

OVERCOMING RESISTANCE IN CANCER

Company Overview

May 2026



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, and commercial opportunities for, our product candidates and programs; plans for the clinical trials and development of enozertinib (ORIC-114) and rinzimetostat (ORIC-944); enozertinib and rinzimetostat clinical outcomes, which may materially change 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 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 Overcoming Resistance In Cancer

Validated Targets in High Unmet Need Populations

- Potential best-in-class PRC2 inhibitor for prostate cancer
- Potential best-in-class TKI for NSCLC with EGFR exon 20 insertion and EGFR atypical mutations

Late-Stage Clinical Pipeline

- Rinzimetostat (ORIC-944) and enozertinib (ORIC-114) rapidly advancing towards potential Phase 3 initiations

Experienced Management Team

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

Strong Financial Position

- Cash and investments of \$420 million expected to fund company into 2H 2028
- Funding through primary endpoint readout from first Phase 3 trial of rinzimetostat

Anticipated Milestones


- Rinzimetostat for mCRPC:
 - ✓ 1Q26: Combination dose optimization data with AR inhibitor
 - 1H26: Initiate first global Phase 3 registrational trial in post-abiraterone mCRPC
 - 2H26: Program update
- Enozertinib for NSCLC:
 - 2H26: 1L EGFR exon 20 monotherapy data and combination data with SC amivantamab ⁽¹⁾
 - 2H26: 1L EGFR atypical monotherapy data

Two potential best-in-class programs approaching Phase 3 initiation; Cash runway into 2H28, beyond rinzimetostat Phase 3 data

Executive Team with Expertise in Building Leading Oncology Companies

Jacob Chacko, MD Chief Executive Officer	<ul style="list-style-type: none"> • 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 	
Kevin Brodbeck, PhD Chief Technical Officer	<ul style="list-style-type: none"> • Previously Chief Technical and Development Operations Officer at Deciphera Pharmaceuticals; led pharmaceutical sciences (CMC) and supply chain operations • SVP of Technical Operations at Nektar Therapeutics; led the global CMC development and manufacturing organization 	
Lori Friedman, PhD Chief Scientific Officer	<ul style="list-style-type: none"> • Previously Head of Translational Oncology at Genentech; advanced >20 drug candidates into development • Director of Signal Transduction at Exelixis 	
Pratik Multani, MD Chief Medical Officer	<ul style="list-style-type: none"> • 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 	
Matt Panuwat Chief Business Officer	<ul style="list-style-type: none"> • 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 	
Dominic Piscitelli Chief Financial Officer	<ul style="list-style-type: none"> • 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 	
Christian Kuhlen, MD General Counsel	<ul style="list-style-type: none"> • Previously General Counsel at Synthorx (acquired by Sanofi), completed \$151 million IPO • General Counsel at Ignyta and Genoptix 	
Edna Chow Maneval, PhD EVP Clinical Development	<ul style="list-style-type: none"> • 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) 	
Keith Lui SVP Commercial & Medical Affairs	<ul style="list-style-type: none"> • Previously SVP of Business Development, Commercial and Medical Affairs at DURECT • Led commercial strategy and launch-readiness at Pharmacyclics, Genentech, Prothena, and Oncopeptides 	

Clinical Pipeline Focused on Advancement of Rinzimetostat and Enozertinib

Program	Indication	Discovery / IND Enabling	Phase 1/2	Pivotal / Phase 3	Clinical Collaboration	Phase 3 Initiations
PRODUCT CANDIDATES						
Rinzimetostat <i>PRC2 inhibitor</i>	Prostate Cancer	<ul style="list-style-type: none"> Combination with darolutamide 				Himalayas-1 Expected in 1H 2026
		<ul style="list-style-type: none"> Combination with apalutamide 			Johnson&Johnson	Potential Himalayas-2 in 2027
Enozertinib <i>EGFR inhibitor</i>	NSCLC EGFR exon 20	<ul style="list-style-type: none"> 1L monotherapy 1L combination with SC amivantamab ⁽¹⁾ 1L combination with chemotherapy 			Johnson&Johnson	Potential Redwood-1 in 2027
	NSCLC EGFR atypical	<ul style="list-style-type: none"> 1L monotherapy 				

Clinical-stage pipeline includes two potential best-in-class programs addressing large solid tumor market opportunities; Both programs approaching initiation of registrational trials

Combination of Rinzimetostat + Darolutamide Compares Favorably to Competitor PRC2 Combination and to AR Inhibitor Monotherapy In Post-Abiraterone mCRPC

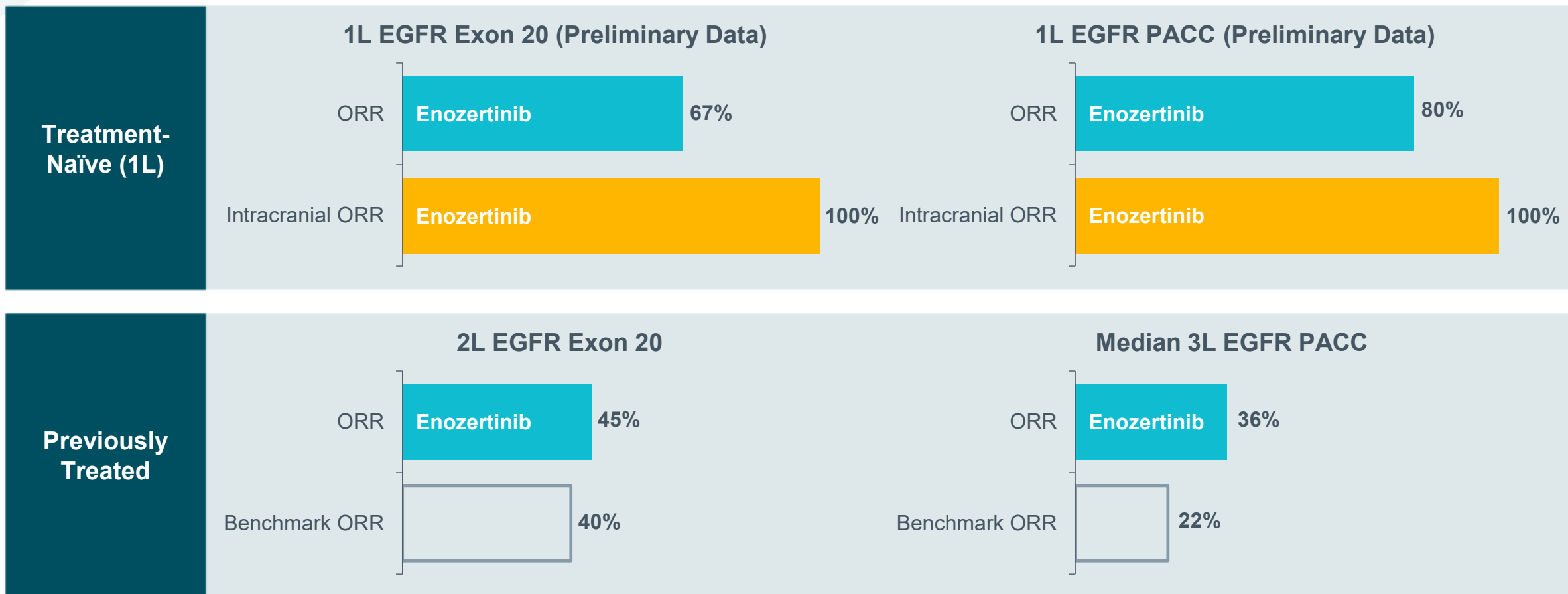
Rinzimetostat Dose Optimization Update (March 2026)

	Enzalutamide	Mevrometostat 1250 mg BID Fasted + Enzalutamide	Rinzimetostat 400 mg QD + Darolutamide
3-Month rPFS	78%	92%	93%
4-Month rPFS	70%	86%	84%
5-Month rPFS	60%	80%	84%
PSA50	15%	34%	33%
SAFETY (All Grade / Grade ≥3)	<ul style="list-style-type: none"> Fatigue (43% / 3%) Nausea (25% / 0%) Anemia (23% / 3%) Diarrhea (18% / 0%) Decreased appetite (18% / 0%) Dysgeusia (8% / 0%) 	<ul style="list-style-type: none"> Diarrhea (78% / 17%) Dysgeusia (59% / 0%) Decreased appetite (59% / 0%) Fatigue (56% / 5%) Anemia (49% / 5%) Nausea (42% / 0%) Alopecia (39% / 0%) Thrombocytopenia (29% / 2%); 2% Gr 4 Neutropenia (22% / 7%); 2% Gr 4 Vomiting (22% / 0%) Arthralgia (22% / 0%) Rash (20% / 2%) <u>AE cutoff of ≥20%</u> 	<ul style="list-style-type: none"> Fatigue (39% / 0%) Diarrhea (22% / 0%) Nausea (22% / 0%) Blood creatinine increased (17% / 0%) Decreased appetite (11% / 0%) Anemia (11% / 0%) <u>AE cutoff of ≥10%</u>

Rinzimetostat + ARi safety profile compatible with long-term dosing, with the majority of AEs Grade 1, and no Grade 4/5 events

Enozertinib Phase 1b Data Establishes Potential Best-in-Class Profile in EGFR Exon 20 and PACC Mutated NSCLC

Enozertinib Updated Phase 1b Data Highlights (ESMO Asia 2025)



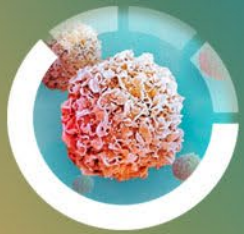
Ongoing development of enozertinib is focused on 1L, where preliminary data demonstrated potential best-in-class systemic and intracranial activity

ORIC's Two Programs Are Approaching Registrational Trials and Each Have Multibillion Dollar Commercial Opportunities in the US Alone

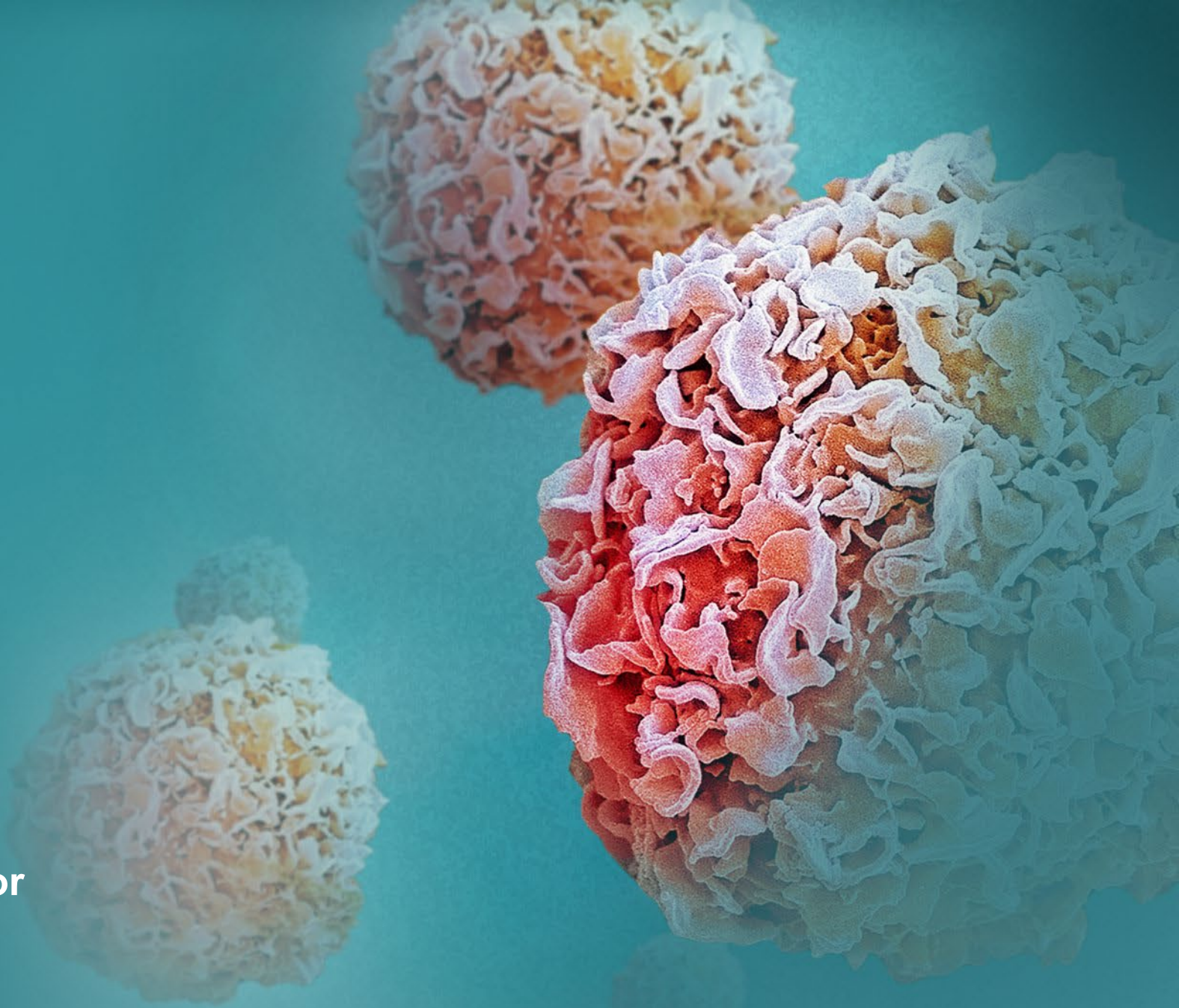
Program	Initial Focus	Estimated Initial US Market Opportunity	Future Development Opportunities										
Rinzimetostat	mCRPC Post-Abiraterone	>\$3.5bn Opportunity Annual US Incidence: 17,000	<table border="1"> <thead> <tr> <th></th> <th>Est. Annual US Incidence</th> </tr> </thead> <tbody> <tr> <td>mCRPC (RLT, TCE, ADC Combo)</td> <td>37,000</td> </tr> <tr> <td>NSCLC (KRASi Combo)</td> <td>45,000</td> </tr> <tr> <td>CRC (KRASi Combo)</td> <td>65,000</td> </tr> <tr> <td>Breast Cancer (ERi Combo)</td> <td>220,000</td> </tr> </tbody> </table>		Est. Annual US Incidence	mCRPC (RLT, TCE, ADC Combo)	37,000	NSCLC (KRASi Combo)	45,000	CRC (KRASi Combo)	65,000	Breast Cancer (ERi Combo)	220,000
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Breast Cancer (ERi Combo)	220,000												
mCRPC Post-AR Inhibitor	>\$3.5bn Opportunity Annual US Incidence: 20,000												
mCSPC	>\$10bn Opportunity Annual US Incidence: 33,000												
Enozertinib	NSCLC EGFR exon 20	>\$1bn Opportunity Annual US Incidence: 4,000	Adjuvant NSCLC EGFR exon 20										
	NSCLC EGFR atypical	>\$2.5bn Opportunity Annual US Incidence: 6,000	Adjuvant NSCLC EGFR atypical										

Rinzimetostat and enozertinib are initially targeting multiple blockbuster commercial opportunities with substantial future upside

ORIC

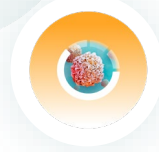


Rinzimetostat
Allosteric PRC2 Inhibitor



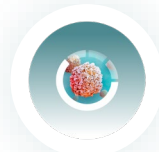
Rinzimetostat: Potential Best-In-Class PRC2 Inhibitor for Prostate Cancer

Rinzimetostat Overview



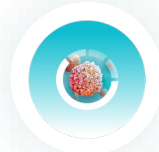
KEY LIMITATIONS of approved and investigational PRC2-directed agents

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



RINZIMETOSTAT may address these limitations

- **Selectively targets PRC2 through allosteric inhibition of the EED subunit**
- **Superior in vitro and in vivo activity** across preclinical prostate cancer models
- **Synergistic activity with AR inhibitors** across preclinical prostate cancer models
- **Strong drug properties** including a 20-hour clinical half-life



PHASE 3 INITIATION expected 1H 2026

- **Selected RP3D for first Phase 3:** 400 mg QD in combination with darolutamide
- **Highly competitive emerging efficacy profile** with landmark rPFS substantially better than SOC therapies in mCRPC
- **Highly differentiated safety profile**
- **First Phase 3 trial in post-abiraterone mCRPC**, with additional trials under consideration

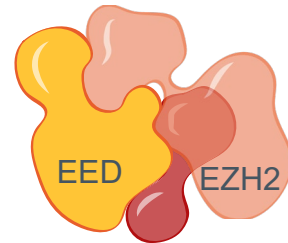
Rinzimetostat is a potential best-in-class therapy for development with AR inhibitors in prostate cancer, demonstrating superior drug properties and favorable combination efficacy & safety

PRC2 Plays a Pivotal Role in Transcriptional Regulation and Cancer Evolution

PRC2 Introduction

PRC2 Is an Epigenetic Modifier

Polycomb Repressive Complex 2 (PRC2)



