

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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934
Date of Report (Date of earliest event reported)
October 23, 2026

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

Delaware
(State or other jurisdiction
of incorporation)

001-39269
(Commission
File Number)

47-1787157
(IRS Employer
Identification No.)

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

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

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

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

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

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

Emerging growth company ☐

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

Item 7.01 Regulation FD Disclosure.

ORIC Pharmaceuticals, Inc. (the “Company”) presented an enozertinib (ORIC-114) program update (the “Program Update”) on October 23, 2026 at ESMO Congress 2026. A presentation containing the data presented in the Program Update is attached as Exhibit 99.1 hereto and is incorporated herein by reference.

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

Item 8.01 Other Events.

The Program Update covered updated data from the Company’s Phase 1b trial of enozertinib, as well as the Company’s plans to initiate a global Phase 3 registrational trial of enozertinib in the first half of 2027:

Enozertinib Phase 1b Data in 1L EGFR Atypical NSCLC

Enozertinib is being evaluated in an ongoing Phase 1b trial in patients with locally advanced or metastatic non-small cell lung cancer (“NSCLC”) with epidermal growth factor receptor (“EGFR”) atypical and EGFR exon 20 insertion mutations. Notably, enrollment allows patients with previously untreated brain metastases (i.e., active, untreated brain metastases). Key objectives of the trial included safety and determination of the recommended Phase 2 dose, along with assessment of antitumor activity based on investigator-assessed objective response rate (“ORR”), blinded independent central review (“BICR”)–assessed ORR, central nervous system (“CNS”)–ORR according to modified RECIST 1.1 and/or Response Assessment in Neuro-Oncology Brain Metastases (“RANO-BM”), as well as duration of response and progression-free survival (“PFS”).

As of the September 4, 2026 cutoff date, data are presented for 26 patients who were treated with 80 mg once daily oral enozertinib, including 23 patients with P-loop and α C-helix compressing (“PACC”) mutations and 3 patients with L861Q mutations without a co-occurring PACC mutation. Brain metastases were present in 65% of patients at baseline, which is more than double the rate versus competitor datasets. Notably, 46% of all patients had previously untreated brain metastases.

Safety Analysis

Enozertinib was well tolerated with predominantly Grade 1 or 2 treatment-related adverse events (“TRAEs”) and no significant off-target toxicities. Most frequent TRAEs included diarrhea, paronychia, and dermatitis acneiform. Six patients (23%) experienced Grade 3 TRAEs, all of which were resolved with dose modifications. There were no Grade 4 or 5 TRAEs and no treatment discontinuations related to TRAEs.

Meaningful Systemic Antitumor Activity

Tumor reductions were observed across all response-evaluable patients¹. Reductions were also observed across a wide range of mutations, including the most prevalent PACC mutations (e.g., G719X, S768I), a broad spectrum of PACC complex mutations, and L861Q mutations. Enozertinib demonstrated meaningful systemic activity, including:

- 84% (21 of 25) confirmed systemic ORR by investigator.
- 80% (20 of 25) confirmed systemic ORR by BICR.

Deep EGFR-mutant ctDNA molecular responses were achieved by Cycle 3 Day 1 in all response-evaluable patients across diverse mutations²:

- 100% of patients achieved MR90, defined as a $\geq 90\%$ EGFR-mutant ctDNA reduction.
- 82% of patients achieved full clearance, which has been associated with improved long-term survival outcomes in prior Phase 3 NSCLC trials.

Compelling Intracranial Antitumor Activity

Enozertinib continues to demonstrate potential best-in-class intracranial efficacy. Notably, no new CNS lesions were observed in patients with or without baseline CNS metastases.

All response-evaluable patients with measurable CNS disease (90% without prior treatment for their CNS metastases) achieved CNS tumor reductions per investigator-assessment³. Enozertinib demonstrated compelling intracranial activity, including:

- 70% confirmed intracranial ORR by investigator.

Intracranial efficacy was also evaluated utilizing the more stringent BICR RANO-BM assessment criteria. Based on this assessment, CNS tumor reductions were observed in nearly all response-evaluable patients, including in patients with previously untreated CNS metastases⁴. Enozertinib demonstrated compelling intracranial activity, including:

- 67% (10 of 15) intracranial ORR by BICR RANO-BM.
- 40% (6 of 15) intracranial complete response rate by BICR RANO-BM, including in three patients with non-measurable CNS disease.

Promising Early Durability

Median progression-free survival and median duration of response data are immature. The Kaplan-Meier 6-month landmark PFS is 88%. Follow-up is ongoing with the majority of patients continuing on treatment.

Redwood-1 Phase 3 Initiation

Supported by potential best-in-class data presented at ESMO Congress 2026 and based on End-of-Phase 1 interactions with the U.S. Food and Drug Administration, the Company plans to initiate Redwood-1, a global Phase 3 registrational trial in EGFR atypical NSCLC in 1H 2027. This trial plans to enroll approximately 360 patients with PACC and L861X mutations, including those with untreated brain metastases, randomized to receive 80 mg once daily oral enozertinib or physician's choice of osimertinib or afatinib. Dual primary endpoints include ORR by BICR for potential accelerated approval as well as PFS by BICR for full approval. Key secondary endpoints include overall survival and intracranial ORR by BICR RANO-BM.

¹ n=25 patients with opportunity for two post-baseline tumor assessments.

² n=22 patients with EGFR mutation in baseline plasma and opportunity for two post-baseline systemic tumor assessments. September 15, 2026 cutoff.

³ n=10 patients with measurable target CNS lesions per investigator assessment.

