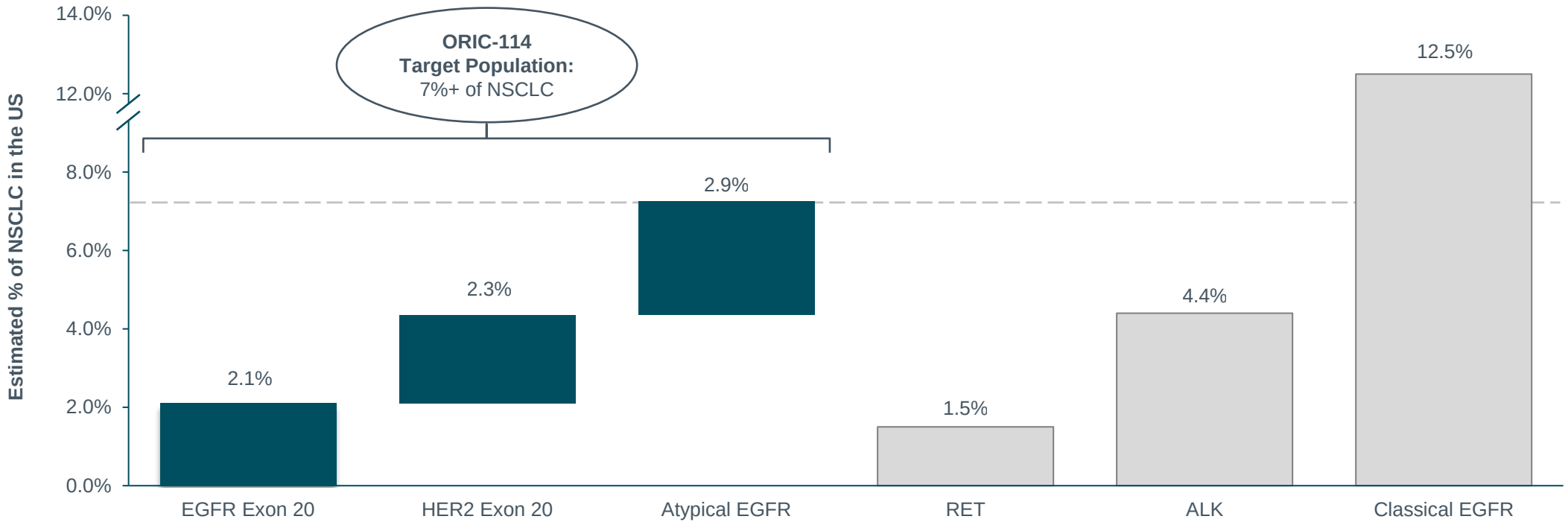
ORIC-114 Planned Next Steps and Potential Registrational Path(s)



Updated Phase 1b data expected in 1H 2025 with the potential initiation of multiple accelerated registrational cohorts expected in 2H 2025; potential for ORIC-114 1L registrational trial(s) initiation in 2026

ORIC-114 Is Pursuing a Significant Commercial Opportunity Across Multiple Patient Populations that Do Not Have CNS Active Agents Approved or in Late-Stage Development

Estimated US Prevalence of Exon 20 Insertions (% of NSCLC)

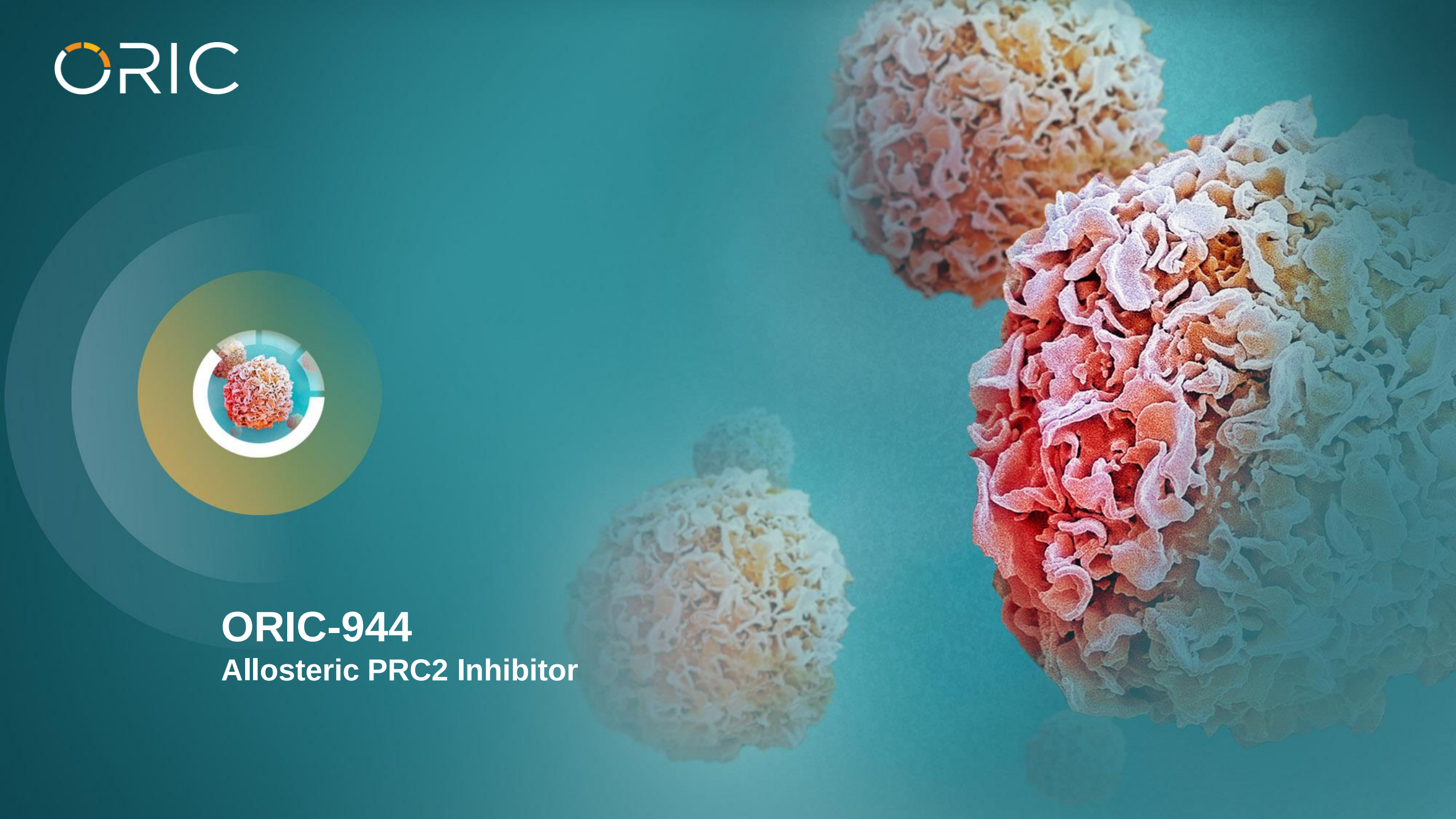


Approved Agents with CNS Activity:	✘	✘	✘	Selpercatinib	Alectinib	Osimertinib
Worldwide Annualized 2024 Estimated Sales:	–	–	–	~$365m (+44% YoY)	~$1,700m (+2% YoY)	$6,500m (+12% YoY)

The commercial opportunity for ORIC-114 may represent over 7% of NSCLC (>13,000 patients) in the US annually

Source: American Cancer Society Cancer Facts & Figures 2024, Gainor et al. Clin Cancer Res (2013), Hirsch et al. Lancet (2017), Rosen et al. Clin Cancer Res (2021), Heymach et al. WCLC (2018), Le et al. WCLC (2024) and Robichaux et al. Nature (2021). Lilly, Roche, and AstraZeneca corporate filings. Note: Worldwide annualized 2024 estimated sales calculated using reported 1Q-3Q24 sales and adjusted for an annual run rate.