Tri-methylation of histone H3K27

Closed chromatin
Gene silencing



PRC2 inhibition



Open chromatin
Gene transcription



PRC2 Is a Clinically Validated Target in Multiple Cancers



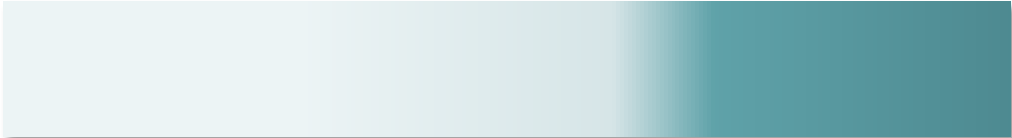



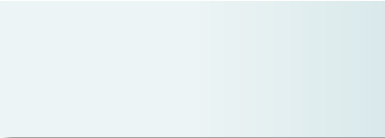

- PRC2 regulates gene expression by modifying chromatin, and is implicated in tumor evolution and cell fate ⁽¹⁾
- PRC2 is clinically validated in prostate cancer
 - Decreased expression of PRC2 target genes is associated with poor prognosis in prostate cancer ⁽²⁾
 - Randomized data with second-generation PRC2 inhibitor demonstrated significant PFS improvement in mCRPC ⁽³⁾
- PRC2 dysfunction has been linked to multiple cancers
 - PRC2 inhibitors approved in follicular lymphoma, epithelioid sarcoma and T cell leukemia/lymphoma
 - Emerging scientific rationale in breast, colon and prostate cancers

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

Rinzimetostat: Next-Generation PRC2 Inhibitor Designed for Best-in-Class Drug Properties

PRC2 Inhibitor Landscape in Prostate Cancer

 Potential Best-in-Class

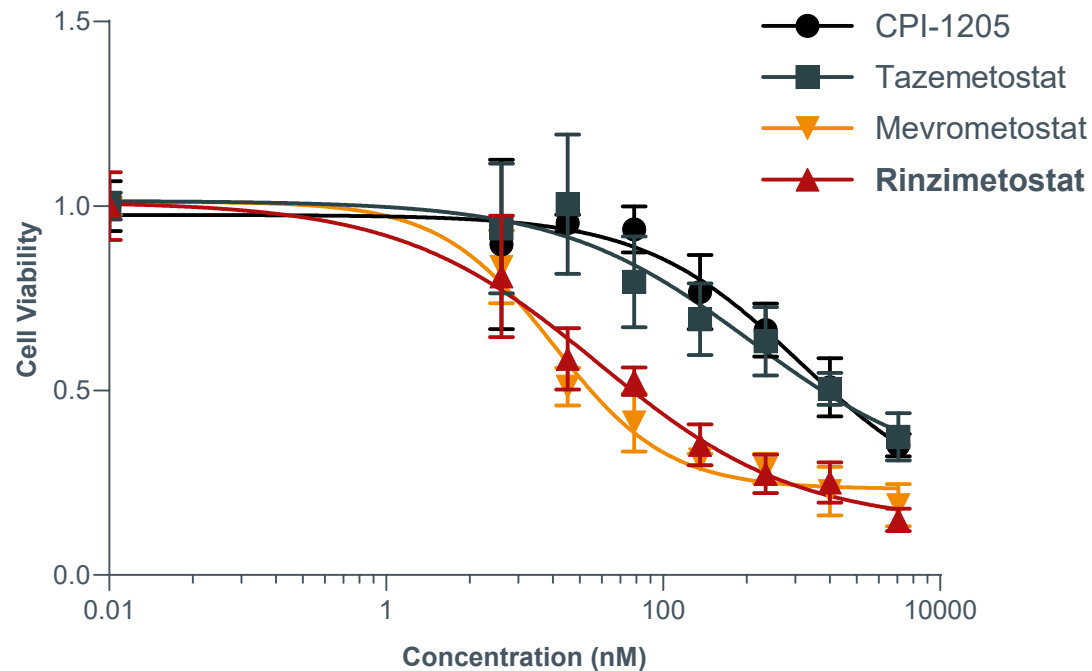
Key Features	CPI-1205 (1 st gen)	Tazemetostat (1 st gen)	Mevrometostat (2 nd gen)	Rinzimetostat (3 rd gen)
Cellular Potency				 Cellular Potency Superior potency vs. 1 st gen programs across prostate cancer models
In Vivo Activity				 In Vivo Activity Improved single agent and combination activity across 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	First Phase 3 initiation expected 1H 2026

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

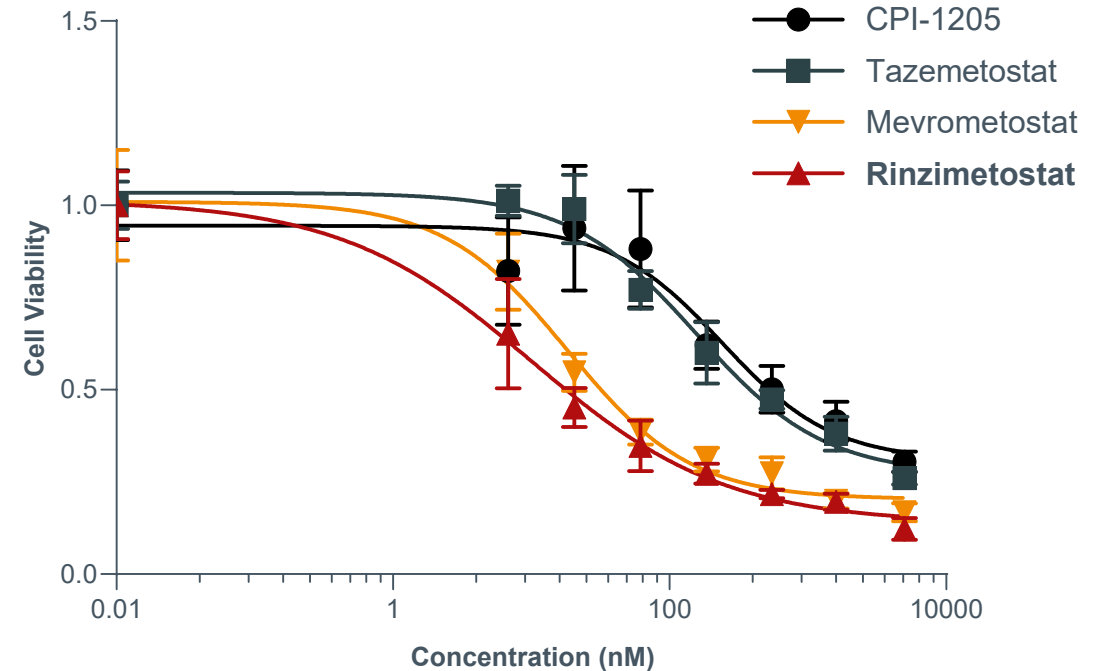
Rinzimetostat Demonstrates Superior In Vitro Potency vs. First-Gen PRC2 Inhibitors

In Vitro Potency in Prostate Cancer Cells

LNCaP
(AR-Positive Prostate Cancer Cells)



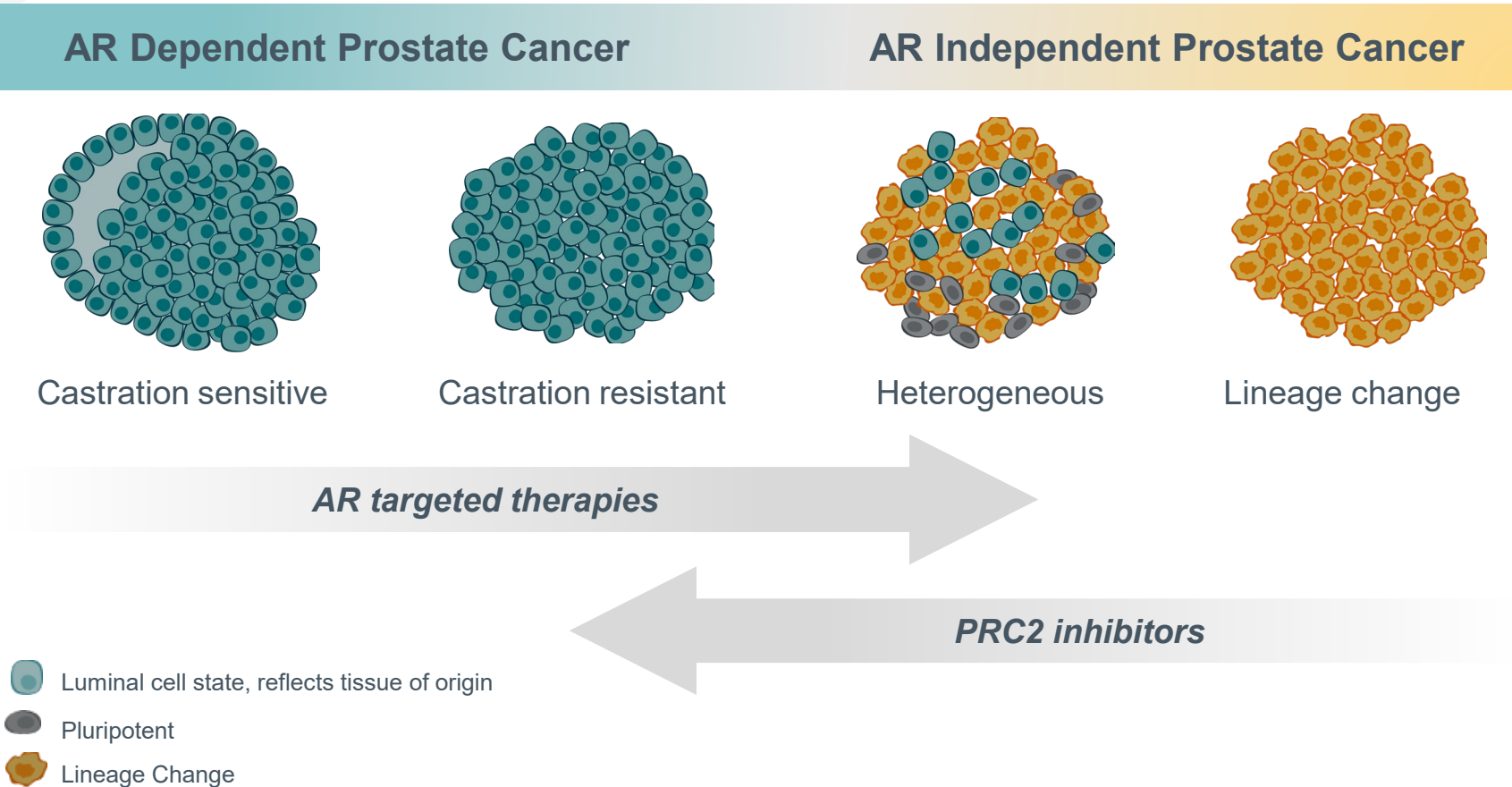
CWR22PC
(AR-Positive Prostate Cancer Cells)



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

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

PRC2 Role in Prostate Cancer

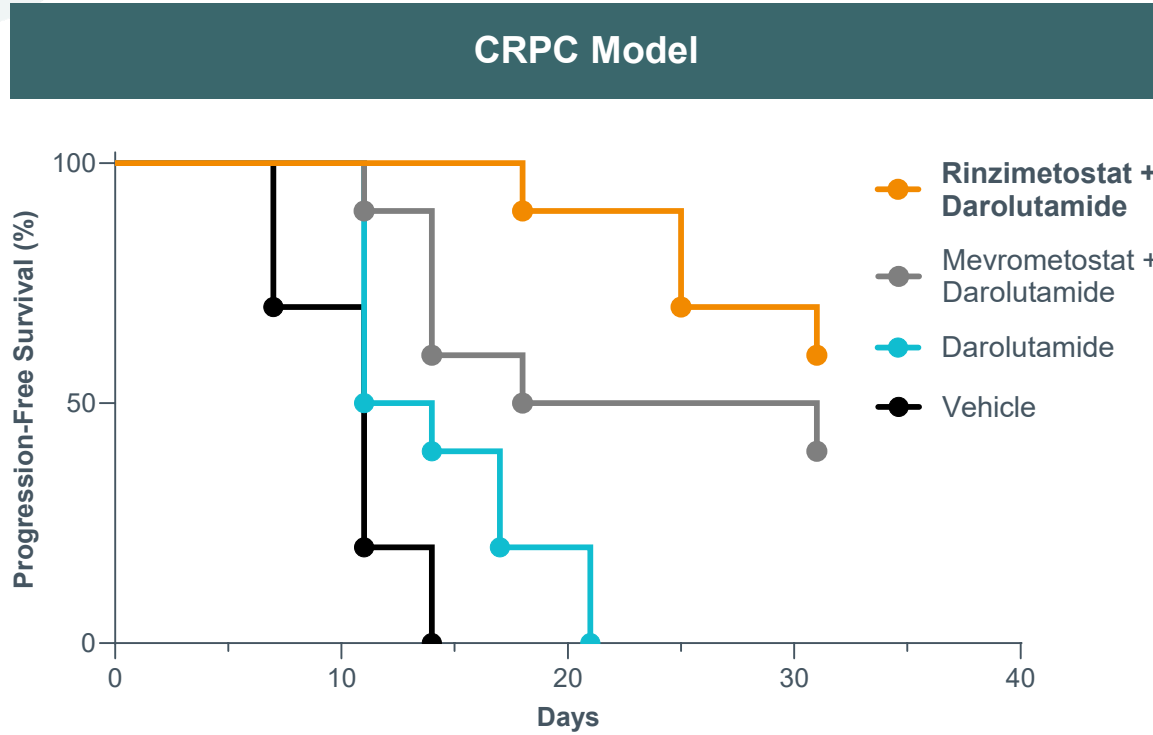


- Prostate cancer cells evade therapies by cellular reprogramming to an AR independent state
- PRC2 inhibition can reverse or prevent this process, such that prostate cancer cells regain or maintain AR dependency
- Randomized data with PRC2 inhibitor + AR inhibitor demonstrated significant PFS improvement

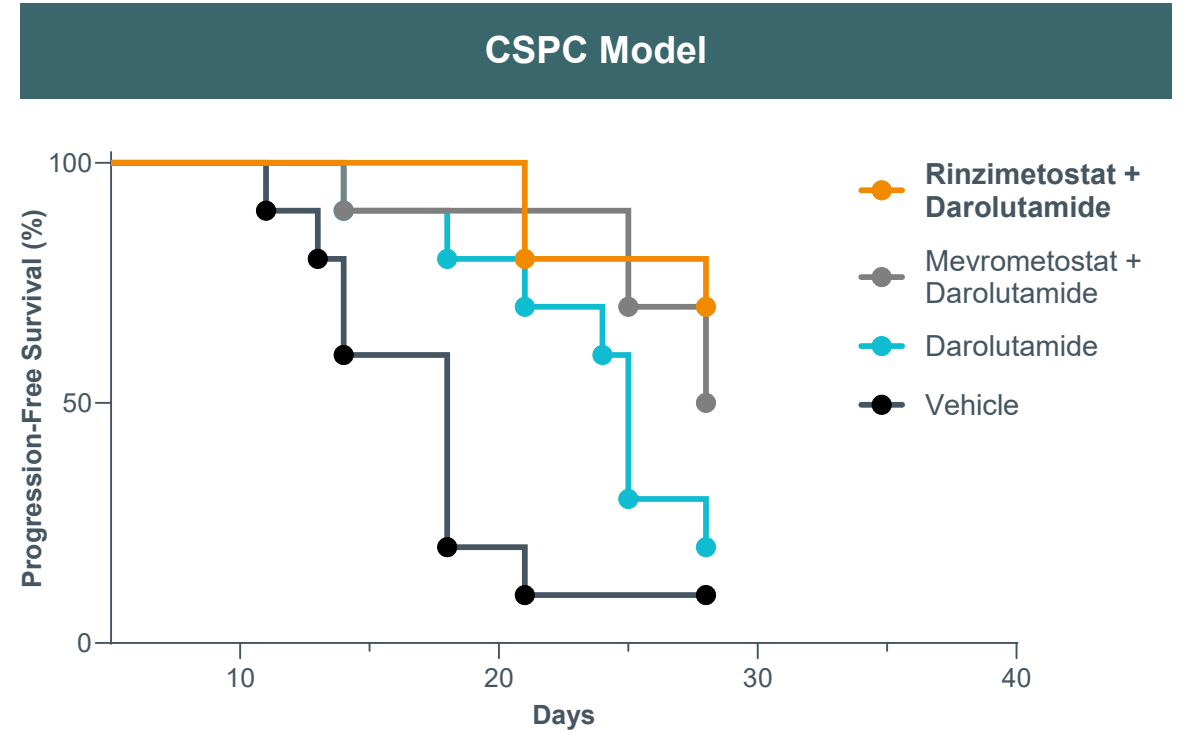
Therapeutic potential of PRC2 inhibitors in prostate cancer is maximized in combination with AR inhibitors

Rinzimetostat Increases Progression-Free Survival in Combination with Darolutamide in Prostate Cancer Xenograft Tumors

Progression-Free Survival in Prostate Cancer Xenografts



	Vehicle	Daro	Mevro	Rinzi	Mevro + Daro	Rinzi + Daro
Median PFS (days)	11	12.5	15.5	27	24.5	Not Reached