⁴ n=15 patients with baseline CNS metastases per BICR assessment.

Cautionary Note Regarding Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements as that term is defined in Section 27A of the Securities Act and Section 21E of the Exchange Act. Statements in this Current Report on Form 8-K that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, the continued clinical development of enozertinib; the potential advantages of enozertinib; statements regarding the potential best-in-class profile of enozertinib; clinical outcomes from studies of enozertinib, which may materially change as patient enrollment continues or more patient data become available; the development plans and timelines for enozertinib, including the expected initiation of the Redwood-1 trial; plans underlying the Company's clinical trials and development; and statements by the Company's chief medical officer and chief executive officer. Words such as "believes," "anticipates," "plans," "expects," "intends," "will," "goal," "potential" and similar expressions are intended to identify forward-looking statements. The forward-looking statements contained herein are based upon the Company's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those projected in any forward-looking statements due to numerous risks and uncertainties, including but not limited to: risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and operating as a clinical stage company; the Company's ability to develop, initiate or complete preclinical studies and clinical trials for, obtain approvals for and commercialize any of its product candidates; changes in the Company's plans to develop and commercialize its product candidates; the potential for clinical trials of enozertinib or any other product candidates to

differ from preclinical, initial, interim, preliminary or expected results; negative impacts of health emergencies, economic instability or international conflicts on the Company’s operations, including clinical trials; the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of the Company’s license and collaboration agreements or its clinical trial collaboration and supply agreements; the potential market for the Company’s product candidates, and the progress and success of competing therapeutics currently available or in development; the Company’s ability to raise any additional funding it will need to continue to pursue its business and product development plans; regulatory developments in the United States and foreign countries; the Company’s reliance on third parties, including contract manufacturers and contract research organizations; the Company’s ability to obtain and maintain intellectual property protection for its product candidates; the loss of key scientific or management personnel; competition in the industry in which the Company operates; general economic and market conditions; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled “Risk Factors” in the Company’s Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the “SEC”) on August 3, 2026, and the Company’s future reports to be filed with the SEC. These forward-looking statements are made as of the date hereof, and the Company assumes no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	<u>Description</u>
99.1	ESMO Congress 2026 Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

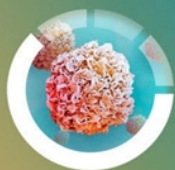
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ORIC PHARMACEUTICALS, INC.

Date: October 23, 2026

By: /s/ Christian V. Kuhlen, M.D., J.D.

Christian V. Kuhlen, M.D., J.D.
General Counsel



OVERCOMING RESISTANCE IN CANCER

**Enozertinib
Program Update**
October 23, 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: the potential best-in-class profile of enozertinib; our development plans and timelines for enozertinib; the potential advantages of, and commercial opportunities for, enozertinib; and enozertinib 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.

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 a 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.



Enozertinib Program Update

Agenda

- Executive Summary
- Preclinical Differentiation
- ESMO 2026 Clinical Data Highlights and Next Steps
- KOL Perspectives on Enozertinib
- Commercial Potential

ORIC Participants

- Jacob Chacko, Chief Executive Officer
- Lori Friedman, Chief Scientific Officer
- Pratik Multani, Chief Medical Officer
- Dominic Piscitelli, Chief Financial Officer
- Matt Panuwat, Chief Business Officer
- Keith Lui, SVP Commercial and Medical Affairs

Guest KOL

- Dr. Joshua Sabari, Assistant Professor of Medicine at NYU Grossman
 - Enozertinib Trial Investigator



Executive Summary

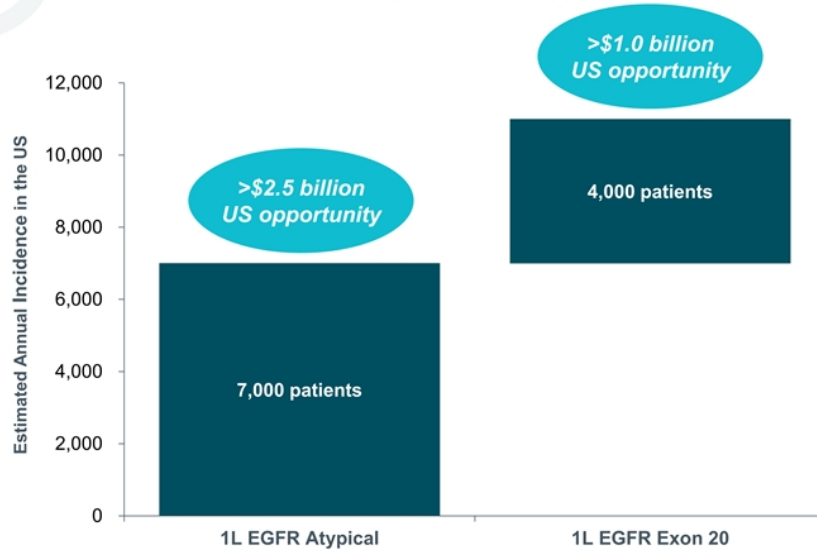
Enozertinib Establishes Potential Best-in-Class Profile in 1L EGFR Atypical NSCLC, with Data Supporting Rapid Advancement to Phase 3

Executive Summary

- 1L EGFR Atypical NSCLC is a **>\$2.5bn market opportunity in the US alone** and lacks a best-in-class therapy with meaningful systemic efficacy, compelling CNS activity, and favorable tolerability
- In a global 1L EGFR Atypical population with **over double the rate of baseline CNS disease** as competitor datasets, including untreated CNS metastases, enozertinib raises the efficacy benchmarks by achieving:
 - **84% confirmed systemic ORR**
 - **70% confirmed CNS ORR**, with **multiple complete responses**
 - **88% 6-month landmark PFS**
- Competitive safety profile: **no significant off-target toxicity** and **no treatment-related discontinuations**
- ORIC plans to **initiate Redwood-1, a global Phase 3 trial** in 1L EGFR Atypical NSCLC, in 1H 2027