ORIC



ORIC-944

Allosteric PRC2 Inhibitor

ORIC-944: Potential Best-In-Class PRC2 Inhibitor to Overcome Limitations of Early Generation PRC2 Inhibitors for Prostate Cancer

KEY LIMITATIONS of approved and investigational agents

- **Poor in vitro and in vivo potency** across preclinical prostate cancer models for early generation PRC2 inhibitors
- **Inadequate clinical drug exposures** due to short half-life and/or CYP autoinduction
- **Suboptimal tolerability** potentially from variability in pharmacokinetic profiles

ORIC-944 may address these limitations

- **Selectively targets PRC2** through the allosteric inhibition of the EED subunit
- **Superior in vitro and in vivo activity** observed across preclinical prostate cancer models
- **Synergistic activity with AR Inhibitors** demonstrated across preclinical prostate cancer models
- **Phase 1b single agent data demonstrated strong drug properties and well tolerated profile**
  - Clinical half-life of ~20 hours and no signs of CYP autoinduction
  - Robust target engagement with once-daily dosing
  - Primarily Grade 1–2 TRAEs

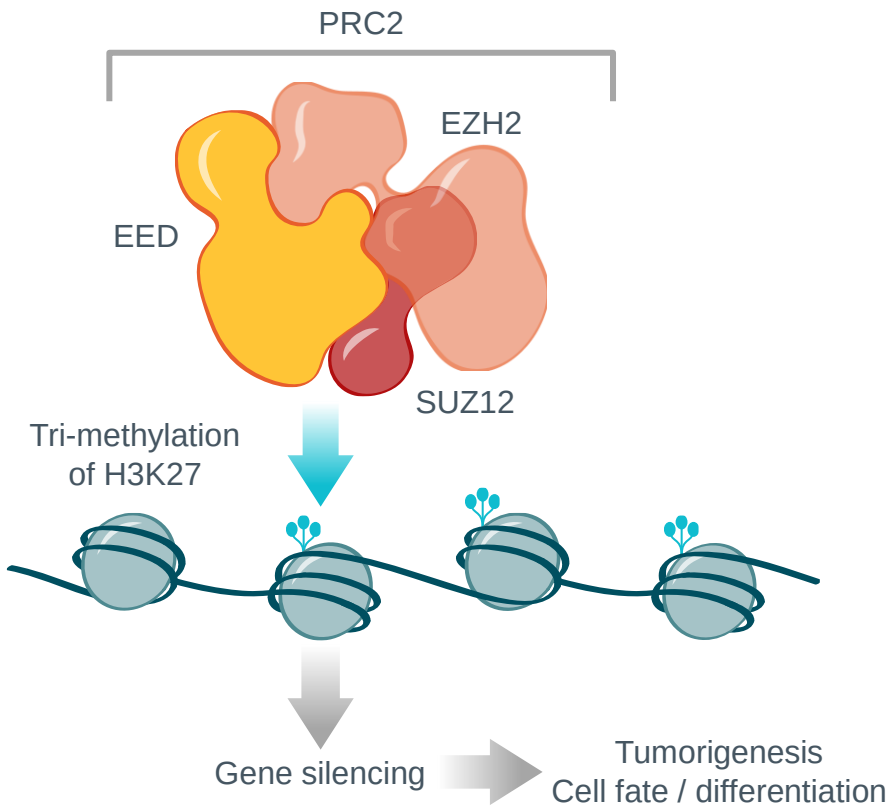
STATUS of development

- **Initiated combination studies** with AR inhibitors mid-2024
- **Established clinical trial collaboration and supply agreements** with Bayer and Johnson & Johnson
- **Presented initial Phase 1b data** for ORIC-944 in combination with apalutamide
- **Phase 1b combination data** with AR inhibitors expected 4Q25 / 1H26

ORIC-944 is a potential best-in-class therapy for combination development with AR inhibitors in prostate cancer with superior drug properties, an excellent PK profile, robust PD activity, and favorable safety profile to date

PRC2 Plays Pivotal Role in Transcriptional Regulation and Cancer

PRC2 Function



PRC2 Background

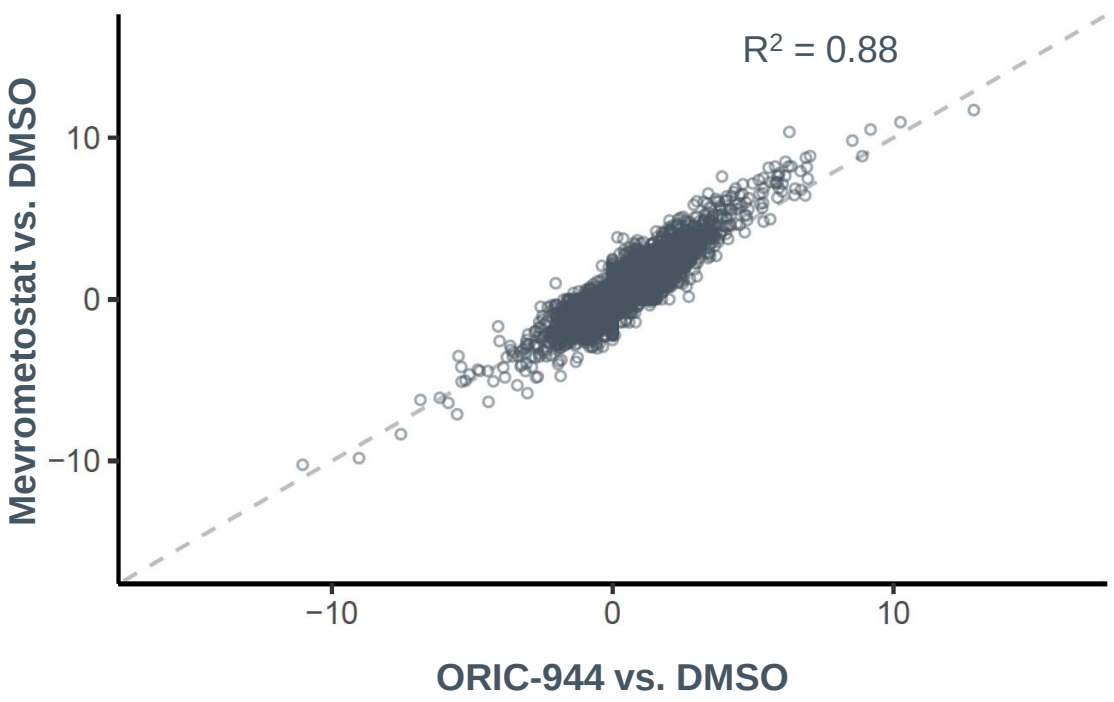
- Two druggable subunits:
  - EED: responsible for histone binding; target of ORIC-944
  - EZH2: responsible for histone methylation; target of first-generation inhibitors
- Dysregulation of PRC2 linked to several cancers
  - Decreased expression of target genes associated with poor prognosis in prostate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

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

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).