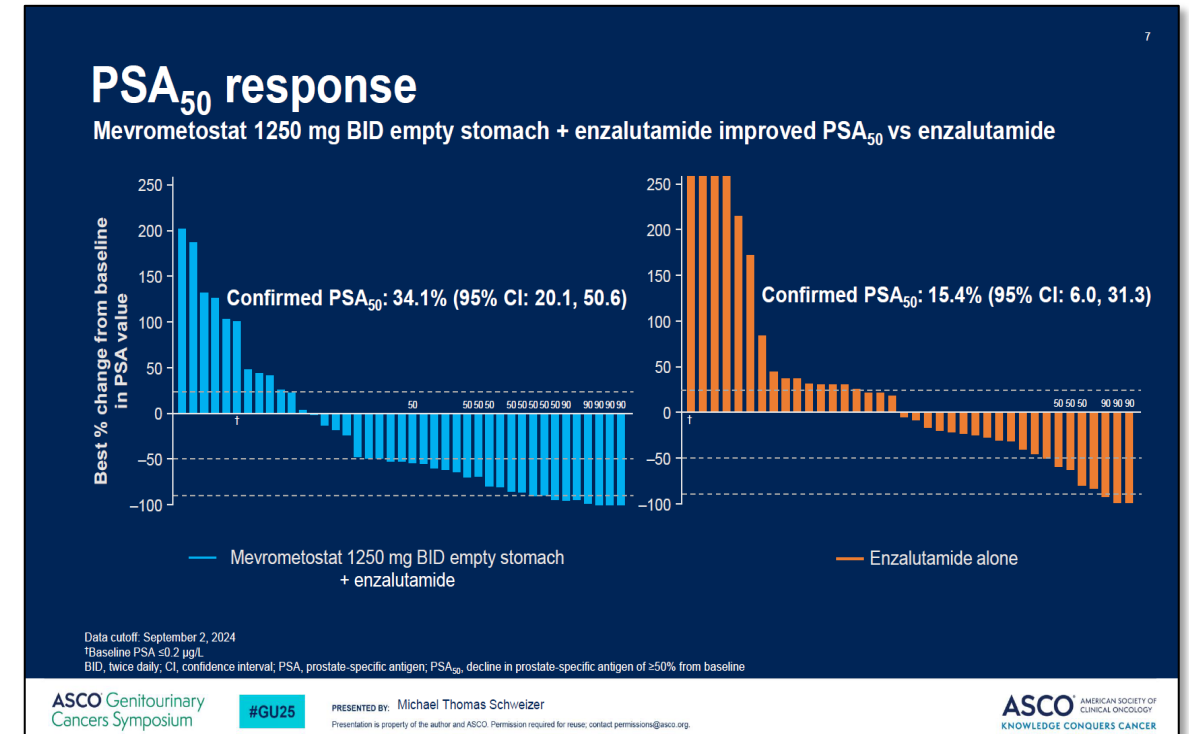
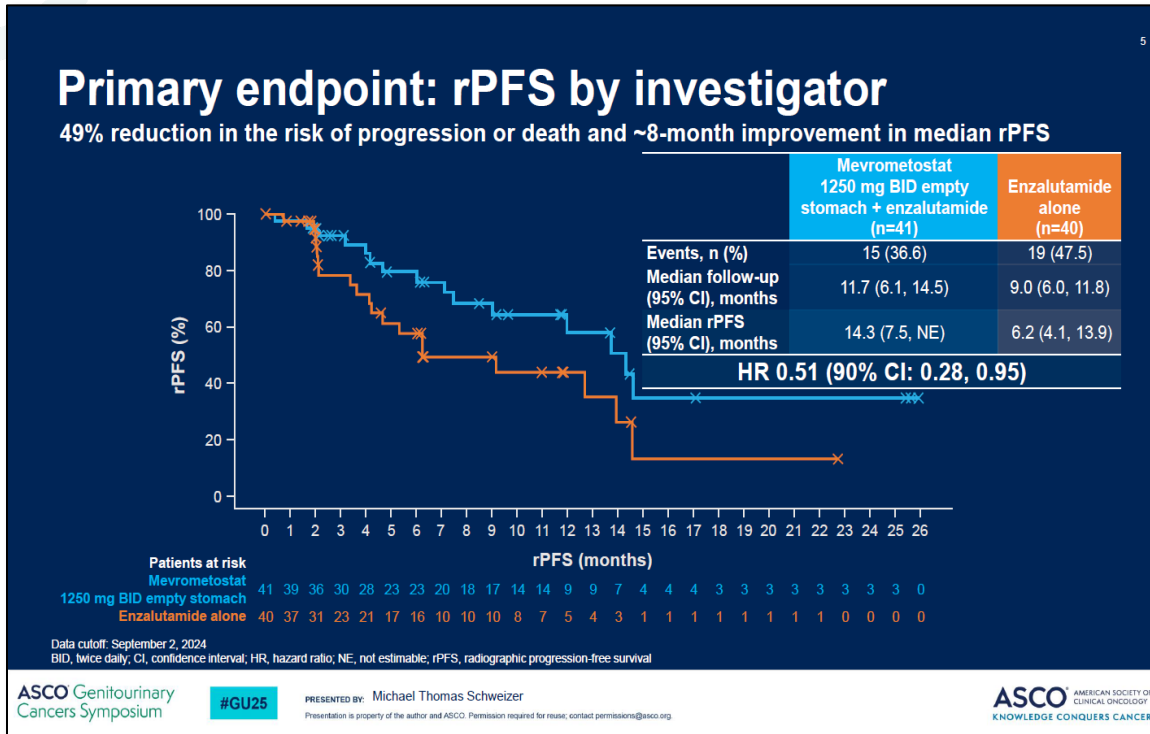


	Vehicle	Daro	Mevro	Rinzi	Mevro + Daro	Rinzi + Daro
Median PFS (days)	18	25	21	19.5	28	Not Reached

Rinzimetostat combination with darolutamide improves progression-free survival in CRPC and CSPC settings in vivo

Mevrometostat Randomized Data Provides Clinical Validation of the Combination of PRC2 Inhibitor and AR Inhibitor in Prostate Cancer

Mevrometostat Plus Enzalutamide Randomized Dose Expansion Results (ASCO GU 2025)



- All patients previously treated with abiraterone and 44% previously treated with chemotherapy
- Mevrometostat plus enzalutamide vs enzalutamide:
 - rPFS of 14.3 months vs. 6.2 months (HR=0.51),
 - cPSA50 of 34.1% vs 15.4%, uPSA50 of 53.7% vs 17.9%

Mevrometostat plus enzalutamide demonstrated improved rPFS, PSA50 and ORR versus enzalutamide in mCRPC patients previously treated with abiraterone, with a manageable (and potentially improvable) AE profile

Rinzimetostat Is Being Explored in Combination with Darolutamide and Apalutamide in Metastatic CRPC

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

Rinzimetostat Combination Dose Exploration

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
- Allows other prior therapies

Rinzimetostat (QD) + darolutamide

Rinzimetostat (QD) + apalutamide

Candidate RP3Ds



Rinzimetostat Combination Dose Optimization

March 2026 Update

Rinzimetostat (QD) + darolutamide

Prior abiraterone

Prior enza, apa, daro

Rinzimetostat (QD) + apalutamide

Prior abiraterone

Prior enza, apa, daro

Primary endpoints: Safety and Recommended Phase 3 Dose

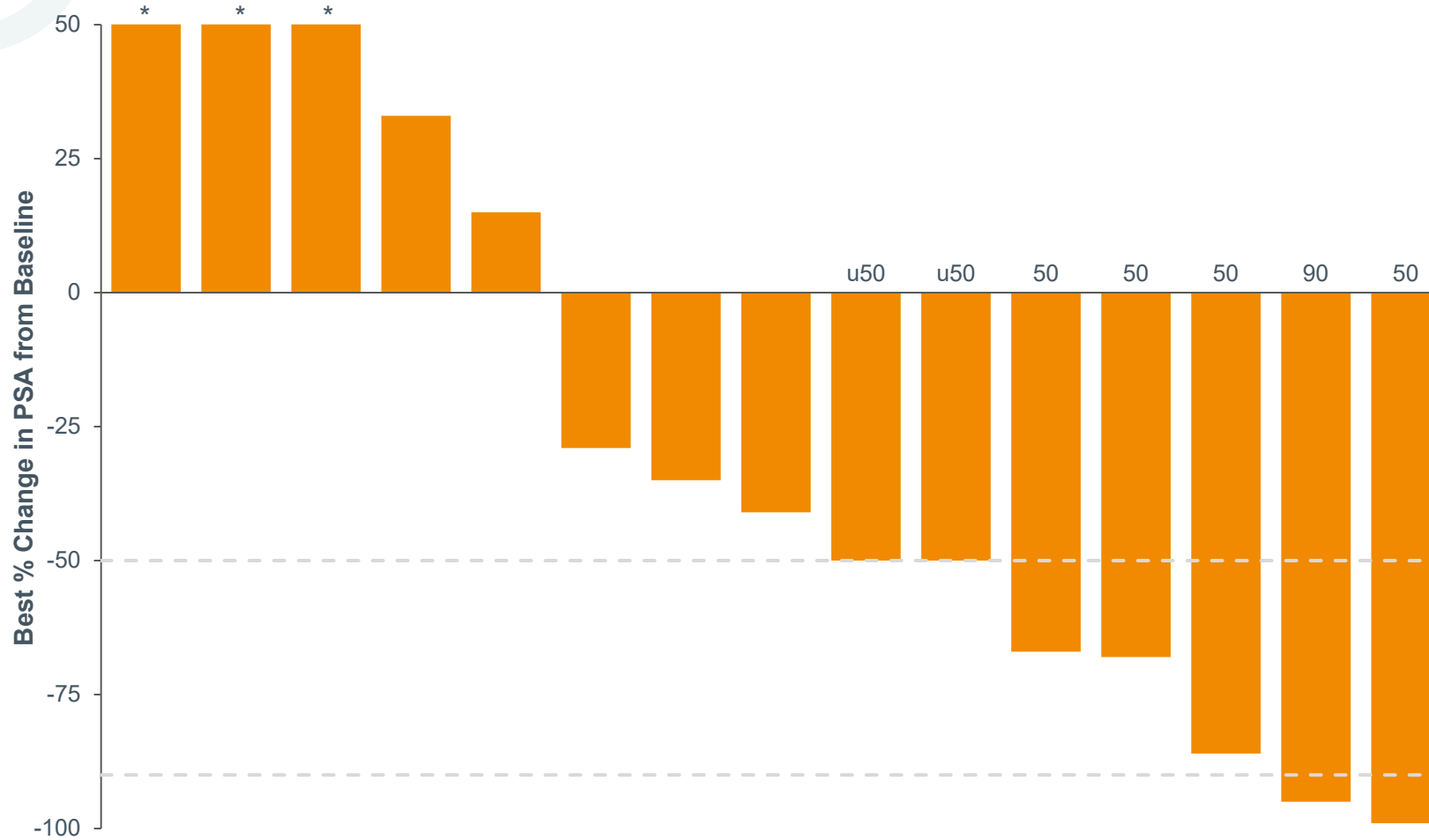
Key secondary endpoints: rPFS, ORR, and DOR

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

Dose optimization data reported in post-abiraterone mCRPC, with Phase 3 trial initiation expected in 1H 2026; ORIC continuing to evaluate rinzimetostat in combination with darolutamide and apalutamide in mCRPC patients

Rinzimetostat in Combination with Darolutamide Continues to Demonstrate Strong Clinical Activity in Post-Abiraterone mCRPC Patients

PSA Response Data of Rinzimetostat 400 mg QD Plus Darolutamide



Notations: * denotes >50% increase; 50 – confirmed PSA50 response; 90 – confirmed PSA90 response; u50 – unconfirmed PSA50 response.

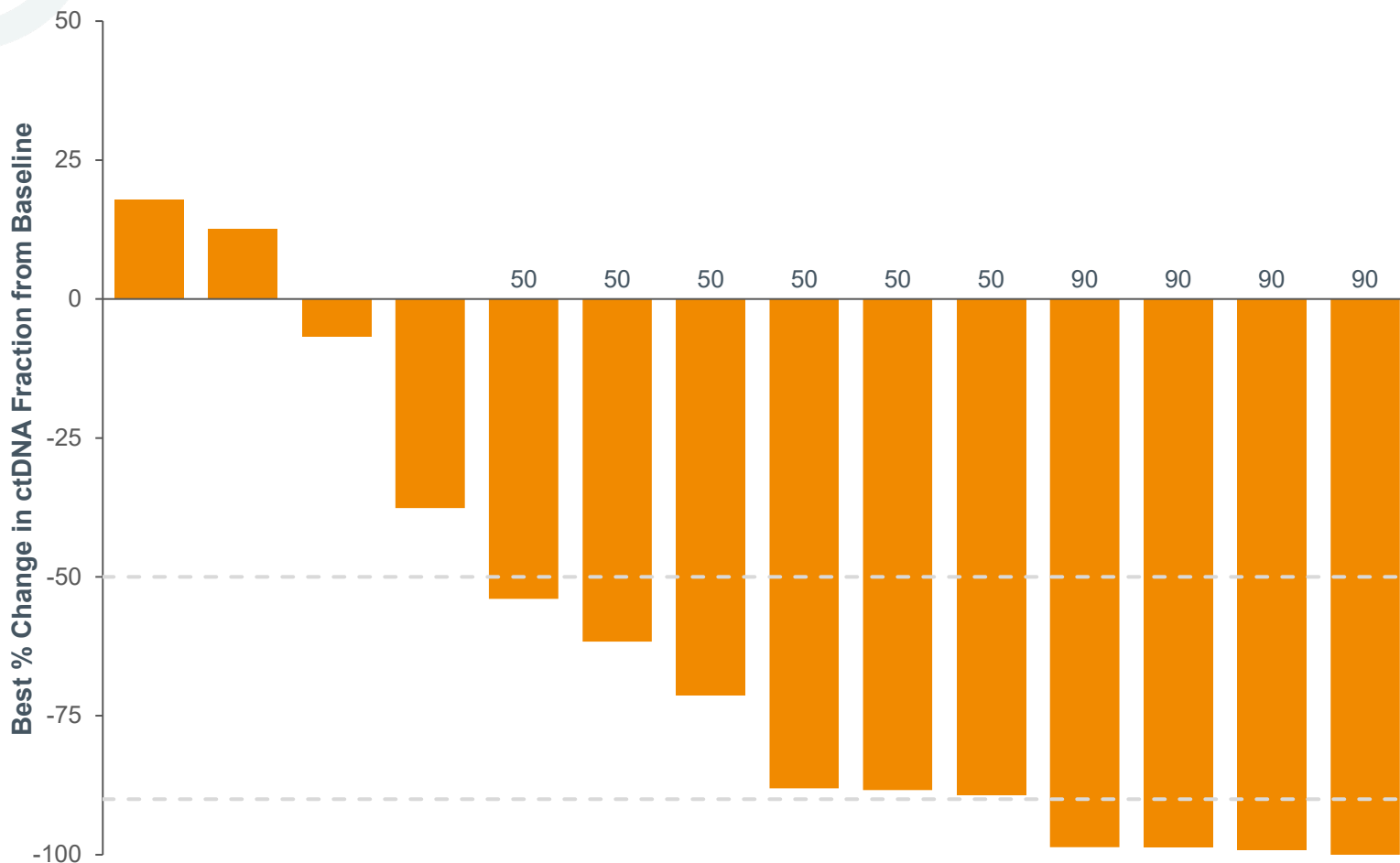
Response	Unconfirmed	Confirmed
PSA50	7/15 (47%)	5/15 (33%)
PSA90	2/15 (13%)	1/15 (7%)

- Rinzimetostat at 400 mg QD plus darolutamide demonstrated strong clinical activity
 - Multiple patients remain on treatment with potential for deepening of responses

Broad and deep PSA responses observed for 400 mg QD rinzimetostat in combination with darolutamide

Rinzimetostat in Combination with Darolutamide Demonstrates Impressive ctDNA Molecular Response in Post-Abiraterone mCRPC Patients

ctDNA Molecular Response Data of Rinzimetostat 400 mg QD Plus Darolutamide



MR50	10/14 (71%)
MR90	4/14 (29%)

- ctDNA molecular responses across a breadth of genotypes including AR mutations, AR amplified, AR wildtype
- Deep ctDNA reductions for the vast majority of patients treated with 400 mg QD rinzimetostat, with 71% of patients demonstrating >50% ctDNA reduction

Notations: 50 – MR50 response; 90 – MR90 response.