Enozertinib Is Pursuing Significant Commercial Opportunities Across Two Patient Populations that Lack an Approved CNS-Active Agent

Potential Enozertinib Commercial Opportunity



Potential commercial opportunity of >\$3.5 billion in the US annually

- Each 1L opportunity has blockbuster potential in the US alone
- Comparable ex-US commercial opportunity
- An oral, well-tolerated, CNS-active agent should garner substantial share
- Additional upside in adjuvant settings

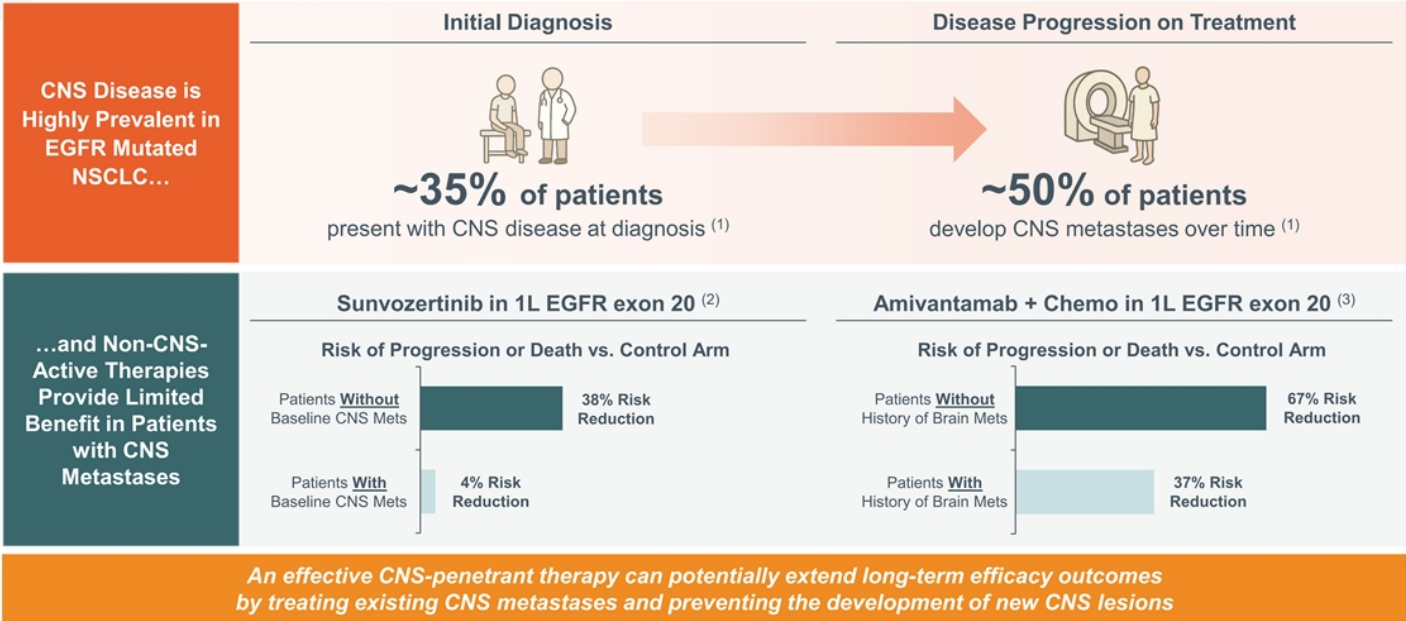
Enozertinib has the potential to address over 11,000 US patients with NSCLC annually, representing a commercial opportunity of >\$3.5 billion in the US alone



Source: American Cancer Society Cancer Facts & Figures 2026, Zhang et al. Oncotarget (2016), Robichaux et al. Nature (2021), Riess et al. Journal of Thoracic Oncology (2018), and ORIC data on file.
Note: Estimated addressable market assumes 11.4-month treatment duration for EGFR exon 20 insertion based on Girard et al. N Engl J Med (2023), 15+ month treatment duration for EGFR atypical, and current price of TKIs. EGFR atypical includes PACC + L861X.

Given the High Rate of CNS Metastases in NSCLC Patients with EGFR Mutations, Strong CNS Activity Is Critical to Driving Long-Term Benefit

CNS Disease Burden And Unmet Need



(1) Wilcox et al. Ann Oncol (2025). Does not include patients with CNS micro-metastases not detectable by conventional imaging. (2) Zhou et al. (2026) supplement. (3) Girard et al. ESMO Presentation (2023).