EED and EZH2 Inhibition Provides Equivalent Activity in Prostate Cancer Models

Equivalent Transcriptional Changes Observed Upon Initial Inhibition by EED and EZH2



Over the Long-term, EED Inhibition May Improve Upon EZH2 with Respect to Resistance

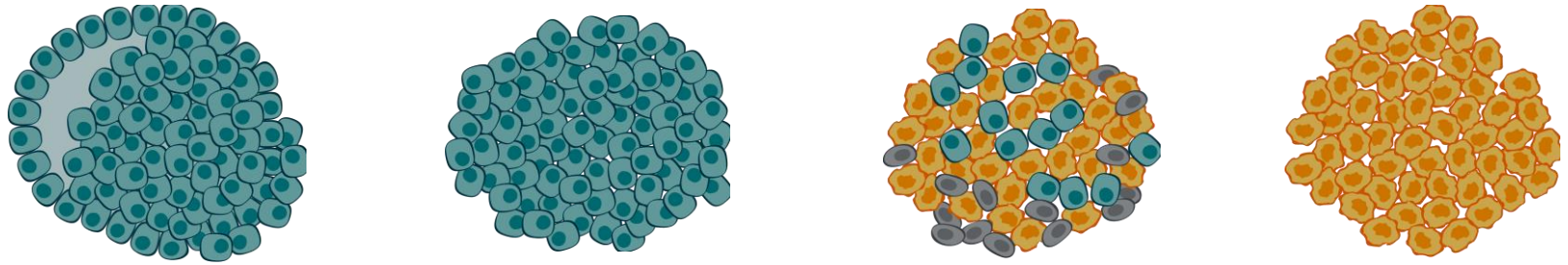
- ORIC-944 allosterically inhibits PRC2 by targeting EED
- Allosteric inhibition of PRC2 through EED may address limitations of EZH2 inhibitors
  - Active against EZH2 resistant PRC2 mutants (1)
  - Prevent acquired resistance through secondary mutations in EZH2 (2)
  - Inhibit compensatory bypass activity of EZH1 (3)

ORIC-944 and mevrometostat treatment result in equivalent transcriptional changes in prostate cancer cells; ORIC-944 may have long term advantages with respect to long-term resistance

Source: Friedman et al. AACR (2024) and ORIC data on file. (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).
Note: LNCaP prostate cells treated for 7 days with either EED inhibitor or EZH2 inhibitor vs DMSO. Transcriptional effects determined by RNA sequencing. Each dot represents a gene's differential expression (t-statistics) by treatment.

PRC2 Epigenetic Dysregulation Plays a Key Mechanistic Role During the Progressive Reprogramming of Prostate Cancers Treated with AR Inhibitors

AR Dependent Prostate Cancer | **AR Independent Prostate Cancer**



Castration sensitive | Castration resistant | Heterogeneous | Lineage change

AR-directed therapeutics

PRC2 inhibitors

Luminal-like: Hormone dependent
Pluripotent
Hormone independent

- Prostate cancer cells evade therapies by cellular reprogramming to an AR independent state
- PRC2 inhibition can reverse this process, such that prostate cancer cells regain AR dependency
- Mechanistic rationale supports combination of PRC2 inhibitors with AR inhibitors

Therapeutic potential of PRC2 inhibitors in prostate cancer is maximized in combination with AR inhibitors

ORIC

Source: Mu et al. Science (2017), Dardenne et al. Cancer Cell (2016), Davies et al. Nat Cell Biol (2021), Nouruzi et al. Nat Commun (2022), and Goel et al. Semin Cancer Bio (2022).

ORIC-944: A Rationally Designed Next-Generation PRC2 Inhibitor

PRC2 Inhibitor Landscape in Prostate Cancer

Potential Best-in-Class

Key Features	CPI-1205 (1st gen)	Tazemetostat (1st gen)	Mevrometostat (2nd gen)	ORIC-944 (3rd gen)	
Cellular Potency				✓ **Cellular Potency**	Superior potency vs. 1st gen programs across prostate cancer models
In Vivo Activity				✓ **In Vivo Activity**	Improved single agent and combination activity across prostate cancer models
Strong Drug Properties (PK, solubility, no CYP autoinduction)				✓ **Strong Drug Properties**	Higher and more consistent clinical exposures
Long Clinical Half-Life				✓ **Long Clinical Half-Life**	Sustained target coverage and QD dosing (~20-hour half-life)
Development Status	Discontinued	Discontinued	Phase 3 trials ongoing	**Phase 1b ongoing**	

ORIC-944 is a potential best-in-class PRC2 inhibitor that addresses the limitations of earlier generation PRC2 inhibitors

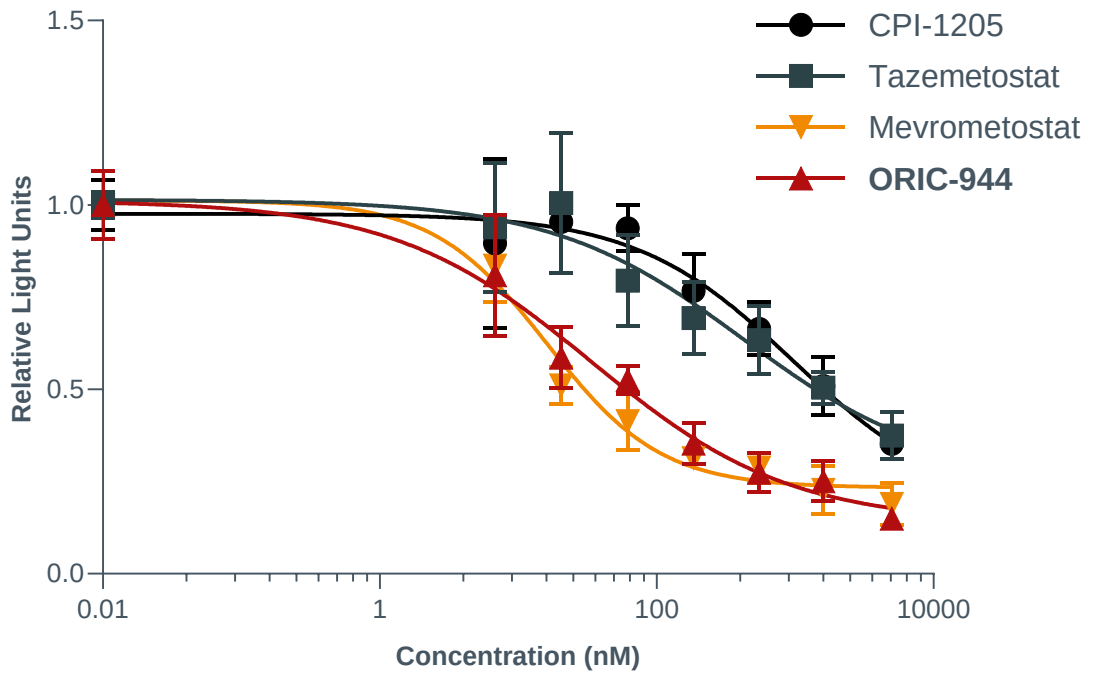
ORIC

Source: Friedman et al. AACR (2024), Vaswani et al. J Med Chem (2016), Motwani et al. and Bradley et al. AACR-EORTC-NCI (2019), Schweizer et al. ESMO (2022), Italiano et al. Lancet (2018), and Harb et al. TAT (2018).
Note: Drug Properties include absorption, CYP profile and metabolism, pharmacokinetic (PK) and solubility profile. Tazemetostat is approved for follicular lymphoma and epithelioid sarcoma, but development in prostate cancer has been discontinued.