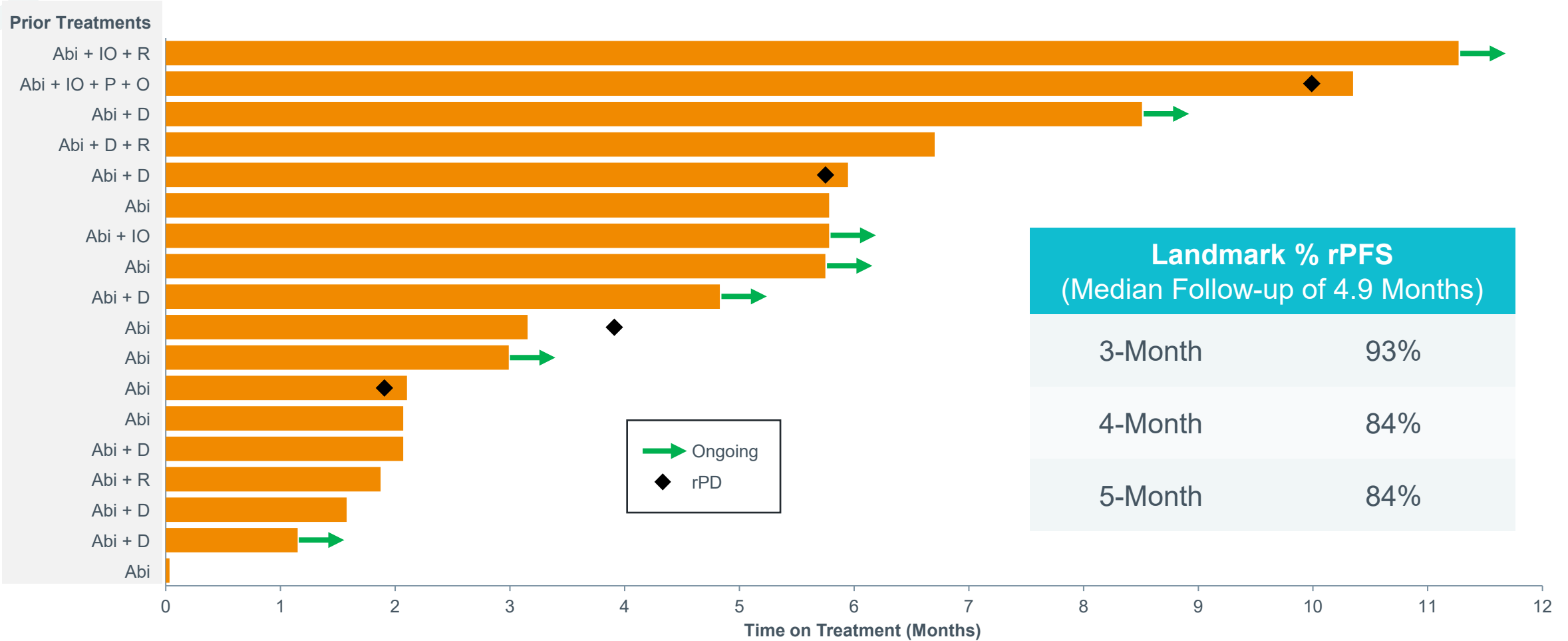
High molecular response rate observed in post-abiraterone patients treated with 400 mg QD rinzimetostat



Source: ORIC data on file as of March 11, 2026.
 Note: All patients treated with 600 mg BID of darolutamide. Excludes one patient without evidence of ctDNA at baseline, and three patients without ctDNA data available. Likely germline variants and clonal hematopoiesis variants were excluded from ctDNA analysis. Molecular response (MR) defined as decrease in ctDNA fraction relative to baseline. Best percent change in ctDNA fraction from baseline assessed at the start of cycle 2, cycle 7, or end of treatment.

Radiographic Progression-Free Survival Data Are Immature, but Early Landmark Analyses Are Promising in Post-Abiraterone mCRPC Patients

Rinzimetostat 400 mg QD Plus Darolutamide Dose Optimization: Time on Treatment



Landmark % rPFS (Median Follow-up of 4.9 Months)	
3-Month	93%
4-Month	84%
5-Month	84%

Many patients remain on treatment with few reports of radiographic progression

Rinzimetostat 400 mg QD in Combination with Darolutamide Has been Generally Well Tolerated in Post-Abiraterone mCRPC Patients

TEAEs Attributed to Rinzimetostat Plus Darolutamide (≥10% Total Incidence)

Rinzimetostat 400 mg QD + Darolutamide Post-Abiraterone mCRPC (n=18)

Preferred Term, n (%)	Grade 1	Grade 2	Grade 3	All Grade
Fatigue	3 (17)	4 (22)	–	7 (39)
Diarrhea	3 (17)	1 (6)	–	4 (22)
Nausea	4 (22)	–	–	4 (22)
Blood creatinine increased	2 (11)	1 (6)	–	3 (17)
Decreased appetite	1 (6)	1 (6)	–	2 (11)
Anemia	1 (6)	1 (6)	–	2 (11)

Adverse Events:

- 6% Grade 3
- No Grade 4 or 5

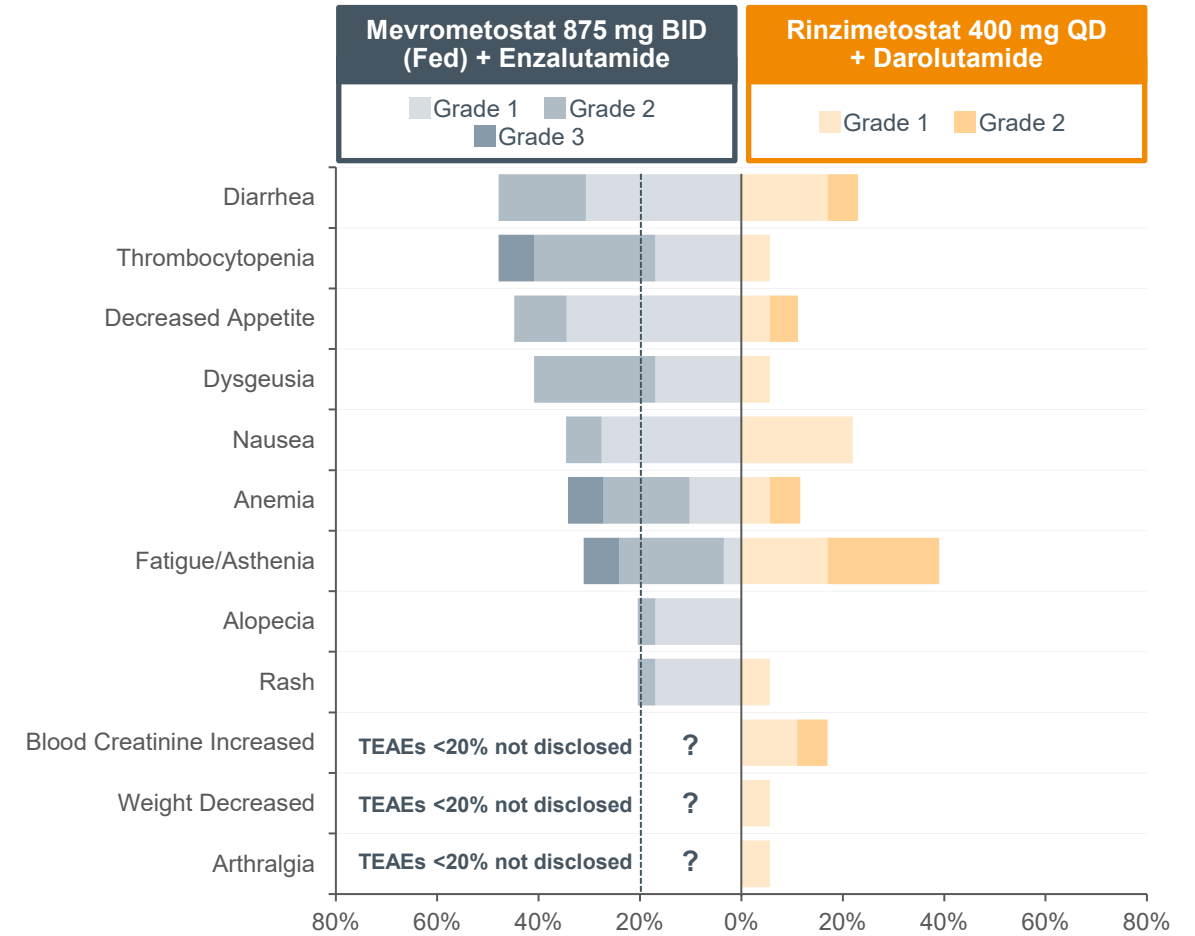
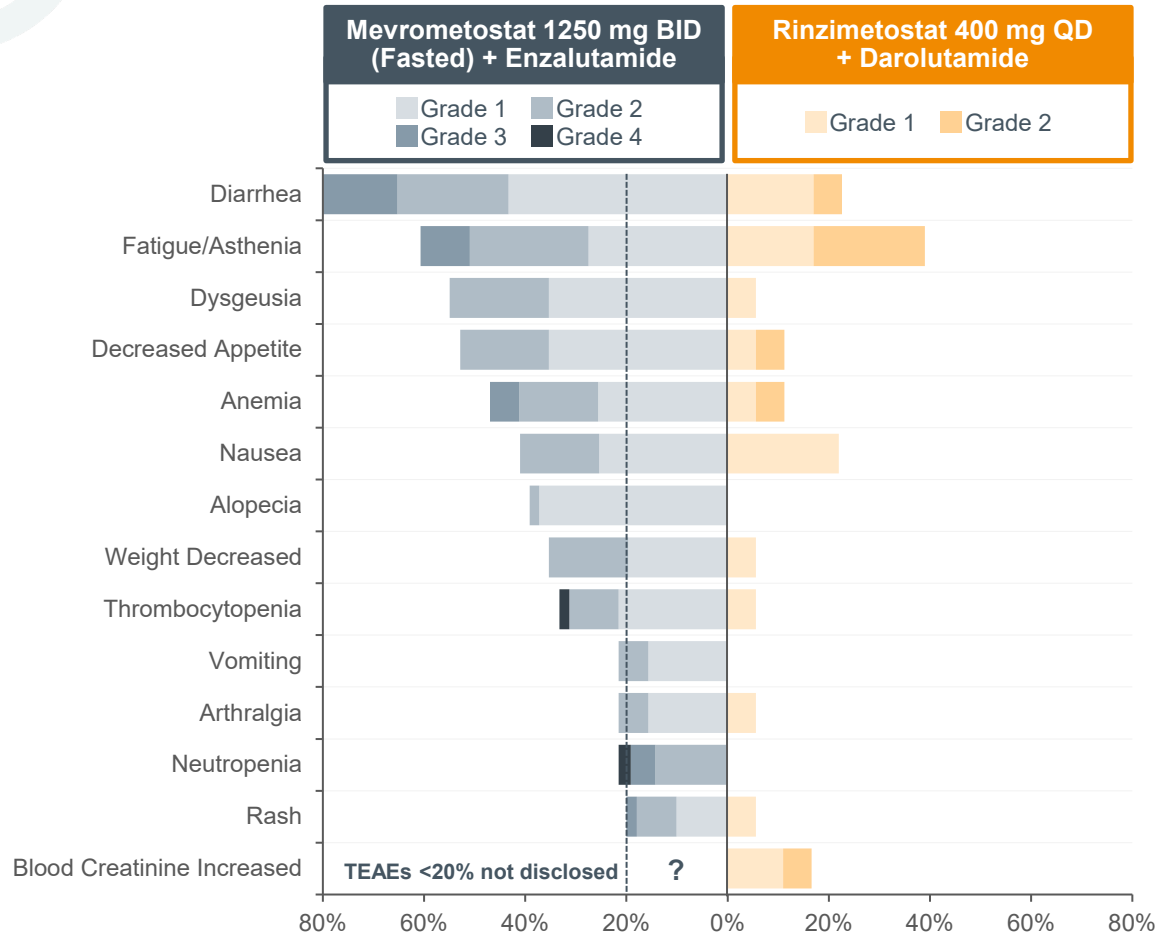
Dose Modifications:

- 6% Dose Interruptions
- No Dose Reductions
- 6% Treatment Discontinuations

In post-abiraterone patients, rinzimetostat in combination with darolutamide is generally well-tolerated, with almost all TRAEs Grade 1 or 2 in severity

Rinzimetostat in Combination with Darolutamide in Post-Abiraterone mCRPC Demonstrates a Clearly Differentiated Safety Profile

Rinzimetostat Adverse Event Comparison to Mevrometostat



Rinzimetostat in combination with darolutamide demonstrates a clearly differentiated safety profile, with the majority of adverse events Grade 1, enabling long-term dosing and sustained patient adherence

Rinzimetostat Demonstrates Competitive Early Landmark rPFS in Post-Abiraterone mCRPC and Does So with a Highly Differentiated Safety Profile

Landmark rPFS and Safety Benchmark Comparisons

	Median Follow-up	3-Month rPFS	4-Month rPFS	5-Month rPFS	Grade ≥3 TRAEs	Dose Reductions / Discontinuations
Mevrometostat 875 mg BID Fed + Enzalutamide (n=14)	9.2 Months	92%	92%	84%	36%	7% / 7%
Mevrometostat 1250 mg BID Fasted + Enzalutamide (n=41)	11.7 Months	92%	86%	80%	49%	37% / 2%
Enzalutamide Monotherapy (n=40)	9.0 Months	78%	70%	60%	23%	8% / 5%
Rinzimetostat 400 mg QD + Darolutamide (n=18)	4.9 Months	93%	84%	84%	6%	None / 6%

Preliminary rinzimetostat rPFS landmark analysis, albeit early, compares favorably to competitor benchmarks with a far cleaner safety profile, despite more heavily pretreated patients

Himalayas-1: Global Phase 3 Study of Rinzimetostat in Combination with Darolutamide in Patients with mCRPC Previously Treated with Abiraterone

Rinzimetostat Global Phase 3 mCRPC Trial



- **Patients with mCRPC**
- **Prior abiraterone** in mCSPC or mCRPC setting
- Up to 1 prior chemotherapy in mCSPC setting



1:1

**Rinzimetostat +
Darolutamide**
(n=300)

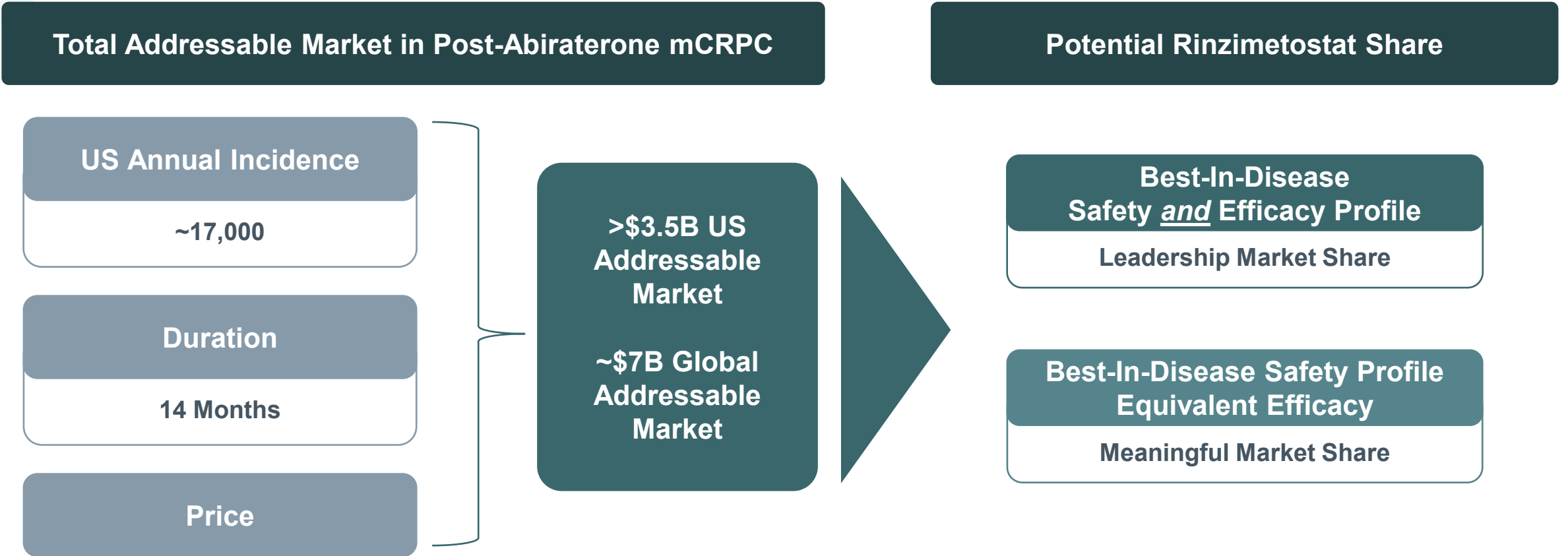
**Physician's Choice
(AR inhibitor or
chemotherapy)**
(n=300)

- **Primary Endpoint:**
 - Radiographic progression-free survival (rPFS)
- **Key Secondary Endpoint:**
 - Overall survival (OS)
- **Other Secondary Endpoints:**
 - PSA response rate
 - ORR (RECIST 1.1 and PCWG3)
 - Patient reported outcomes

Rinzimetostat's first global registrational Phase 3 trial is designed to evaluate combination with darolutamide compared to AR inhibitor and chemotherapy

Rinzimetostat Is Initially Pursuing a Significant Addressable Market in Post-Abiraterone mCRPC