Best-in-Class TKIs with Compelling CNS Activity Are Approved Across Multiple NSCLC Drivers, but Not Yet for EGFR Atypical and Exon 20 NSCLC

Selected Examples of Best-in-Class TKIs in NSCLC by Driver Mutation

	EGFR Classical ⁽¹⁾	ALK	RET	ROS1	EGFR Atypical and EGFR Exon 20
Meaningful systemic efficacy	✓	✓	✓	✓	No agent yet combines all attributes
Compelling CNS activity	✓	✓	✓	✓	
Well-tolerated	✓	✓	✓	✓	
Best-in-class profiles with 1L approval					

There are no approved CNS-active, best-in-class therapies for EGFR atypical and exon 20 insertion mutations in NSCLC

Enozertinib Demonstrated Higher Systemic and CNS ORRs than Competitor Programs, Despite Enrolling Patients with Significantly More Challenging Disease

Key Benchmarks for 1L NSCLC with EGFR Atypical Mutations

	Afatinib (Approved)	Osimertinib (NCCN Guidelines)	Investigational Therapies (Late-Stage)	Enozertinib
ENROLLMENT				
Mutations included	Only S768I, L861Q, G719X	Only S768I, L861Q, G719X	PACC +/- L861Q	PACC + L861Q
% Baseline CNS mets	NR	25%	≤32%	65%
Untreated CNS mets allowed	No	Yes	Mixed	Yes
CLINICAL ACTIVITY				
Systemic ORR	66%	50%	57% to 68%	84%^{INV} / 80%^{BICR}
CNS ORR	NR	40%	NR to 29%	70%^{INV} / 67%^{BICR RANO-BM}
6-month PFS	~65%	~65%	~75%	88%
SAFETY				
Significant off-target toxicities	Yes	Yes	Yes	None
Discontinuations due to TRAE	14%	13%	0% to 24%	0%

Enozertinib demonstrated potential best-in-class systemic and CNS response rates in a population with more than double the rate of baseline CNS disease as competitor datasets



Source: Giotrif (afatinib) label, 14% discontinuation rate per LUX-Lung 3; Tagrisso (osimertinib) label, 13% discontinuation rate per FLAURA; Cho et al. (2020); Yang et al. (2015); Le et al. WCLC (2025); Neal et al. ASCO (2026); Le et al. Cancer Cell (2026); Ahn et al. ESMO (2026).
Note: Investigational therapies include amivantamab + lazertinib and firmonertinib.



Preclinical Differentiation



Enozertinib Is a Promising Candidate for NSCLC Patients with EGFR Atypical Mutations, Including Those with CNS Metastases

Enozertinib Target Candidate Profile



Robust Potency

- Robust in vitro potency & in vivo efficacy against a breadth of EGFR mutations



Exquisite Selectivity

- Exquisite selectivity that limits potential for off-target toxicity



Highly Brain Penetrant

- High brain exposure and intracranial tumor regression in preclinical studies



Enozertinib Preclinical Profile Validated with Clinical Data

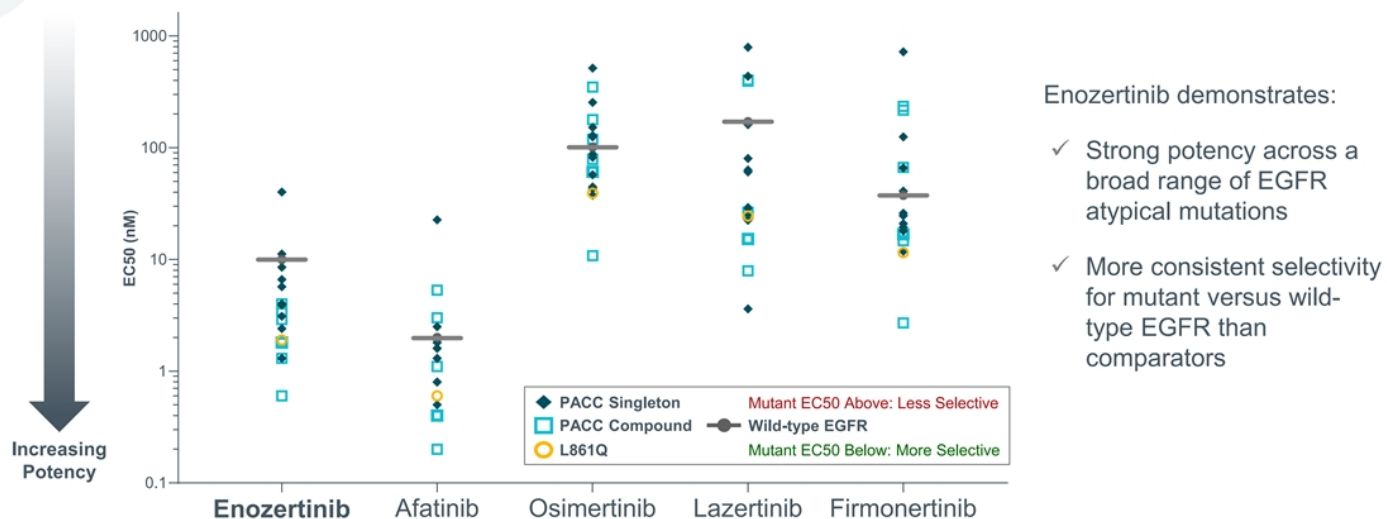


- ✓ **Potency:** meaningful systemic ORR
- ✓ **Selectivity:** no significant off-target toxicity
- ✓ **CNS-penetrance:** compelling CNS ORR

Enozertinib is a potential best-in-class inhibitor of EGFR atypical mutations, with superior potency and selectivity, and excellent brain-penetrance driving intracranial responses

Enozertinib Demonstrates Superior Relative Potency for EGFR Atypical Mutations Versus Competitors