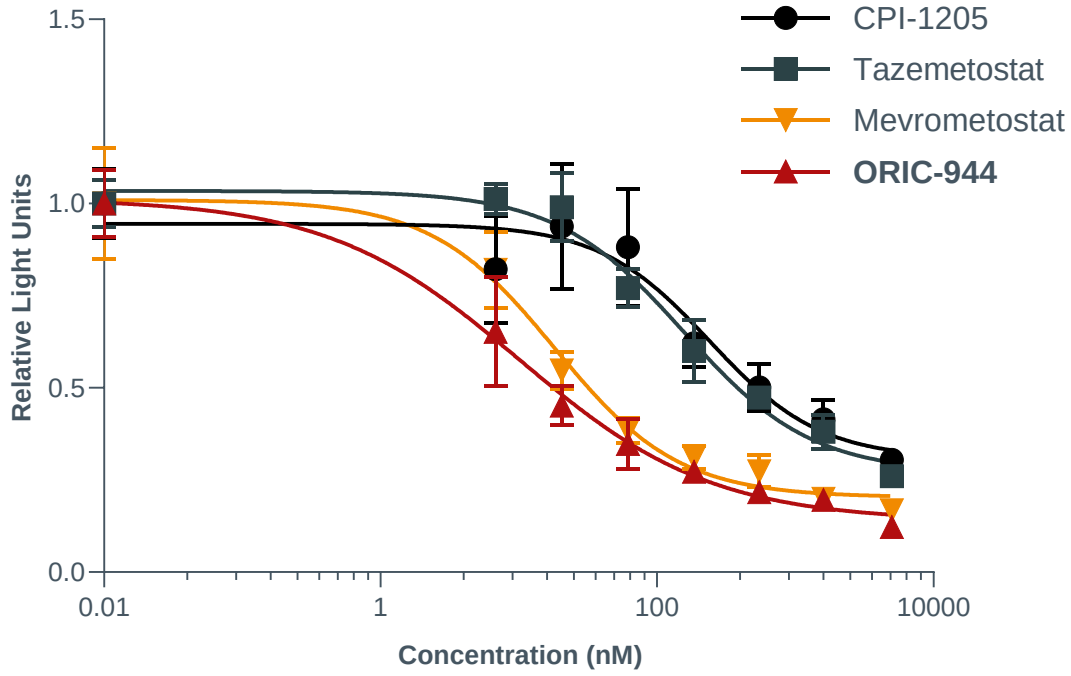
ORIC-944 Demonstrates Superior In Vitro Potency vs. First-Gen PRC2 Inhibitors

In Vitro Potency in Prostate Cancer Cells

LNCaP
(AR-Positive Cells)



CWR22PC
(AR-Positive Cells)



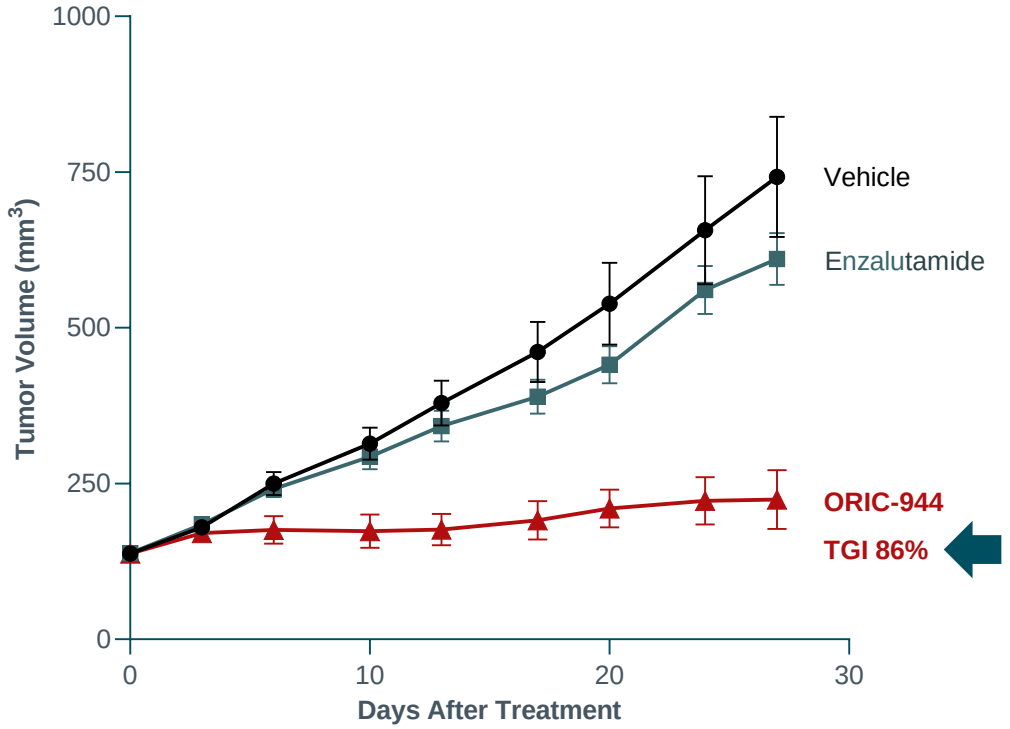
ORIC-944 demonstrates potency in AR+ prostate cancer cell lines comparable to mevrometostat and superior to tazemetostat and CPI-1205

Note: Head-to-head in vitro cell viability assays.

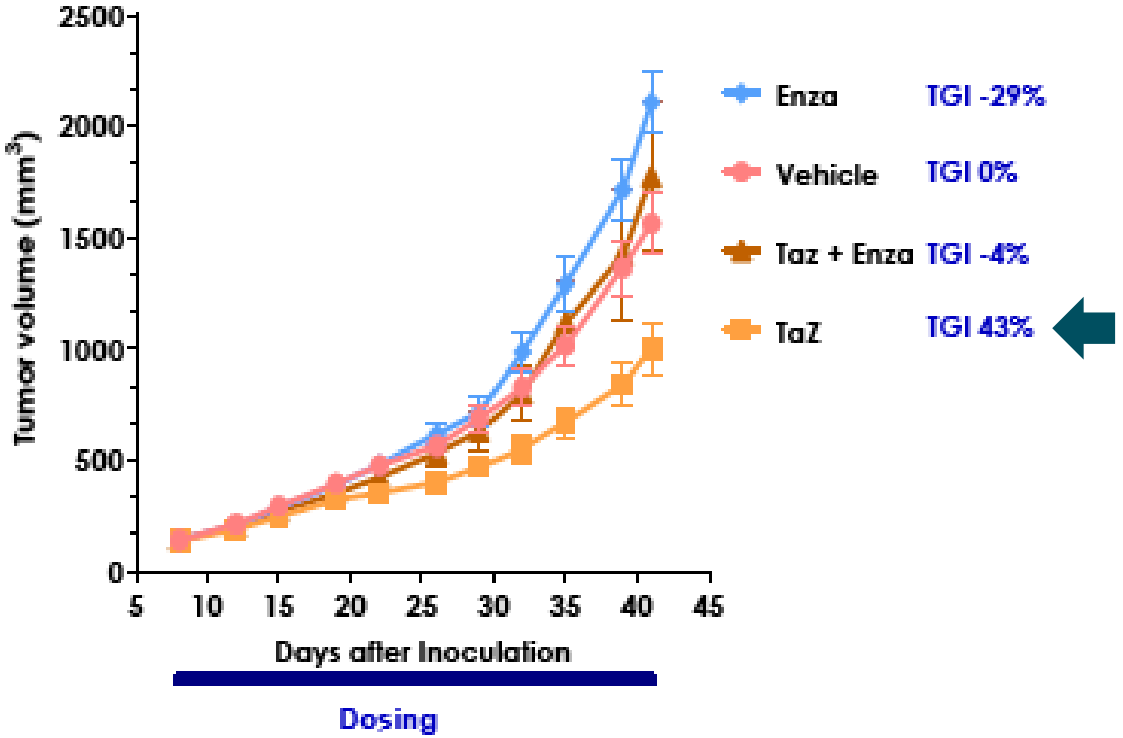
ORIC-944 Single-Agent Activity in Preclinical Prostate Cancer Model Compares Favorably to Previously Reported Data from Epizyme with Tazemetostat