Rinzimetostat Total Addressable Market in Post-Abiraterone mCRPC

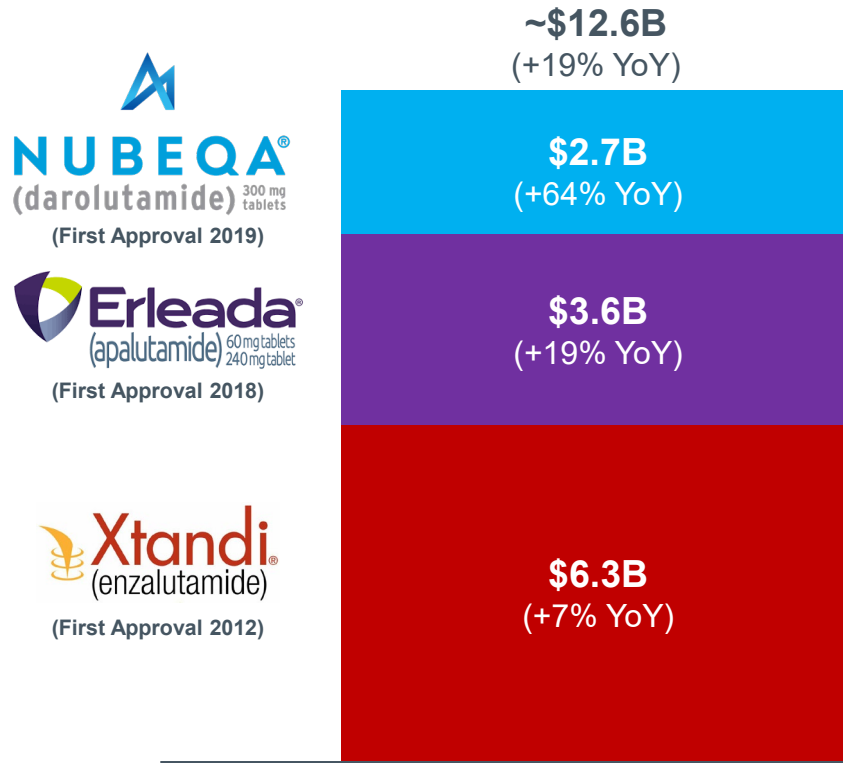


Post-abiraterone mCRPC is a large addressable market with limited effective therapeutic options that are oral and well-tolerated; Rinzimetostat is positioned to capture substantial share with its potential best-in-disease profile

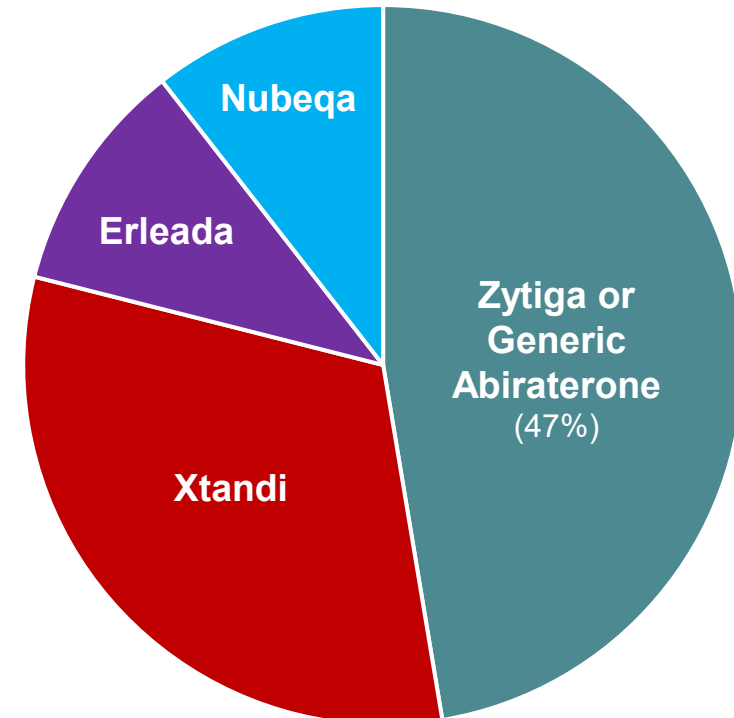
PRC2 Inhibitors Have the Potential to Expand the ARPI Market, which Currently Represents \$11B and Growing Despite Significant Generic Usage

Worldwide Sales and Market Share for Androgen Receptor Pathway Inhibitors

Worldwide Sales (2025)



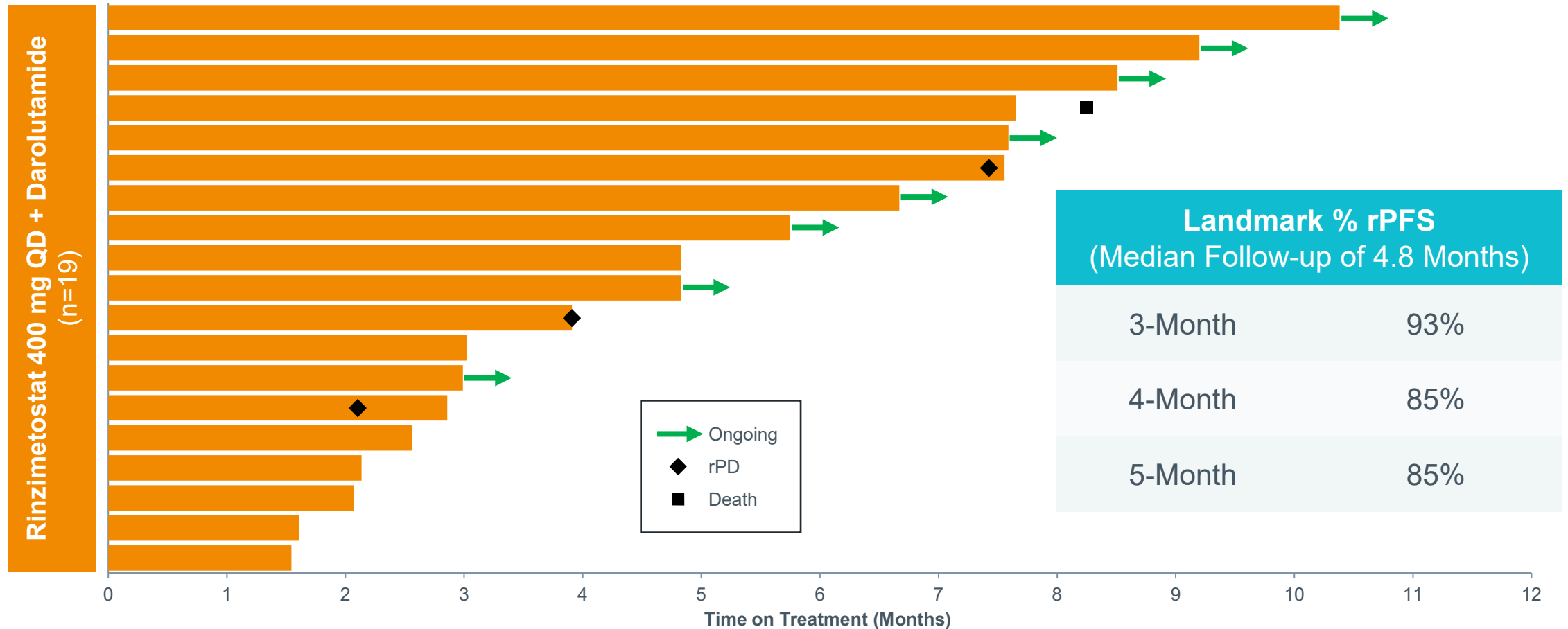
Market Share in Major Markets (2024)



PRC2 inhibitors have the potential to be combined with ARPIs to significantly improve clinical benefit, and expand the already significant commercial opportunity in prostate cancer

Rinzimetostat Is Being Explored in Other Patient Populations that Could Form the Basis of Future Phase 3 Trials, Including Post-AR Inhibitor mCRPC

Rinzimetostat 400 mg QD Plus Darolutamide in Post-ARi mCRPC: Time on Treatment



Preliminary data in second mCRPC population, albeit early, are promising

PRC2 Inhibitors Are Associated with Significant Radiographic Progression-Free Survival in Post-AR Inhibitor mCRPC, Comparing Favorably to Available Therapies

Therapies for 1L+ mCRPC (Post-AR Inhibitor)

Treatment	Status	5-Month rPFS	Median rPFS (months)
Enzalutamide (Xtandi®)	Approved	N/A	N/A
Abiraterone (Zytiga®)	Approved	41%	3.4
Cabazitaxel (Jevtana®)	Approved	65%	8.2
Mevrometostat + Enzalutamide	N/A	68%	11.7
Rinzimetostat + Darolutamide	Phase 1b	85%	Not mature

PRC2 inhibitors in combination with an AR inhibitor have demonstrated much longer rPFS (key regulatory primary endpoint) than what has been reported with other approved and emerging therapies

Rinzimetostat Commercial Opportunity Is Significant in Each Segment of the Prostate Cancer Treatment Continuum

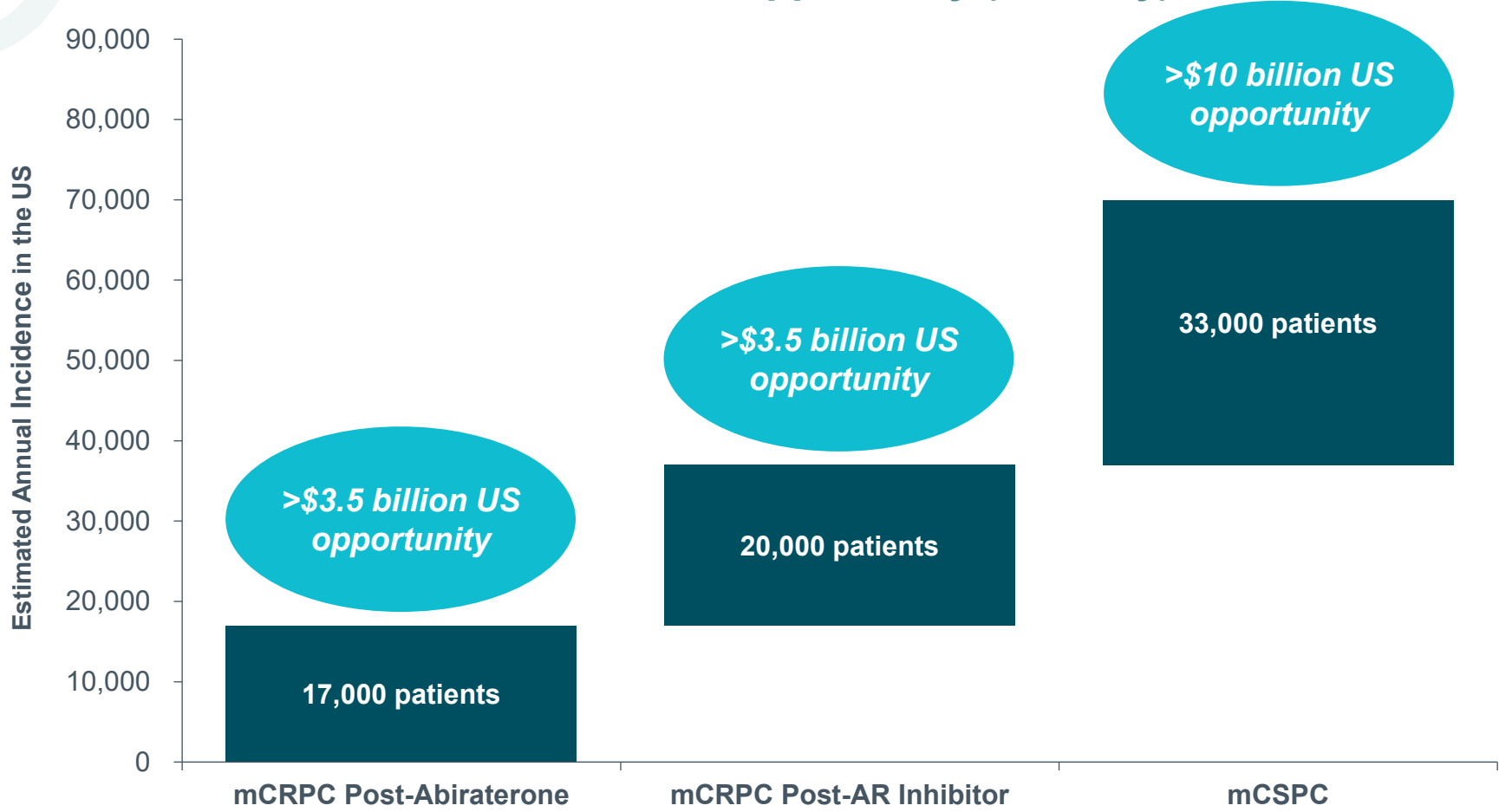
PRC2 Inhibitor Commercial Opportunity in Prostate Cancer (US Only)

	nmCSPC	mCSPC	nmCRPC	mCRPC		
				ARPI-Naïve	Prior Abiraterone	Prior AR Inhibitor
US Incidence (Estimated)	118,000	33,000	12,000	16,000	17,000	20,000
ARPI Efficacy Benchmarks (rPFS)	>85 months	>33 months	>36 months	>16 months	4-6 months	3 months
ARPI + PRC2i Efficacy Potential (rPFS)	TBD	TBD	TBD	TBD	14 months	12 months
Rinzimetostat Opportunity	Future Development Opportunities				\$7B+ Addressable US Market	

Near term development of rinzimetostat will focus on previously treated mCRPC populations that represent a \$7B+ addressable market in the US; future development in earlier disease settings represents an even more significant opportunity

Rinzimetostat Has the Potential to Address Multiple Large Market Opportunities in Prostate Cancer, with Several Development Opportunities in Other Solid Tumors

Potential Rinzimetostat Commercial Opportunity (US Only)

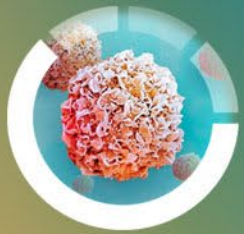


Future Development Opportunities

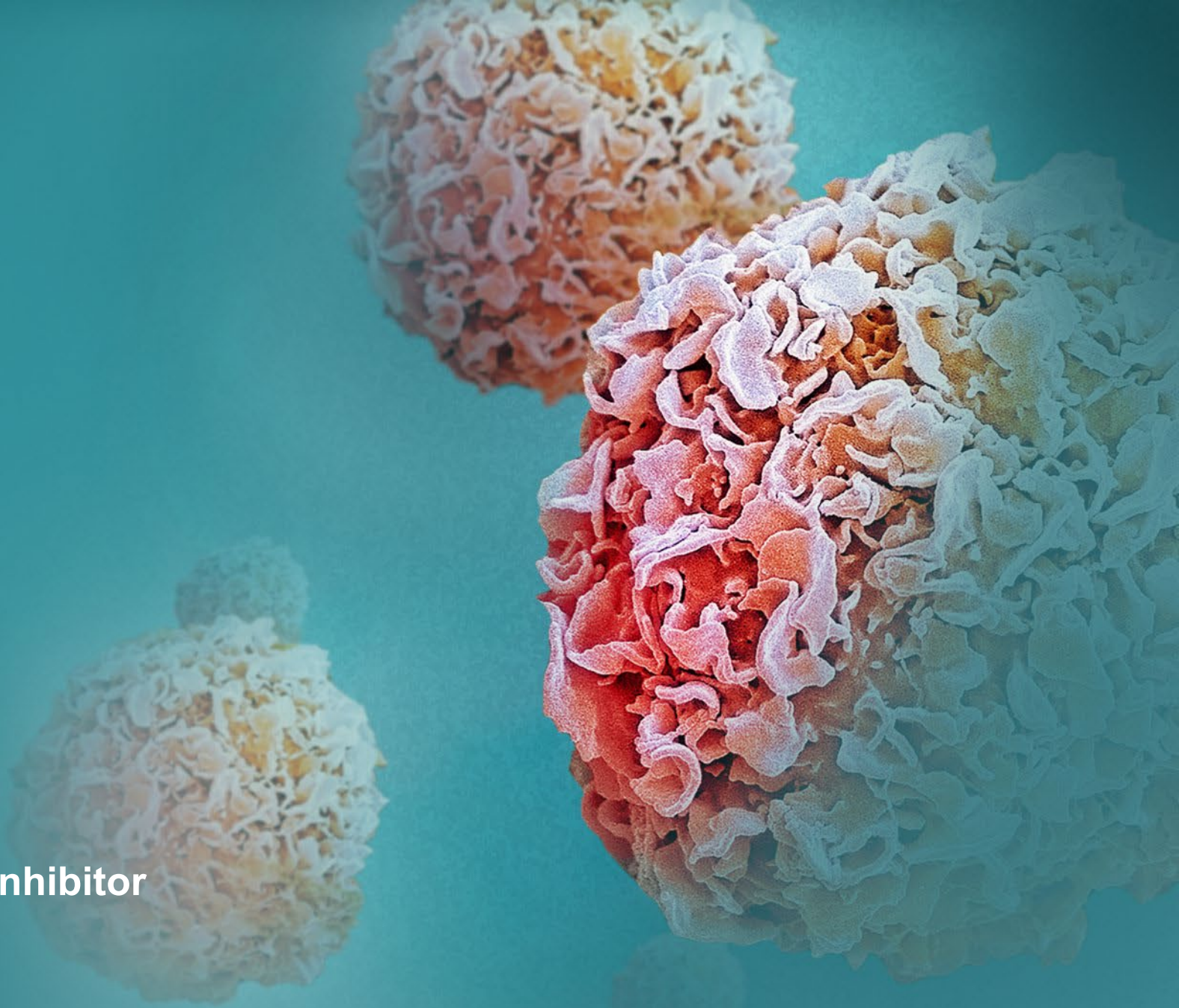
Opportunity	Est. Annual US Incidence
mCRPC (RLT, TCE, ADC Combo)	37,000
NSCLC (KRASi Combo)	45,000
CRC (KRASi Combo)	65,000
Breast Cancer (ERi Combo)	220,000