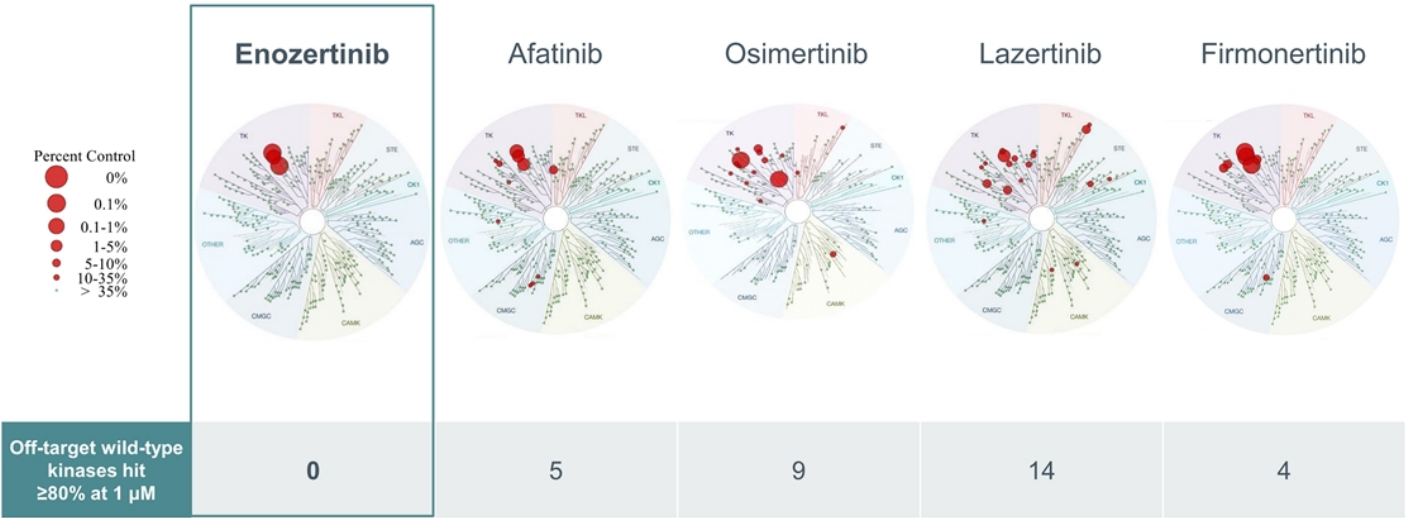
Comparison of Cell Potency and EGFR Wild-Type Selectivity



Enozertinib demonstrates more favorable EGFR mutant potency and selectivity versus competitors, leading to the potential for a superior therapeutic index in patients

Enozertinib Was Designed to Selectively Target EGFR with No Off-Target Hits

Kinome Selectivity Comparison



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

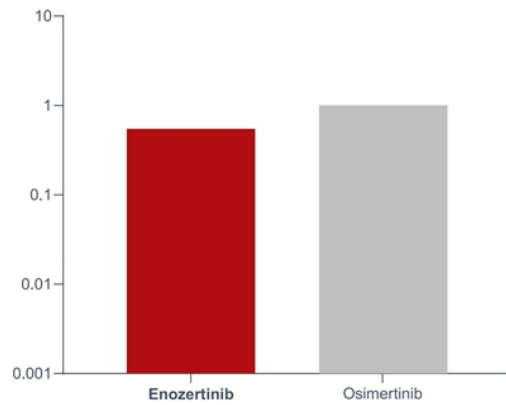


Source: Junttila et al. Cancer Res (2026) and Junttila et al. ESMO (2023).
Note: Kinase binding profiles across 468 kinases at 1 μM assessed using KINOMEScan. Red circles indicate kinases impacted within 10% of control. Table reports the number of off-target (non-EGFR/HER2) wildtype kinases inhibited 80% or more.
(1) Survozeritinib kinome tree generated from Wang et al. Cancer Discov (2022), only 117 kinases tested.

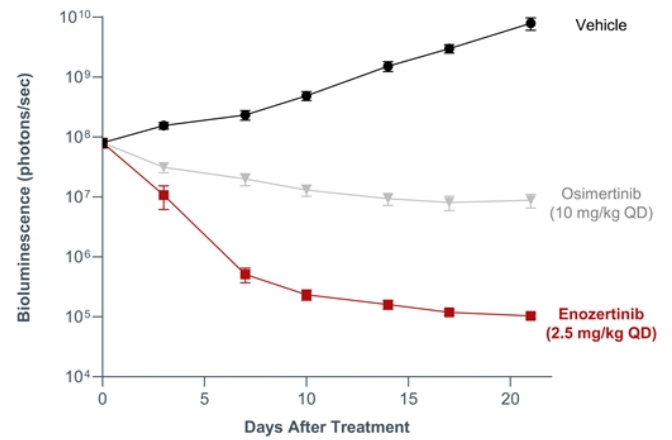
Brain Penetration of Enozertinib Leads to Intracranial Tumor Regressions In Vivo

Preclinical CNS Exposure and Intracranial Efficacy

Enozertinib Exhibits High Ratio of Free (Unbound) Brain/Plasma Exposure in Mice



Enozertinib CNS Efficacy vs Osimertinib in Intracranial NSCLC EGFR Classical Mutant In Vivo Model