Review of Published Preclinical Data: Prostate Cancer In Vivo Efficacy

ORIC-944 In Vivo Efficacy by ORIC



Tazemetostat In Vivo Efficacy by Epizyme



ORIC-944 single agent activity appears superior to data reported by Epizyme with tazemetostat in an enzalutamide-resistant in vivo prostate cancer model

Source: Daemen et al. AACR Poster (2021) and Motwani et al. AACR-EORTC-NCI Poster (2018). Note: 22Rv1 prostate cancer mouse model. Enzalutamide dose used was 30 mg/kg QD in both studies. Dose used for ORIC-944 was 200 mg/kg QD and 125 mg/kg BID for tazemetostat. Taz, tazemetostat. Enza, enzalutamide.

ORIC-944 Synergizes with AR Inhibitors in Preclinical Prostate Cancer Models

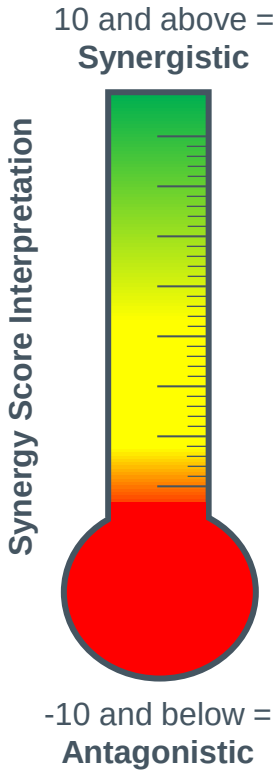
Combination Potential of PRC2 and AR Inhibition

Preclinical Synergy Assessment

- Synergy observed with ORIC-944 combination with enzalutamide in preclinical prostate cancer model
  - Cellular growth assay over 14 days
  - Dose-ranging concentrations of enzalutamide and PRC2 inhibitor, alone and in combination
  - Synergy scoring via multiple models
- Synergy also demonstrated with ORIC-944 in transcriptional based analysis, in combination with other AR inhibitors, and in additional prostate cancer cell lines

Synergy Score Results

Synergy Analysis	**ORIC-944 + enzalutamide**	PF-1497 + enzalutamide
Bliss	**10.6**	9.9
Loewe	**15.8**	14.1
HSA	**16.7**	15.4



ORIC-944 synergizes with AR inhibitors in prostate cancer models, providing rationale for clinical development

Source: Data in C4-2 prostate cancer cells shown.

Pfizer Phase 1 Data Clinically Validates Synergy of PRC2 Inhibitor and AR Inhibitor in Prostate Cancer

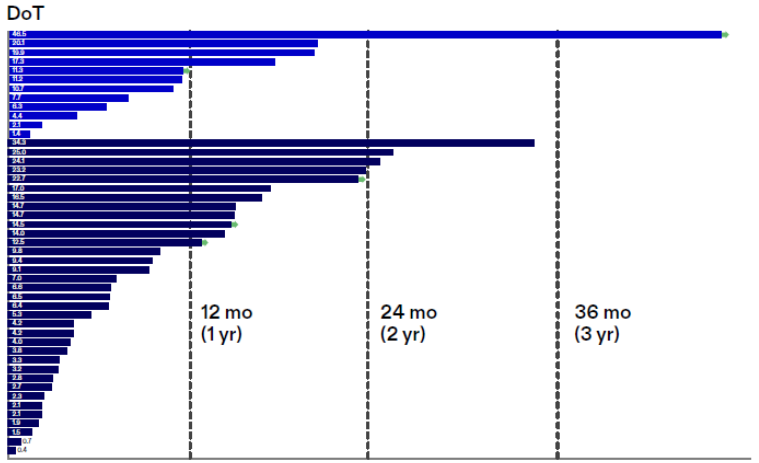
Updated mevrometostat Phase 1 Data in Prostate Cancer (Pfizer Oncology Innovation Day)

NEW DATA

Compelling Activity in Heavily Pre-Treated Patients With mCRPC Supports Phase 3 Program

Phase 1 Dose Escalation in 2L+ mCRPC (N=47)[1]

EZH2i + XTANDI Post-abi, N=12	EZH2i + XTANDI Post-XTANDI, N=35
Median rPFS = 17.1 mo (95% CI: 6.2, NE)	Median rPFS = 11.7 mo (95% CI: 4.2, NE)
Median DoT = 47 weeks (IQR: 23–80)	Median DoT = 28 weeks (IQR: 12–63)
Median number of prior anti-cancer therapies = 3 (range 1, 8)	
Most common TRAE were diarrhea (42.6%), dysgeusia (42.6%), and anemia (36.2%)	
Grade ≥3 TRAEs were reported in 17.0% of pts	
Discontinuation due to TRAE: 3/47 (6.3%)	



- Historical control of post-abi median rPFS = **4.8 months**[2]

ClinicalTrials.gov: NCT03460977.
[1]Data on file (initial data presented at ESMO2022), [2]deWit, et al. *N Eng J Med.* 2019.
Abi, abiraterone; AE, adverse event; ARPi, androgen receptor signalling pathway inhibitor; DoT, duration of treatment; Enza, enzalutamide; EZH2, enhancer of zeste homolog 2; IQR, interquartile range; mCRPC, metastatic castration-resistant prostate cancer; rPFS, radiographic progression-free survival; TRAE, treatment-related adverse event; 2L, second line.

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*"Based on the strong signal, **we are planning to initiate two pivotal studies in metastatic CRPC later this year**"*

"[As with Xtandi], there's nothing stopping us from building another wall of data now with an EZH2 inhibitor on top as appropriate"

Roger Dansey,
Chief Development Officer

"It's really the totality of the data that's driving our conviction to move to Phase 3"