Rinzimetostat has the potential to address ~70,000 patients in the US with prostate cancer annually

ORIC



Enozertinib
Brain-Penetrant EGFR Inhibitor



Enozertinib: Potential Best-in-Class TKI for EGFR Exon 20 and EGFR Atypical NSCLC

Enozertinib Overview



KEY LIMITATIONS of approved and investigational agents

- **Lack of CNS activity:** ~50% of patients develop brain metastases and derive limited benefit with non-CNS-active drugs
- **Tolerability issues:** high rates of treatment discontinuations due to on- and off-target toxicity



CLINICAL DATA establishes enozertinib's potential best-in-class profile

- **Competitive systemic activity:** response rates at or above competitor benchmarks
- **Convincing CNS activity:** 100% intracranial ORR in patients with measurable disease
- **Well-tolerated safety profile:** no significant off-target toxicity, resulting in low rate of discontinuations



PRIORITIZING 1L for future development

- **Selected Phase 3 monotherapy dose:** 80 mg once-daily
- **Enrollment and follow-up continues in 1L cohorts**
 - EGFR exon 20: monotherapy, combination with SC amivantamab⁽¹⁾, and combination with chemotherapy
 - EGFR atypical: monotherapy
- **Data expected 2H26,** ahead of potential initiation of Phase 3 trial(s)

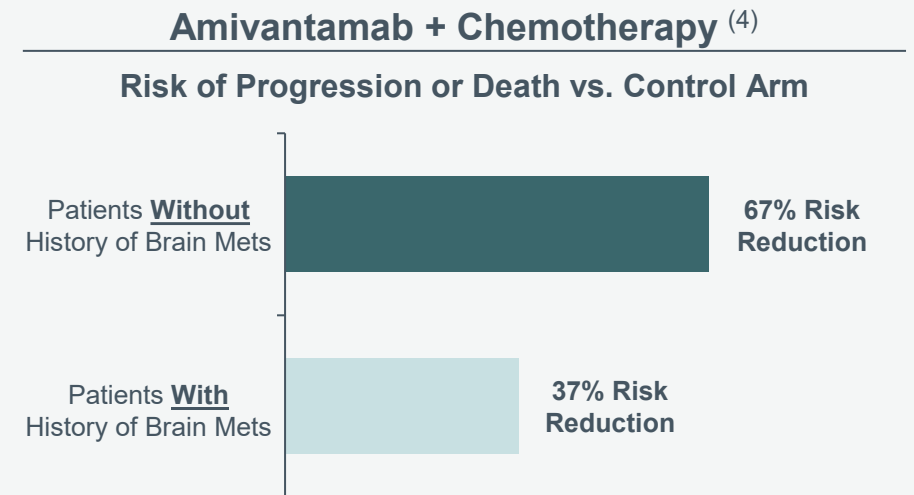
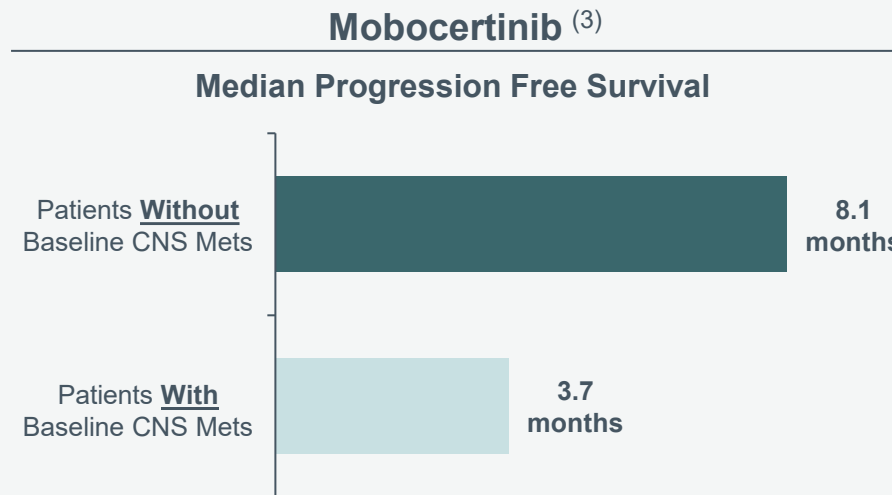
Enozertinib is a potential best-in-class therapy with excellent selectivity and brain-penetrance that has demonstrated highly competitive clinical data in EGFR exon 20 and EGFR PACC

High Burden of CNS Disease in NSCLC Patients with EGFR Mutations Leads to Disease Progression and Limited Survival with Current Therapies

CNS Disease Highly Prevalent in EGFR Mutated NSCLC...



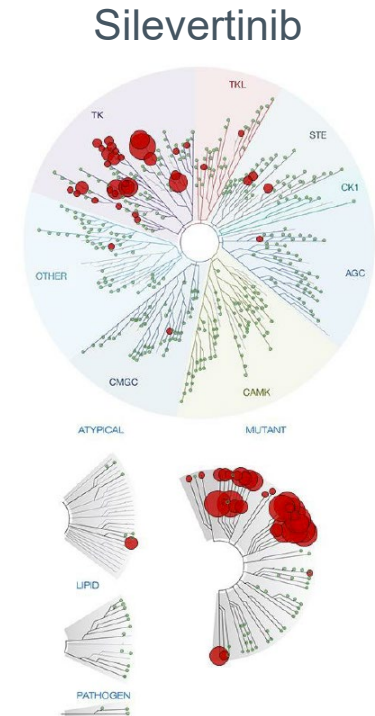
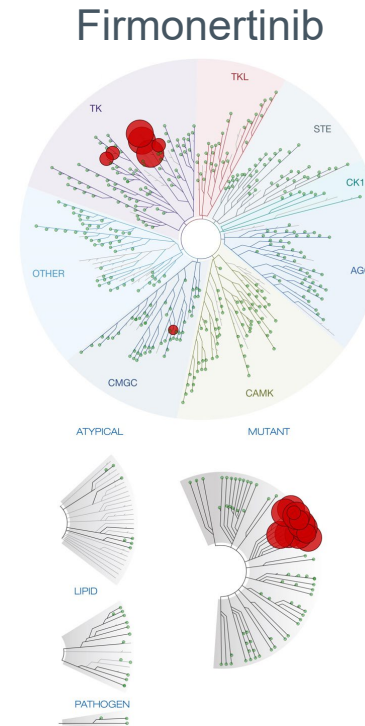
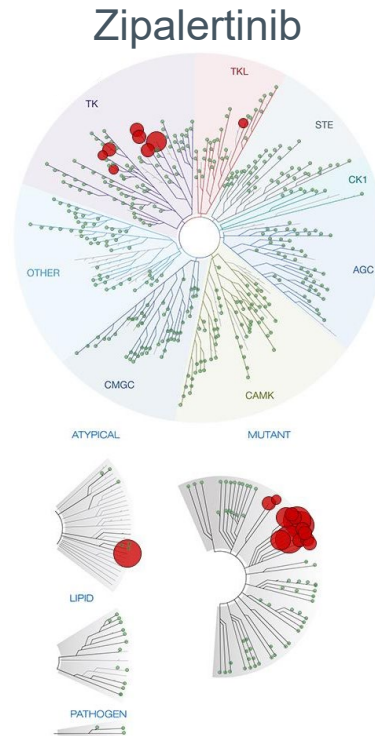
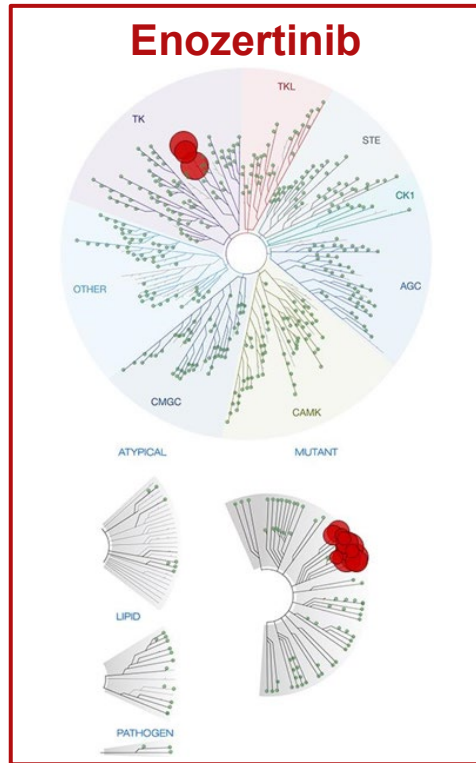
...And Patients With CNS Metastases Derive Limited Benefit From Non-CNS-Active Drugs



An effective, brain-penetrant therapy can potentially drive long-term outcomes and extend survival through durable CNS control

Enozertinib Was Designed to Selectively Target EGFR with High Potency Against Exon 20 and Atypical Mutations

Kinome Selectivity Comparison



Off-target Wildtype Kinases Inhibited $\geq 80\%$ at 1 μM

Enozertinib	Zicalertinib	Firmonertinib	Silevertinib
0	7	4	25

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

Phase 1b Trial of Enozertinib in NSCLC Patients

Phase 1b, Multicenter, Open-Label Trial

Key Eligibility

- Advanced NSCLC
 - EGFR exon 20
 - EGFR atypical
- **Untreated, stable, asymptomatic brain metastases allowed**

**EGFR
exon 20**

**EGFR
atypical**

Monotherapy

Combination with SC amivantamab ⁽¹⁾

Combination with chemotherapy

Monotherapy

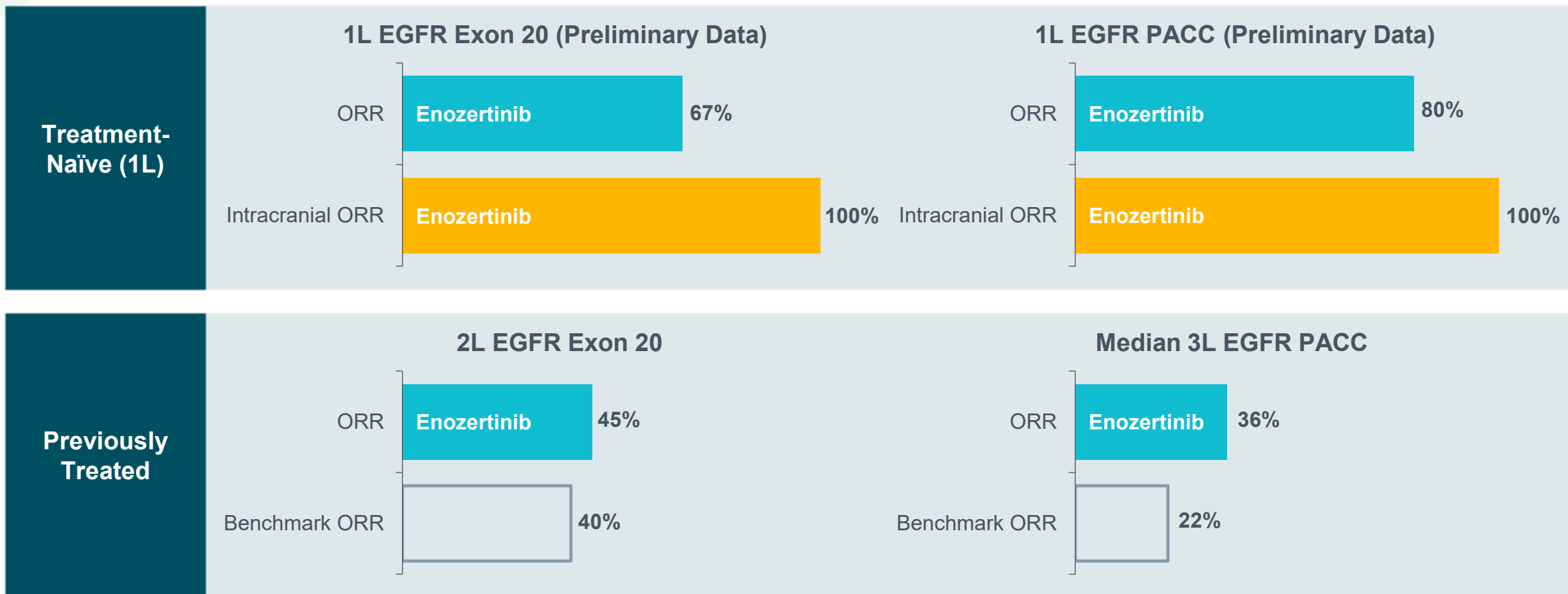
Primary endpoints: Safety and candidate RP2Ds, dose expansion (RP2D selection) and ORR (per RECIST v1.1)

Key secondary endpoints: PK, safety, DOR, CBR and PFS, including intracranial ORR/PFS (per RECIST v1.1 and RANO-BM)

Robust clinical activity demonstrated in 1L and 2L+ NSCLC patients with EGFR exon20 and EGFR PACC mutations

Enozertinib Phase 1b Data Establishes Potential Best-in-Class Profile in EGFR Exon 20 and PACC Mutated NSCLC

Enozertinib Updated Phase 1b Data Highlights (ESMO Asia 2025)



Ongoing development of enozertinib is focused on 1L, where preliminary data demonstrated potential best-in-class systemic and intracranial activity

Enozertinib Has Been Generally Well Tolerated Despite Less Stringent Enrollment Criteria for Baseline CNS Disease

1L EGFR exon 20 NSCLC

Event, n (%)	80 mg (n=18)	120 mg (n=15)
TRAEs Grade ≥3	4 (22)	9 (60)
Dose reduction due to TRAE	3 (17)	12 (80)
Discontinued due to TRAE	2 (11)	0

- Well tolerated safety profile with TRAEs predominantly Grades 1-2
- No significant off-target toxicities (e.g., myelosuppression, QTc prolongation, hepatotoxicity)
- Low rate of discontinuations due to TRAEs
- Higher rate of dose reductions at 120 mg (80%) vs 80 mg (17%)
 - 58% of reductions at 120 mg dose by ~8 weeks (2 cycles)

Treatment-Related Adverse Events (TRAEs) in ≥20% of Patients

Event, n (%)	80 mg (n=18)		120 mg (n=15)	
	Grade 1-2	Grade 3	Grade 1-2	Grade 3
Diarrhea	15 (83)	2 (11)	9 (60)	1 (7)
Paronychia	8 (44)	0	11 (73)	1 (7)
Stomatitis	7 (39)	1 (6)	4 (27)	0
Dermatitis acneiform	5 (28)	0	4 (27)	6 (40)
Rash	4 (22)	1 (6)	2 (13)	1 (7)
Nausea	6 (33)	0	3 (20)	0
Pruritis	4 (22)	0	3 (20)	0
Mucosal inflammation	4 (22)	0	5 (33)	1 (7)
Dry skin	1 (6)	0	6 (40)	0
Alopecia	1 (6)	0	8 (53)	0
Rash maculo-papular	5 (28)	0	2 (13)	0

High rate of dose reductions in 120 mg cohort led to subsequent cohort of patients being dosed at 80 mg QD

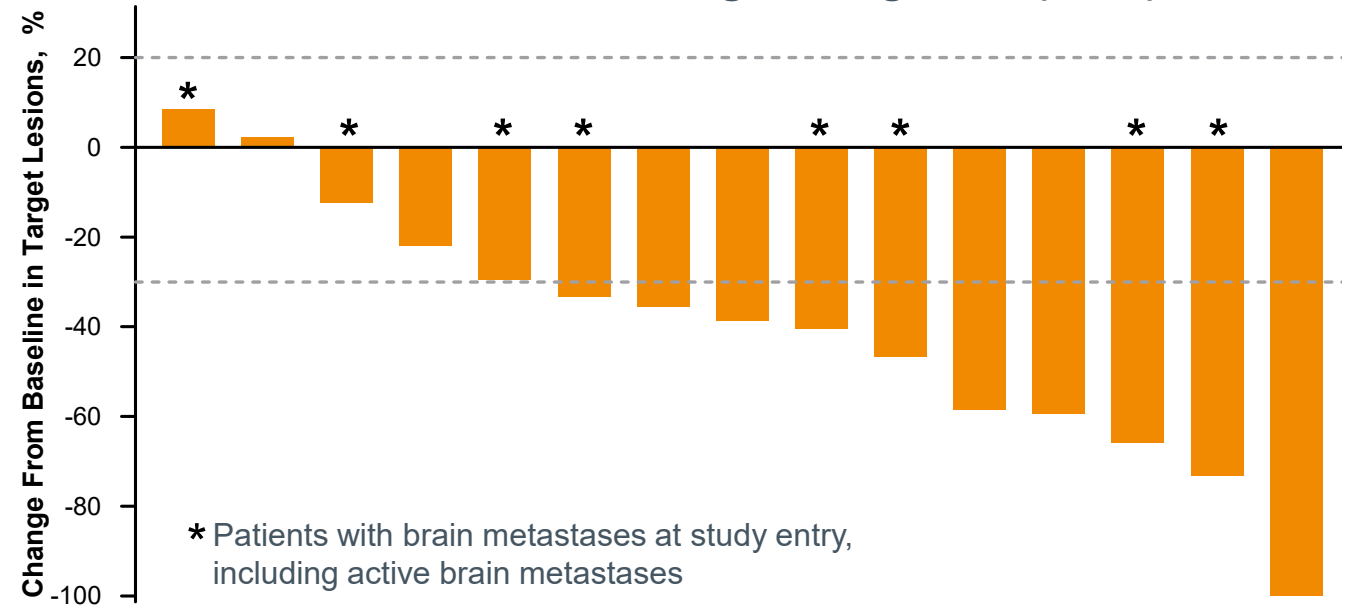
Enozertinib Achieved Strong Antitumor Activity, Including in Patients with CNS Disease at Baseline