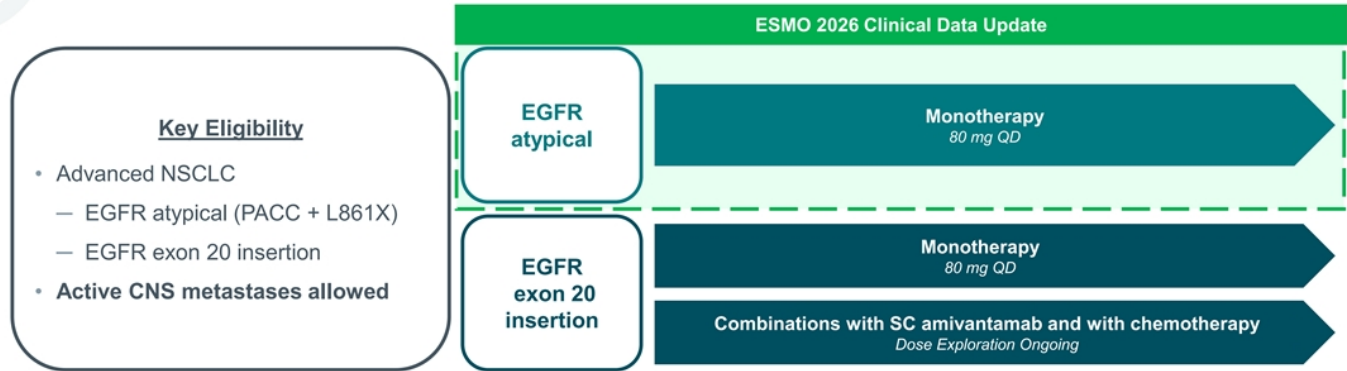
Enozertinib demonstrates excellent CNS exposure and strong tumor regressions in an intracranial NSCLC model



ESMO 2026 Clinical Data Highlights

Enozertinib Phase 1b Trial Enrolled NSCLC Patients with EGFR Atypical and Exon 20 Mutations

Phase 1b, Multicenter, Open-Label Trial



Primary endpoints: Safety, selection of recommended phase 2 dose (RP2D), and PK

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

Enozertinib previously demonstrated strong clinical activity in 1L NSCLC patients with EGFR atypical or exon 20 mutations; ESMO 2026 data further reinforce potential best-in-class profile in 1L EGFR atypical NSCLC



Note: ClinicalTrials.gov identifier: NCT05315700. Combination of enozertinib with SC amivantamab is being evaluated in a dedicated dose exploration trial via clinical collaboration with Johnson & Johnson.

Enozertinib Phase 1b Trial Enrolled 1L EGFR Atypical NSCLC Patients, Including an Exceptionally High Proportion with Baseline CNS Metastases

Demographics and Baseline Characteristics

Characteristic	N=26
Age, years, median (range)	66 (26–79)
Female, n (%)	10 (38)
Race: Asian / White, %	77 / 23
Never smoker, n (%)	9 (35)
ECOG performance: 0 / 1, %	27 / 73
Brain metastases at baseline, n (%) ⁽¹⁾	17 (65)
Previously untreated brain metastases, n (%)	12 (46)

Characteristic	N=26
Atypical mutation type	
PACC, n (%)	23 (88)
L861Q, n (%) ⁽²⁾	3 (12)
Compound mutations, n (%) ⁽³⁾	18 (69)

65% of patients had baseline CNS metastases, with nearly half of all patients having previously untreated CNS metastases



Source: Ahn et al. ESMO (2026).
Note: Data as of September 4, 2026.

(1) As determined by investigator. (3) Includes tumors harboring more than one EGFR mutation.
(2) Without PACC mutations.

Enozertinib Was Generally Well Tolerated with No Significant Off-Target Toxicity

Safety and Tolerability Profile

TRAEs, n (%)	N=26
Grade 3	6 (23)
Serious adverse events	1 (4)
Dose interruptions	9 (35)
Dose reductions	10 (39)
Treatment discontinuations	0

- TRAEs predominantly Grades 1-2
- All Grade 3 TRAEs resolved with dose modifications
- No Grade 4 or 5 TRAEs
- No significant off-target toxicities (e.g., cardiac, hematologic and hepatic)
- No discontinuations due to TRAEs

TRAEs in ≥20% of Patients	N=26	
Preferred term, n (%)	Grade 1–2	Grade 3
Diarrhea	15 (58)	2 (8)
Paronychia	15 (58)	1 (4)
Dermatitis acneiform	12 (46)	2 (8)
Rash	14 (54)	0
Stomatitis	12 (46)	0
Pruritus	7 (27)	0
Decreased appetite	6 (23)	0
Dry skin	6 (23)	0
Nausea	6 (23)	0

Enozertinib was generally well tolerated with mainly Grade 1 or 2 adverse events, no significant off-target toxicity, and no discontinuations due to TRAEs

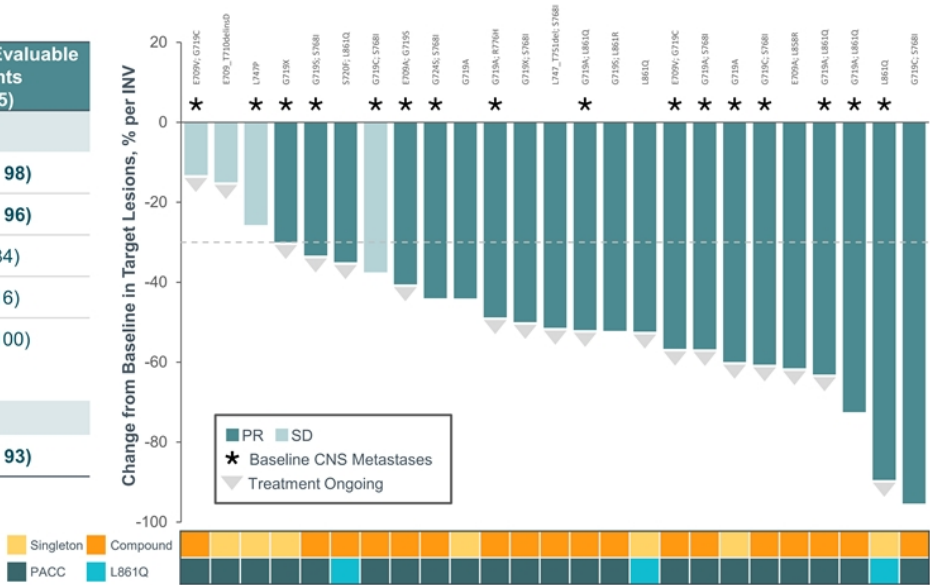


Source: Ahn et al. ESMO (2026).
Note: Data as of September 4, 2026.