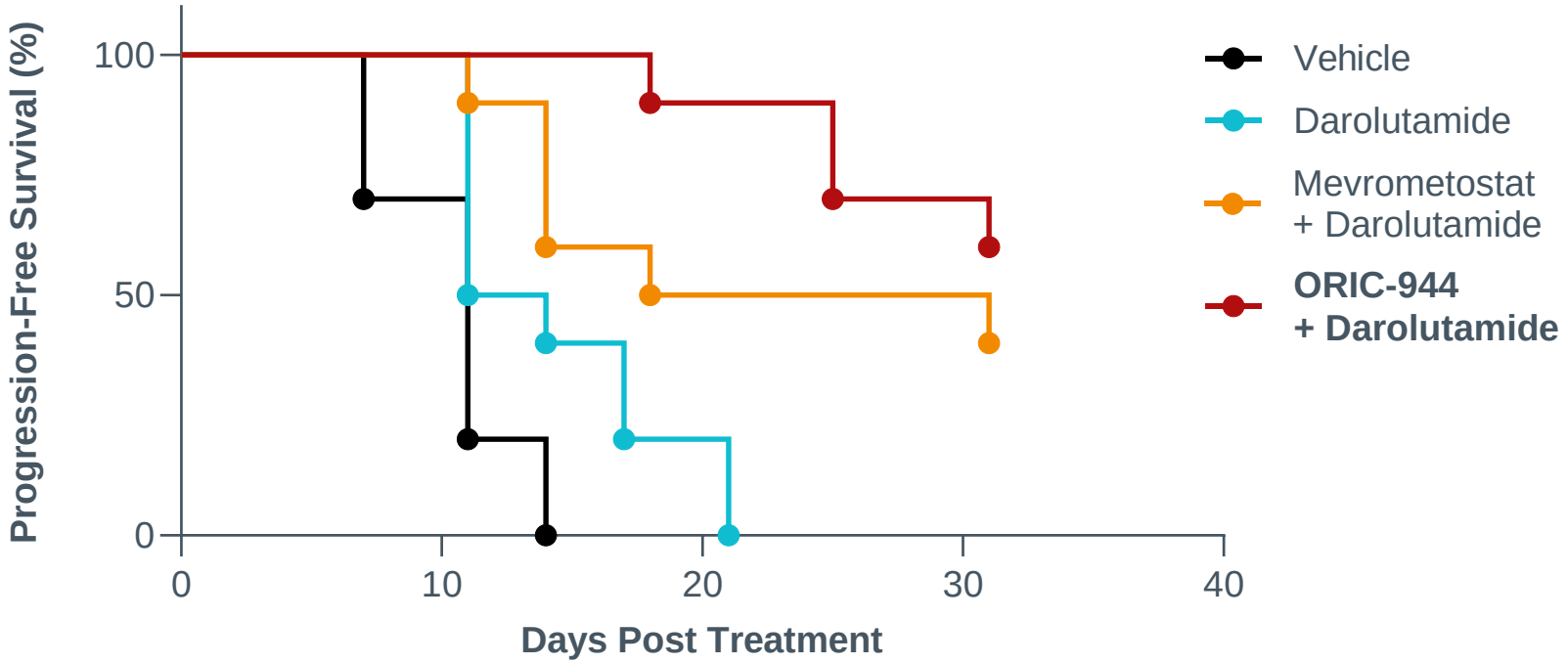
Dana Kennedy
Therapeutic Area Development Head for Genitourinary Cancer

Durable antitumor activity was observed in both Xtandi naïve and experienced patients with mCRPC, both of which are notably longer than historical controls

Source: Pfizer Oncology Innovation Day call on February 29, 2024.

ORIC-944 Increases Progression-Free Survival in Combination with AR Inhibitor in Prostate Cancer Xenograft Tumors

Progression-Free Survival in Prostate Cancer In Vivo Model



	Vehicle	Darolutamide	Mevrometostat + Darolutamide	ORIC-944 + Darolutamide
Median survival (days)	11	12.5	24.5	**Not reached**

ORIC-944 combination with darolutamide improves progression-free survival in a treatment refractory setting in vivo

Note: C4-2 model grown in castrated mice. Darolutamide 50 mg/kg BID, mevrometostat 100 mg/kg BID, and ORIC-944 100 mg/kg QD. No drug-related tolerability issues. Progression event for either tumor volume >800 mm3 or morbidity.

First-In-Human Phase 1b Study of ORIC-944 in Metastatic Prostate Cancer

Phase 1b, Multicenter, Open-Label Study

Single Agent Dose Escalation

Key Eligibility

- Metastatic prostate cancer
- Progressed:
  - ≥1 AR inhibitor(s)
  - ≤2 chemo regimens
- ECOG 0-1

Screening / Enrollment

ORIC-944

- Single agent
- i3+3 design
- Oral once daily dosing

Single Agent Objectives

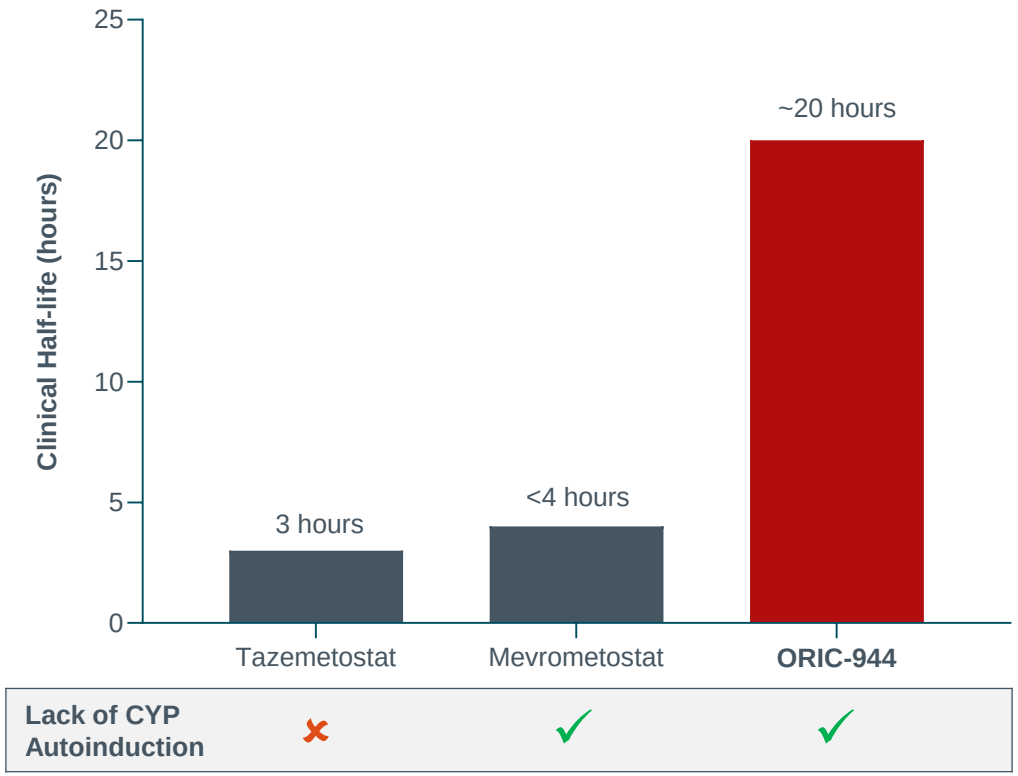
- Strong drug properties
  - Long half-life
  - Dose proportional exposures
  - No CYP autoinduction
- Robust target engagement
- Well tolerated

Phase 1b designed to confirm ORIC-944 differentiated single agent profile and to position ORIC-944 as a potential best-in-class PRC2 inhibitor for combination development in prostate cancer

ORIC-944 Has Demonstrated a Potential Best-in-Class Pharmacokinetic Profile

Preliminary Phase 1b Pharmacokinetic Data

Clinical Half-Life Comparison



Key Takeaways

- Excellent pharmacokinetic profile observed to date
  - Increased exposure with dose level
  - Low inter-patient variability
- No signs of CYP autoinduction that is observed with first-generation PRC2 inhibitors
- Clinical half-life of ~20 hours is superior to other PRC2 inhibitors and supports QD dosing
- Exposures at ≥600 mg QD exceed target Cmin that provides 90% TGI in preclinical in vivo prostate cancer models