1L EGFR exon 20 NSCLC

Systemic Objective Response Rate

Evaluable Population ⁽¹⁾	120 mg (n=15)
Best ORR, [†] % [95% CI]	67 [38, 88]
Confirmed ORR, % [95% CI]	60 [32, 84]
Partial response, n (%)	9 (60)
Stable disease, n (%)	5 (33)
Progressive disease, n (%)	1 (7)
Disease control rate (CR + PR + SD), % [95% CI]	93 [68, 100]

Best % Change in Lesions in Patients Receiving 120 mg Dose (n=15)



- Initial cohort of efficacy evaluable patients were treated at 120 mg; given 80% dose reduction rate, most patients effectively received 80 mg
- Subsequent cohort of patients were treated at 80 mg; follow-up is still in progress

Enozertinib demonstrates strong ORR and disease control in 1L NSCLC patients with EGFR exon 20 mutations

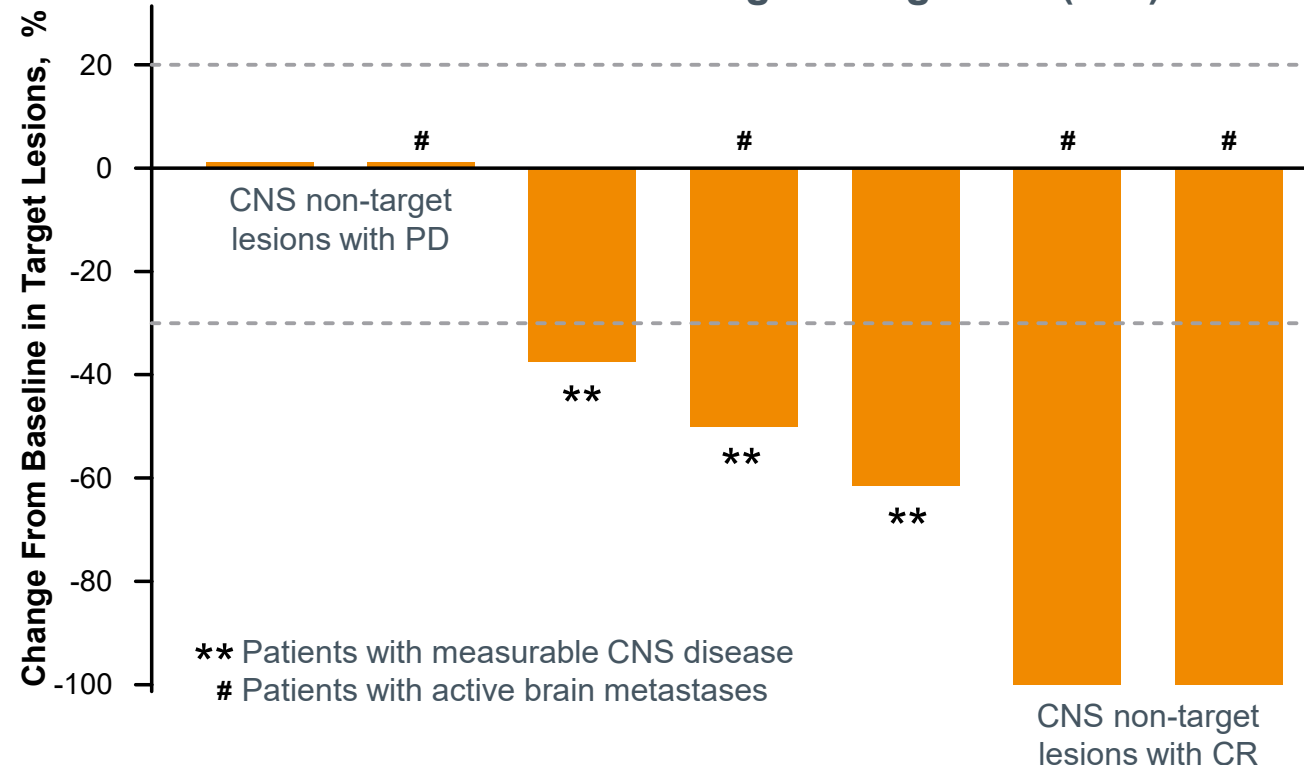
Enozertinib Achieved Strong CNS Antitumor Activity as Measured by BICR-RANO

1L EGFR exon 20 NSCLC

CNS Response [†]	120 mg (n=7) ⁽¹⁾
Best ORR,[‡] % [95% CI]	71 [29, 96]
Confirmed ORR, % [95% CI]	71 [29, 96]
Complete response, n (%)	2 (29)
Partial response, n (%)	3 (43)
Stable disease, n (%)	0
Progressive disease, n (%)	2 (29)
Disease control rate (CR + PR + SD), % [95% CI]	71 [29, 96]

- 3 patients with measurable CNS disease:
 - 100% confirmed intracranial ORR
- 4 patients with non-measurable CNS disease:
 - 2 confirmed complete responses

Best % Change in CNS Lesions in Patients Receiving 120 mg Dose (n=7)



Strong CNS ORR (100% in measurable CNS disease by BICR-RANO), including in patients with active brain metastases, showcases enozertinib's CNS activity and positions it favorably for future clinical development in 1L NSCLC patients with EGFR exon 20

Complete Intracranial and Partial Systemic Responses in a Treatment-Naïve EGFR Exon 20 Mutant NSCLC Patient With Active CNS Metastases

Patient: 60-year-old female

Prior Therapy: None

CNS Metastases at Baseline: 5 active non-target lesions (no prior radiation or surgery)

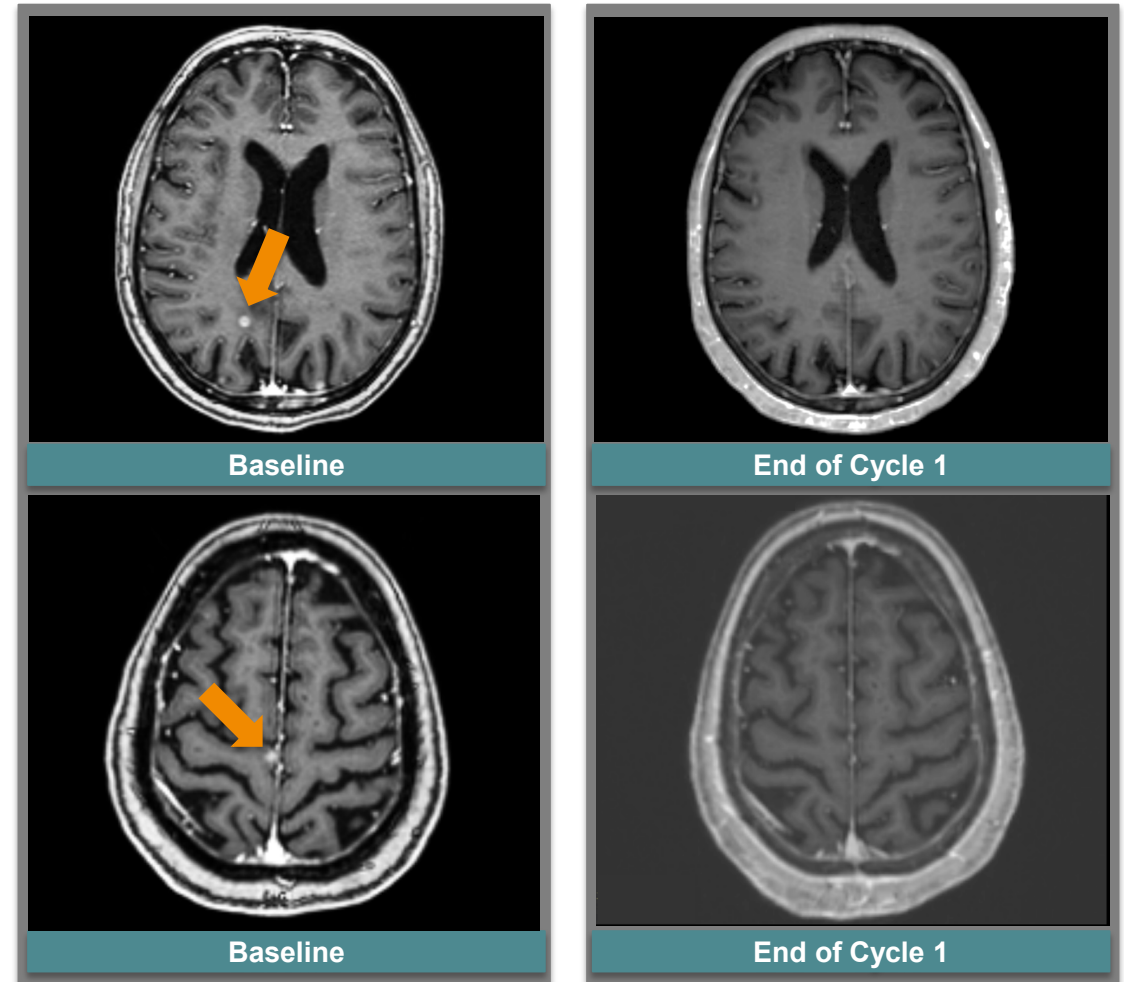
Enozertinib Dose: 120 mg oral, once-daily

Systemic Response: Partial response after Cycle 1 (47% reduction)

CNS Response: Complete response after Cycle 1 (disappearance of all 5 CNS lesions)

Treatment-Related Adverse Events: Grade 1 paronychia, Grade 2 mucositis, dose reduced to 80 mg for Grade 3 palmar erythrodysesthesia

Duration of Treatment: Cycle 6 (ongoing at data cutoff)

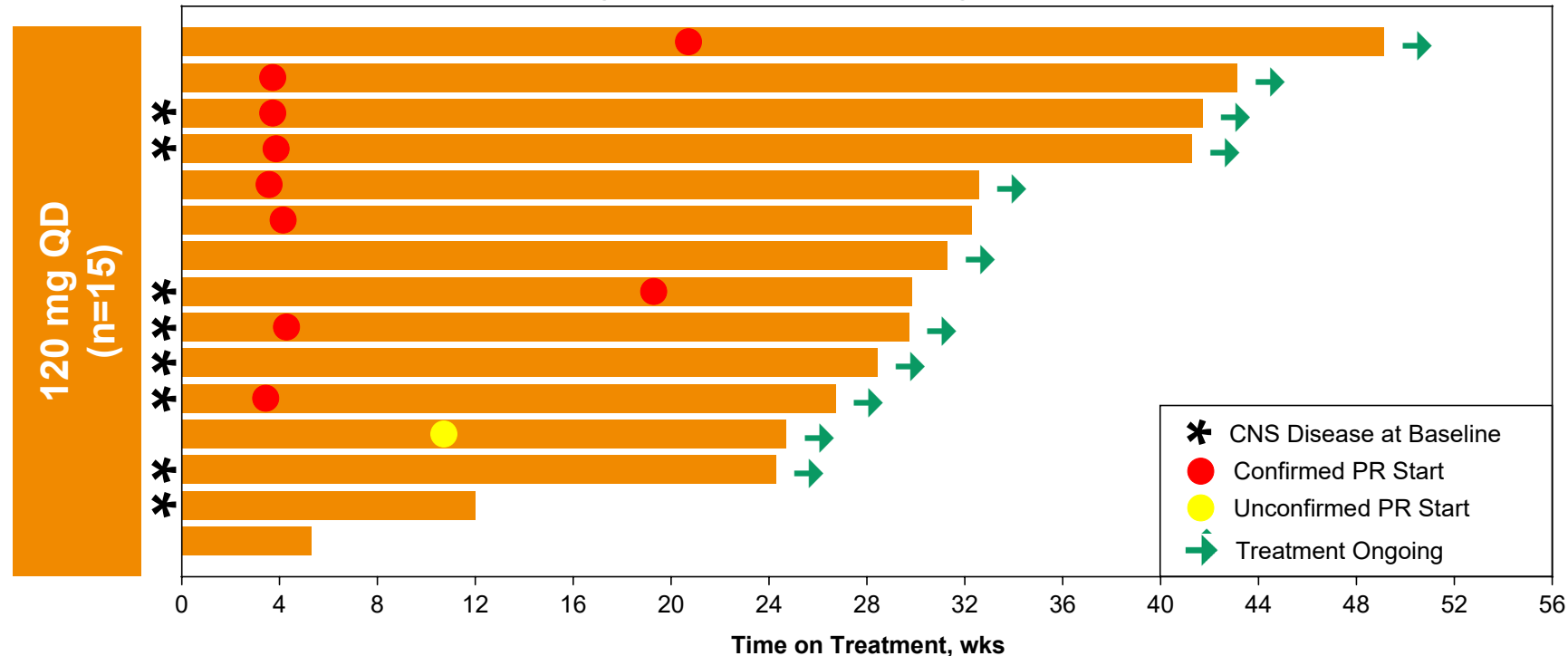


Enozertinib demonstrated robust systemic activity and complete intracranial response in a patient with active brain metastases

Tumor Responses on Enozertinib Were Generally Achieved Early and the Vast Majority of Patients Remain on Treatment

1L EGFR exon 20 NSCLC

- Initial cohort of efficacy evaluable patients were treated at 120 mg; given 80% dose reduction rate, most patients effectively received 80 mg
- Subsequent cohort of patients were treated at 80 mg; follow-up is still in progress



- Responses generally occur by 4 weeks, but tumor regression continues over time, with late responses seen after 4+ months on treatment
- Median follow-up of 32.6 weeks; 80% (8 of 10) of responders are still on treatment

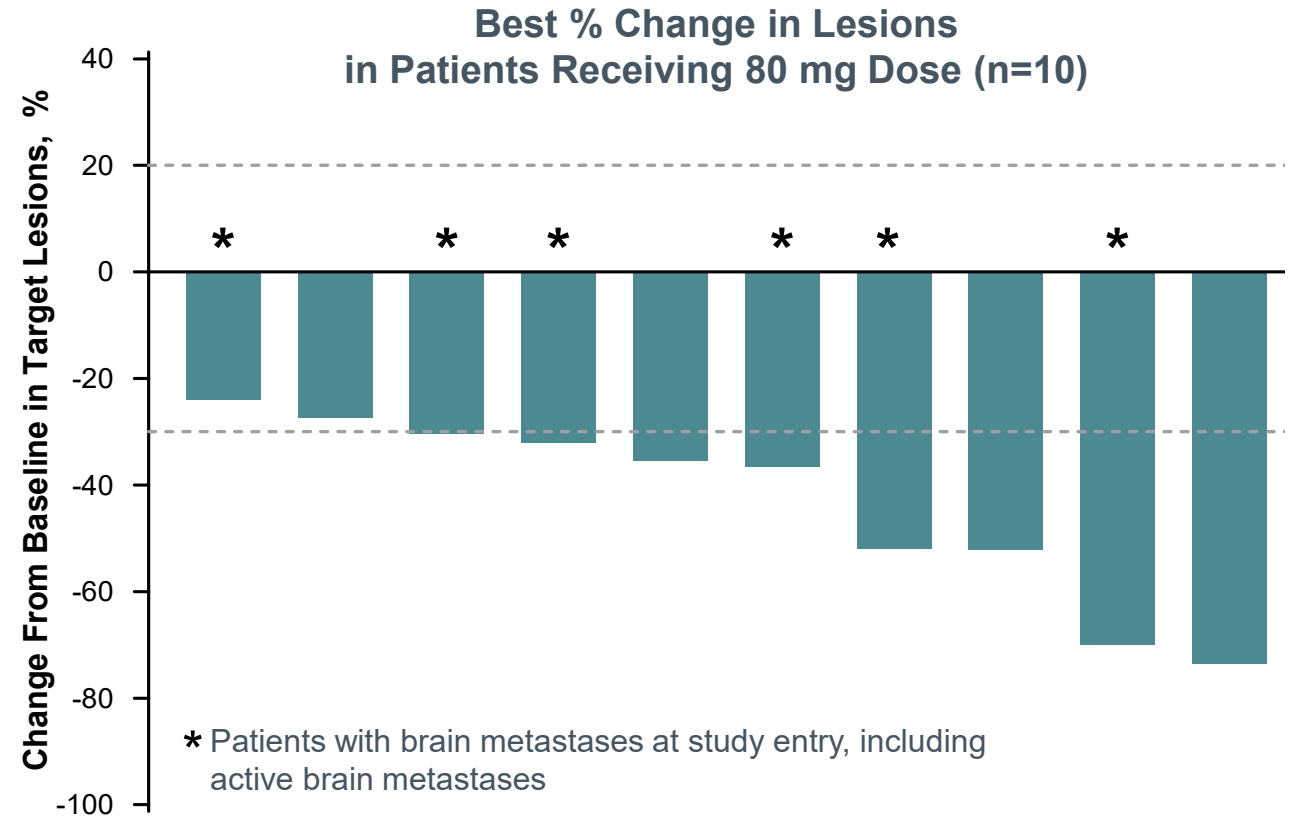
80% of responders are still on therapy, most at a reduced 80 mg dose; all subsequent enrollment was at 80 mg, with follow-up in progress