Enozertinib Demonstrated Impressive Antitumor Activity in 1L EGFR Atypical NSCLC Patients, Including in Patients with Baseline CNS Metastases

Systemic ORR

Systemic ORR	Response-Evaluable Patients (n=25)
Investigator-assessed	
Best ORR, % (95% CI)	88 (69, 98)
Confirmed ORR, % (95% CI)	84 (63, 96)
Partial response, n (%)	21 (84)
Stable disease, n (%)	4 (16)
DCR, n (%)	25 (100)
BICR-assessed	
Confirmed ORR, % (95% CI)	80 (59, 93)



Despite enrolling a population with more than double the rate of baseline CNS metastases versus competitor datasets, enozertinib demonstrated a meaningfully higher best-in-class systemic response rate



Source: Ahn et al. ESMO (2026).
Note: Data as of September 4, 2026. BICR – blinded independent central review. INV – investigator. Investigator and BICR assessments per RECIST v1.1. Response-evaluable includes all patients with opportunity for two post-baseline systemic tumor assessments.

Enozertinib Achieved Deep ctDNA Molecular Responses in 1L EGFR Atypical NSCLC Patients with All Reductions Observed Early in Treatment

ctDNA Molecular Response Data



- Deep EGFR-mutant ctDNA reductions achieved in all evaluable patients (n=22) across diverse mutations
 - 100% of patients achieved MR90 ⁽¹⁾
 - 82% of patients achieved full clearance
- Phase 3 NSCLC trials have shown that EGFR-mutant ctDNA clearance associates with improved long-term survival outcomes ⁽²⁾

All patients had ≥90% reduction by C3D1, with ctDNA clearance observed in 82% of patients



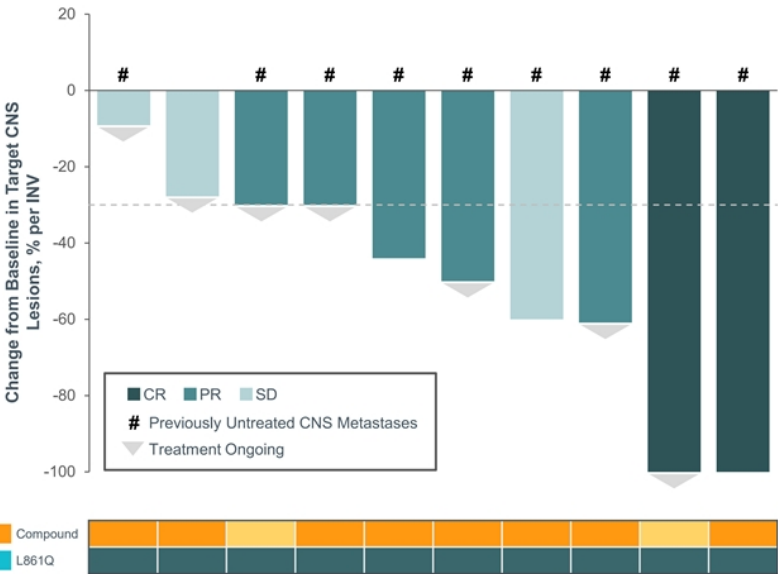
Source: Ahn et al. ESMO (2026).
Note: Data as of September 15, 2026. Evaluable includes all patients with EGFR mutation detected in plasma at baseline and opportunity for two post-baseline systemic tumor assessments. ctDNA assessed with Guardant Infinity Liquid assay. Clearance is defined as change from detected to undetected mutant EGFR in plasma after up to two treatment cycles and is shown as -100 on waterfall plot.
(1) MR90 defined as ≥90% EGFR-mutant ctDNA reduction. (2) Gray et al. Clin Cancer Res (2023).

Enozertinib Demonstrated Strong CNS Antitumor Activity in 1L EGFR Atypical NSCLC Patients Per Investigator Assessment...

Intracranial ORR in Patients with Measurable Target CNS Lesions Per Investigator Assessment

Intracranial Objective Response Rate	Response-Evaluable (n=10)
Best ORR, % (95% CI)	80 (44, 98)
Confirmed ORR, % (95% CI)	70 (35, 93)
Complete response, n (%)	2 (20)
Partial response, n (%)	5 (50)
Stable disease, n (%)	3 (30)
DCR, n (%)	10 (100)

- No new CNS lesions in patients with or without baseline CNS metastases



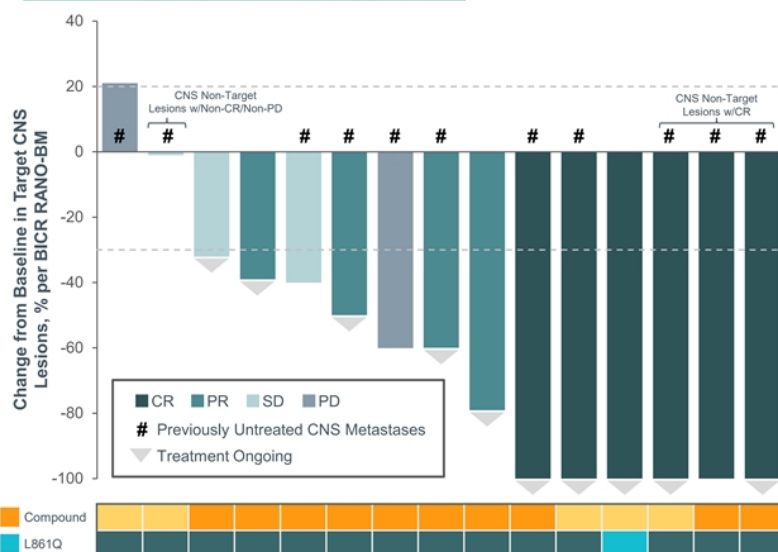
In the context of 90% of patients having no prior treatment for their CNS metastases, all patients achieved CNS tumor reductions