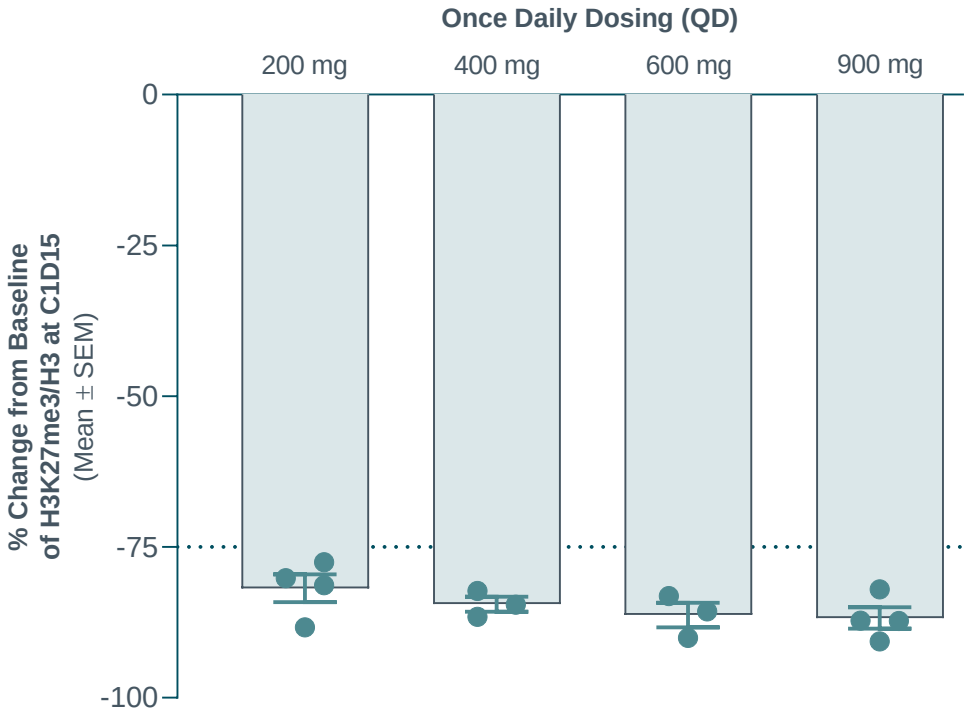
Dose exploration continues with favorable plasma half-life and exposures consistent with best-in-class drug properties

Note: All data as of December 10, 2023.
Source: Tazemetostat half-life from FDA label. Mevrometostat half-life estimated from Schweizer et al. ESMO Poster (2022).

ORIC-944 Has Demonstrated Robust and Consistent Target Engagement

Preliminary Phase 1b Pharmacodynamic Data

Inhibition of PRC2 Activity
(% H3K27me3 Reduction in Monocytes)



Key Takeaways

- Robust target engagement demonstrated with once-daily monotherapy dosing
- Maximal decrease (≥75%) in H3K27me3 in monocytes from peripheral blood samples achieved across multiple dose levels, starting as low as 200 mg QD
- Low inter-patient variability observed

ORIC-944 has demonstrated promising pharmacodynamic data, indicating strong target engagement

Note: All data as of December 10, 2023. % H3K27me3 inhibition in monocytes from Phase 1b patients shown on plot. Samples collected at cycle 1 day 15, or at cycle 1 day 22 for 2 patients at 400 mg QD. H3K27me3, trimethylation of lysine 27 of histone H3.

ORIC-944 Has Been Generally Well-Tolerated to Date

Treatment-Related Adverse Events Occurring in ≥10% of Patients in Single Agent Dose Escalation

Dose Level (QD)	100 mg (N=3)		200 mg (N=4)		400 mg (N=3)		600 mg (N=3)		700 mg (N=3)		800 mg (N=3)		900 mg (N=6)		Total (N=25)	
Preferred Term, n (%)	**All Grade**	**Grade 3**	**All Grade**	**Grade 3**	**All Grade**	**Grade 3**	**All Grade**	**Grade 3**	**All Grade**	**Grade 3**	**All Grade**	**Grade 3**	**All Grade**	**Grade 3**	**All Grade**	**Grade 3**
Diarrhea	–	–	–	–	2 (67)	–	2 (67)	–	1 (33)	–	3 (100)	–	2 (33)	–	10 (40)	–
Fatigue	–	–	1 (25)	–	1 (33)	–	2 (67)	–	–	–	1 (33)	–	3 (50)	–	8 (32)	–
Decreased appetite	1 (33)	–	1 (25)	–	1 (33)	–	2 (67)	–	–	–	2 (67)	–	1 (17)	–	8 (32)	–
Nausea	–	–	1 (25)	–	1 (33)	–	2 (67)	–	–	–	–	–	3 (50)	–	7 (28)	–
Anemia	1 (33)	–	–	–	–	–	–	–	–	–	2 (67)	1 (33)	2 (33)	2 (33)	5 (20)	3 (12)
Platelet count decreased	–	–	–	–	1 (33)	–	1 (33)	–	–	–	–	–	3 (50)	2 (33)	5 (20)	2 (8)
White blood cell count decreased	–	–	–	–	–	–	1 (33)	–	–	–	–	–	2 (33)	1 (17)	3 (12)	1 (4)
Blood creatinine increased	–	–	1 (25)	–	1 (33)	–	–	–	–	–	–	–	1 (17)	–	3 (12)	–
Dizziness	–	–	1 (25)	–	–	–	1 (33)	–	–	–	–	–	1 (17)	–	3 (12)	–
Vomiting	–	–	–	–	–	–	2 (67)	–	–	–	–	–	1 (17)	–	3 (12)	–
							Optimal single agent dose									

ORIC-944 single agent was well-tolerated up to 900 mg QD, well beyond efficacious dose projections and maximal PD activity

Note: All data as of December 10, 2024. Severity grade according to NCI CTCAE v5.0. No Grade 4 or Grade 5 events reported.

ORIC-944 Advanced into Combination Development with AR Inhibitors

Phase 1b, Multicenter, Open-Label Study (in collaboration with Johnson & Johnson and Bayer)

ORIC-944 Combination Dose Escalation

Key Eligibility

- Patients with mCRPC
- Previously treated with an ARPI (e.g., abiraterone, enzalutamide, apalutamide or darolutamide)
- May have received up to 1 line of chemotherapy

ORIC-944 (QD) + apalutamide (240 mg QD)

ORIC-944 (QD) + darolutamide (600 mg BID)

Candidate RP2Ds Selected

ORIC-944 Combination Dose Optimization

Prior abiraterone	ORIC-944 + apalutamide
	ORIC-944 + darolutamide
Prior AR inhibitor (enzalutamide, apalutamide or darolutamide)	ORIC-944 + apalutamide
	ORIC-944 + darolutamide