Early Enozertinib Data in 1L EGFR PACC Patients Demonstrated Impressive Antitumor Activity, Including in Patients with CNS Disease at Baseline

1L EGFR PACC NSCLC

Preliminary Response Assessment	80 mg (n=10)
Best ORR, ‡ %	80
Partial response, n (%)	8 (80)
Stable disease, n (%)	2 (20)
Progressive disease, n (%)	0 (0)
Disease control rate (CR + PR + SD), %	100

- Safety profile to date in line with 80 mg dose level in other cohorts



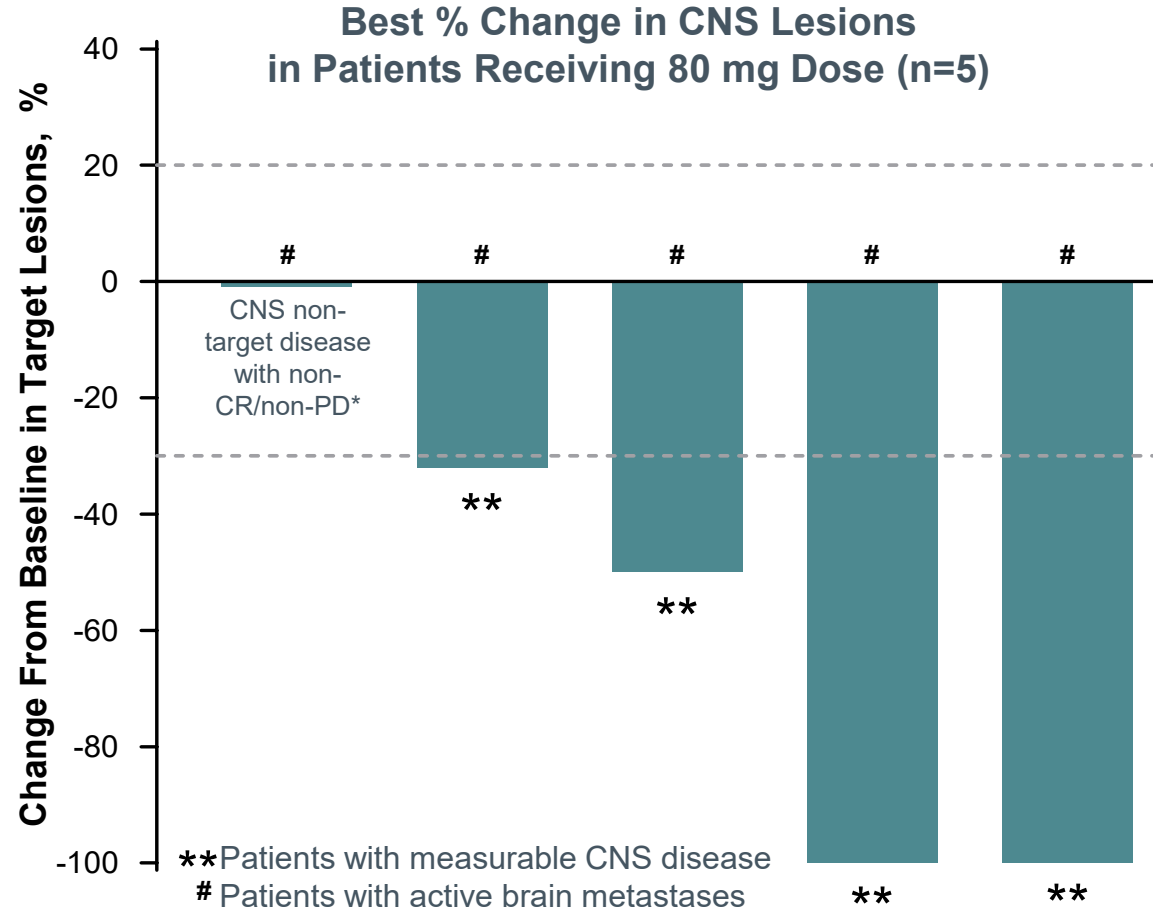
Early enozertinib data in 1L NSCLC patients with EGFR PACC mutations shows impressive responses, with additional data expected in 2H 2026

Early Enozertinib Data in 1L EGFR PACC Patients Demonstrated Strong CNS Antitumor Activity

1L EGFR PACC NSCLC

Preliminary CNS Response	80 mg (n=5) ⁽¹⁾
Best ORR, ‡ %	80
Complete response, n (%)	1 (20)
Partial response, n (%)	3 (60)
Stable disease, n (%) *	1 (20)
Progressive disease, n (%)	0 (0)
Disease control rate (CR + PR + SD), %	100

- 4 patients with measurable CNS disease:
 - 100% intracranial ORR, including 1 complete response
- 1 patient with non-measurable CNS disease:
 - Best response of non-CR / non-PD



Early enozertinib data in 1L NSCLC patients with PACC mutations shows impressive CNS antitumor activity (100% ORR in measurable CNS disease), including in patients with active brain metastases, with additional data expected in 2H 2026

Partial Intracranial and Systemic Responses in a Treatment-Naïve EGFR PACC Mutant NSCLC Patient with Active CNS Disease

Patient: 67-year-old male

PACC Mutation: G719A

Prior Therapy: None

CNS Metastases at Baseline: 1 target lesion
(no prior radiation or surgery)

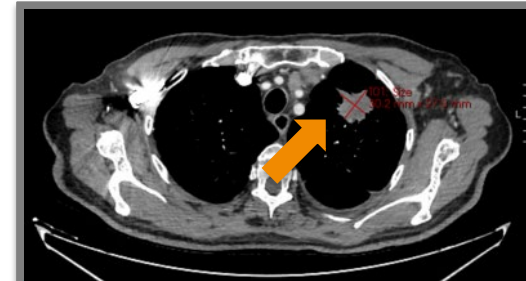
Enozertinib Dose: 80 mg oral, once-daily

Systemic Response: Partial response after Cycle 1
(43% reduction)

CNS Response: Partial response after Cycle 1
(66% reduction); complete response after Cycle 4

Treatment-Related Adverse Events: Grade 1 acneiform rash

Duration of Treatment: Cycle 5 (ongoing at data cutoff)



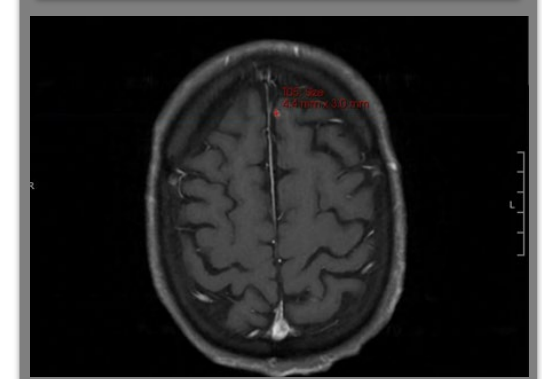
Baseline



BOR Timepoint



Baseline

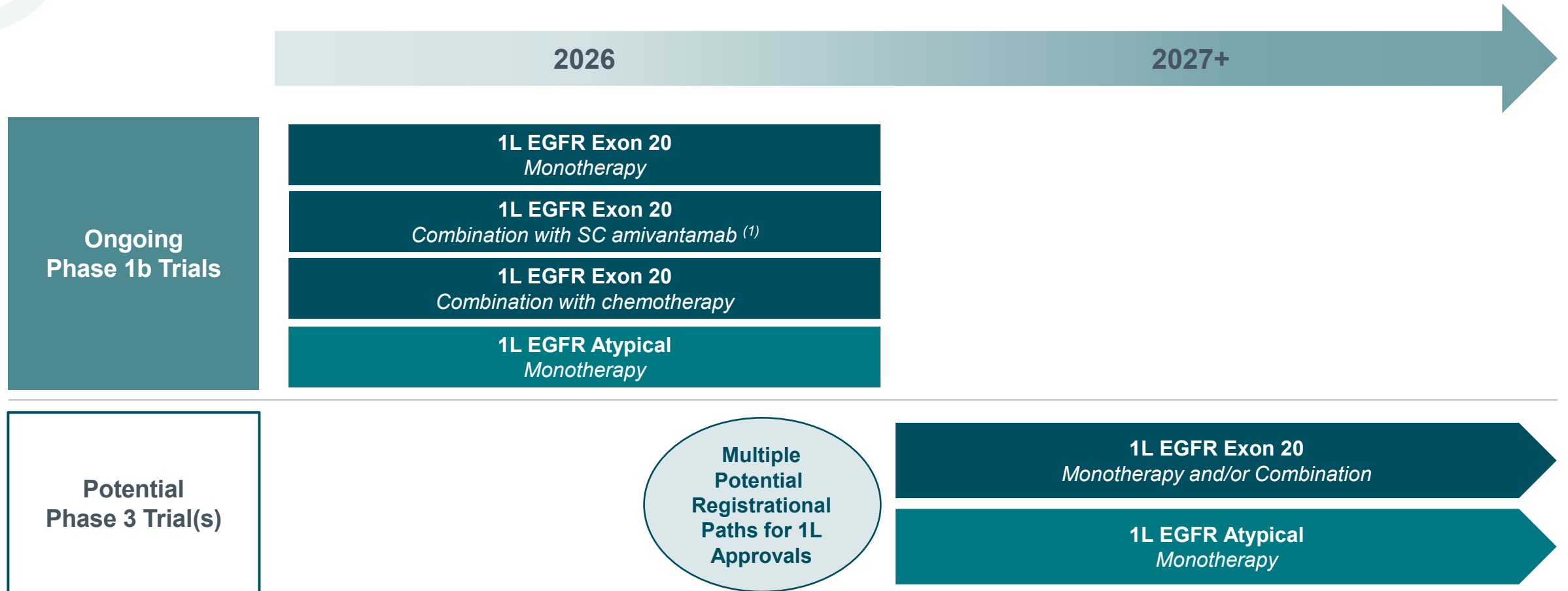


BOR Timepoint

Enozertinib demonstrated robust systemic activity and complete intracranial response in a patient with active brain metastasis

Enozertinib Development Is Focused on First-Line NSCLC Patients with EGFR Exon 20 and EGFR Atypical Mutations

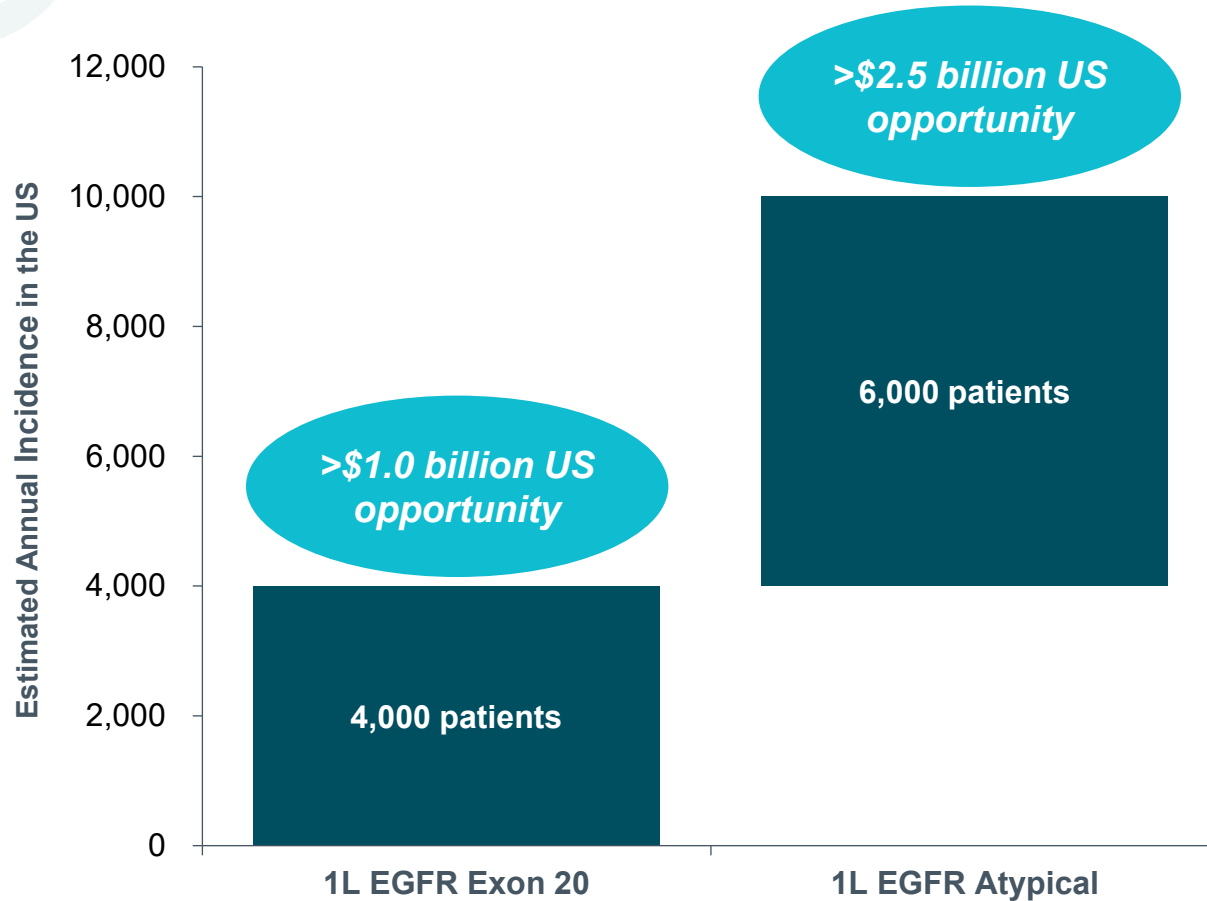
Enozertinib Next Steps



Additional data expected in 2H 2026, ahead of potential initiation of Phase 3 trial(s)

Enozertinib Is Pursuing a Significant Commercial Opportunity Across Patient Populations that Lack an Approved CNS Active Agent

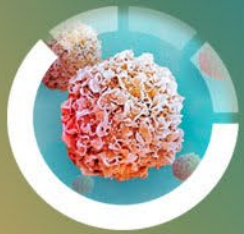
Potential Enozertinib Commercial Opportunity (US Only)



- ~10,000 patients (~5% of NSCLC) diagnosed annually
- EGFR exon 20 mutant NSCLC: no approved CNS-active therapies
- EGFR atypical NSCLC: no approved therapies


Potential commercial opportunity of ~\$3.0 to \$4.0 billion in the US annually

Enozertinib has the potential to address ~9,000 patients with NSCLC annually, representing a commercial opportunity of ~\$3.0 to \$4.0 billion in the US alone



Key Takeaways

Clinical Pipeline Focused on Advancement of Rinzimetostat and Enozertinib

Program	Indication	Discovery / IND Enabling	Phase 1/2	Pivotal / Phase 3	Clinical Collaboration	Phase 3 Initiations
PRODUCT CANDIDATES						
Rinzimetostat <i>PRC2 inhibitor</i>	Prostate Cancer	<ul style="list-style-type: none"> • Combination with darolutamide 				Himalayas-1 Expected in 1H 2026
		<ul style="list-style-type: none"> • Combination with apalutamide 			Johnson&Johnson	Potential Himalayas-2 in 2027
Enozertinib <i>EGFR inhibitor</i>	NSCLC EGFR exon 20	<ul style="list-style-type: none"> • 1L monotherapy • 1L combination with SC amivantamab ⁽¹⁾ • 1L combination with chemotherapy 			Johnson&Johnson	Potential Redwood-1 in 2027
	NSCLC EGFR atypical	<ul style="list-style-type: none"> • 1L monotherapy 				

Clinical-stage pipeline includes two potential best-in-class programs addressing large solid tumor market opportunities; Both programs approaching initiation of registrational trials

ORIC Pharmaceuticals: Dedicated to Overcoming Resistance In Cancer

Validated Targets in High Unmet Need Populations

- Potential best-in-class PRC2 inhibitor for prostate cancer
- Potential best-in-class TKI for NSCLC with EGFR exon 20 insertion and EGFR atypical mutations

Late-Stage Clinical Pipeline

- Rinzimetostat (ORIC-944) and enozertinib (ORIC-114) rapidly advancing towards potential Phase 3 initiations

Experienced Management Team

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

Strong Financial Position

- Cash and investments of \$420 million expected to fund company into 2H 2028
- Funding through primary endpoint readout from first Phase 3 trial of rinzimetostat

Anticipated Milestones

- Rinzimetostat for mCRPC:
 - ✓ 1Q26: Combination dose optimization data with AR inhibitor
 - 1H26: Initiate first global Phase 3 registrational trial in post-abiraterone mCRPC
 - 2H26: Program update
- Enozertinib for NSCLC:
 - 2H26: 1L EGFR exon 20 monotherapy data and combination data with SC amivantamab ⁽¹⁾
 - 2H26: 1L EGFR atypical monotherapy data

Two potential best-in-class programs approaching Phase 3 initiation; Cash runway into 2H28, beyond rinzimetostat Phase 3 data