Primary endpoints: Safety and recommended Phase 2 dose

Key secondary endpoints: rPFS, ORR, DOR

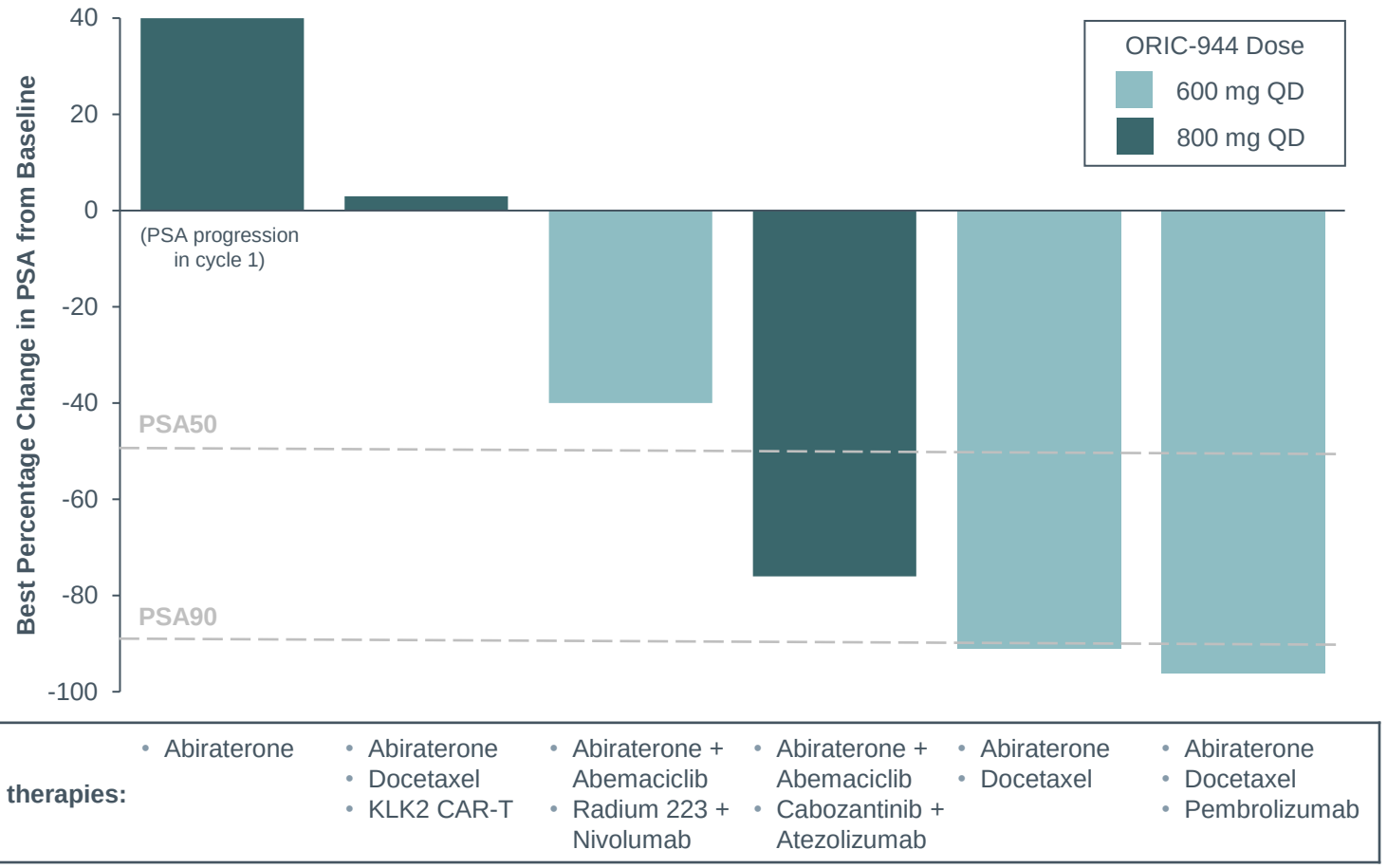
Exploratory endpoints: H3K27 trimethylation, PRC2 target gene expression, PSA, and genomics

Initiated combinations of ORIC-944 with apalutamide and with darolutamide in mid-2024

Note: ClinicalTrials.gov identifier: NCT05413421. RP2D, recommended Phase 2 dose, rPFS, radiographic progression free survival, ORR, objective response rate, DOR, duration of response, PSA, prostate-specific antigen

ORIC-944 Plus Apalutamide Has Demonstrated Preliminary Clinical Activity in Patients with mCRPC During Initial Dose Escalation Cohorts

Phase 1b PSA Response Data of ORIC-944 Plus Apalutamide (in collaboration with Johnson & Johnson)



- Clinical activity observed in initial cohorts (n=6)
  - Confirmed PSA50 response in 3 patients
  - Confirmed PSA90 response in 2 patients
  - All PSA responses maintained ≥12 weeks
  - Durable confirmed PSA90 response up to 38 weeks (ongoing)
- Once daily oral regimen generally well tolerated
  - Primarily Grade 1 and Grade 2 TRAEs consistent with PRC2 and AR inhibition
  - One Grade 3 TRAE of fatigue (1)
  - First two dose cohorts cleared without DLT; dose escalation ongoing
  - No discontinuations due to safety
- Exploration of ORIC-944 plus darolutamide with first cohort complete and second cohort enrolling
  - Preliminary clinical activity consistent with ORIC-944 and apalutamide combination

PSA responses observed with the combination of ORIC-944 and apalutamide in heavily pretreated mCRPC patients; updated combination data expected in 4Q25 / 1H26

Note: Data as of December 10, 2024. All PSA responses confirmed. All patients treated with 240 mg QD of apalutamide. Prior therapies exclude androgen depravation therapy. Treatment related adverse events (TRAEs) include any adverse event attributed to either ORIC-944 or apalutamide. (1) Grade 3 TRAE of fatigue observed in one patient, who remains on treatment without dose modification. Fatigue is a known adverse event of androgen receptor pathway inhibitors. Abiraterone refers to abiraterone acetate. DLT, dose limiting toxicity.

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Key Takeaways

Clinical Pipeline Focused on Advancement of ORIC-114 and ORIC-944

Program	Indication	Discovery / IND Enabling	Phase 1/2	Pivotal / Phase 3	Clinical Collaboration	Anticipated Data Milestones
PRODUCT CANDIDATES						
ORIC-114 *EGFR/HER2 inhibitor*	EGFR exon 20 NSCLC (1)	• 1L combination with SC amivantamab • 1L monotherapy • 2L monotherapy			Johnson&Johnson	Mid-2026 1H26 1H25
	Atypical EGFR NSCLC	• 1L monotherapy • 2L+ monotherapy				Mid-2026 2H25
	HER2 exon 20 NSCLC	• 2L+ monotherapy				1H25
ORIC-944 *PRC2 inhibitor*	Prostate Cancer	• Combination with apalutamide			Johnson&Johnson	4Q25 / 1H26
		• Combination with darolutamide			BAYER	4Q25 / 1H26
DISCOVERY RESEARCH PROGRAMS						
Multiple programs targeting resistance mechanisms	Solid tumors					

(1) Clinical collaboration with Johnson & Johnson to evaluate ORIC-114 plus subcutaneous (SC) amivantamab in patients with first-line NSCLC with EGFR exon 20 insertion mutations.

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

Lead Programs Advancing toward Pivotal Studies

- Potential best-in-class TKI targeting NSCLC with EGFR exon 20, HER2 exon 20, and EGFR atypical mutations
- Potential best-in-class PRC2 inhibitor targeting mCRPC

Dual Engine for Pipeline Expansion

- Pipeline built from internal R&D and external business development
- Targeting one new IND candidate every 18 months

Experienced Management Team

- Heritage of discovering, developing, and commercializing oncology therapies at Ignyta, Medivation, Aragon, Pharmacyclics, and Genentech

Strong Financial Position

- Cash and investments of $282 million expected to fund company into late 2026 (1)

Anticipated Data Milestones

- ORIC-114 (NSCLC):
  - 1H25: 2L EGFR exon 20 and 2L+ HER2 exon 20
  - 2H25: 2L+ EGFR atypical
  - 1H26: 1L EGFR exon 20
  - Mid-2026: 1L EGFR exon 20 combination with SC amivantamab and 1L EGFR atypical
- ORIC-944 (mCRPC):
  - 4Q25 / 1H26: Combination with AR inhibitors

Two potential best-in-class programs expected to enter pivotal studies in 2H25 (ORIC-114) and early 2026 (ORIC-944)

(1) Unaudited balance as of September 30, 2024.