...and Enzertinib's CNS Antitumor Activity Was Equally Impressive Utilizing the More Stringent BICR RANO-BM Assessment Criteria

Intracranial ORR in Patients with CNS Lesions Per BICR RANO-BM Assessment

Intracranial Objective Response Rate	Response-Evaluable (n=15)
Confirmed ORR, % (95% CI)	67 (38, 88)
Complete response, n (%)	6 (40)
Partial response, n (%)	4 (27)
Stable disease, n (%) ⁽¹⁾	3 (20)
Progressive disease, n (%)	2 (13)
DCR, n (%)	13 (87)

- **Six complete responses**, including in three patients with non-measurable CNS disease



CNS tumor reduction observed in nearly all patients, including in patients with previously untreated CNS metastases; Six complete responses were observed, including in three patients with non-measurable CNS disease

Enozertinib Demonstrated Early Tumor Responses in 1L EGFR Atypical NSCLC Patients, with Most Remaining on Treatment

Time on Treatment



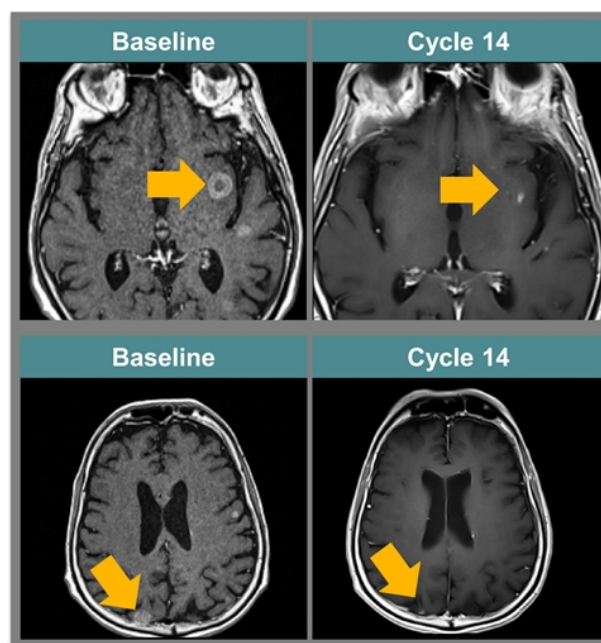
The Kaplan-Meier 6-month landmark PFS is 88%; follow-up is ongoing with the majority of patients continuing on treatment



Source: Ahn et al. ESMO (2026).
 Note: Data as of September 4, 2026.
 (1) Patient discontinued due to unrelated adverse event.

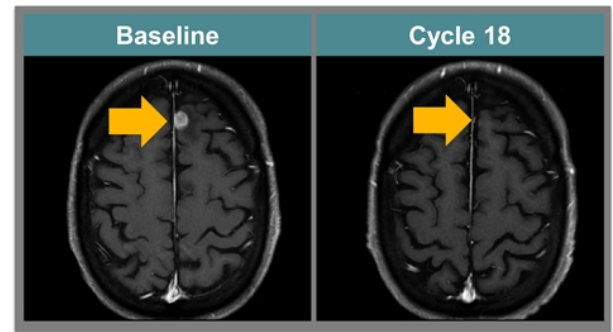
Patient Vignette 1: Complete Intracranial Response in Patient with Treatment-Naïve EGFR Atypical Mutation and Previously Untreated CNS Metastases

- **Patient:** 59-year-old male with G719C-S768I mutation
- **Baseline CNS Metastases:** 3 target lesions and 2 non-target lesions, all previously untreated
- **Enozertinib Dose:** 80 mg oral, once-daily
- **Systemic Response:** Confirmed partial response (-81%) after Cycle 4
- **CNS Response:** Partial response after Cycle 3 and complete response after Cycle 14
- **Treatment-Related Adverse Events:** Grade 2 dermatitis acneiform (resolved), Grade 1 diarrhea (resolved), and Grade 1 dry skin
- **Duration of Treatment:** Cycle 18 (ongoing)



Patient Vignette 2: Complete Intracranial Response in Patient with Treatment-Naïve EGFR Atypical Mutation and Previously Untreated CNS Metastases

- **Patient:** 67-year-old male with G719A mutation
- **Baseline CNS Metastases:** 1 target lesion, previously untreated
- **Enozertinib Dose:** 80 mg oral, once-daily
- **Systemic Response:** Partial response (~60%) after Cycle 1
- **CNS Response:** Partial response after Cycle 1; complete response after Cycle 4
- **Treatment-Related Adverse Events:** Grade 1 acneiform rash
- **Duration of Treatment:** Cycle 18 (ongoing)





Next Steps in 1L EGFR Atypical

Enozertinib Demonstrated Higher Systemic and CNS ORRs than Competitor Programs, Despite Enrolling Patients with Significantly More Challenging Disease

Key Benchmarks for 1L NSCLC with EGFR Atypical Mutations

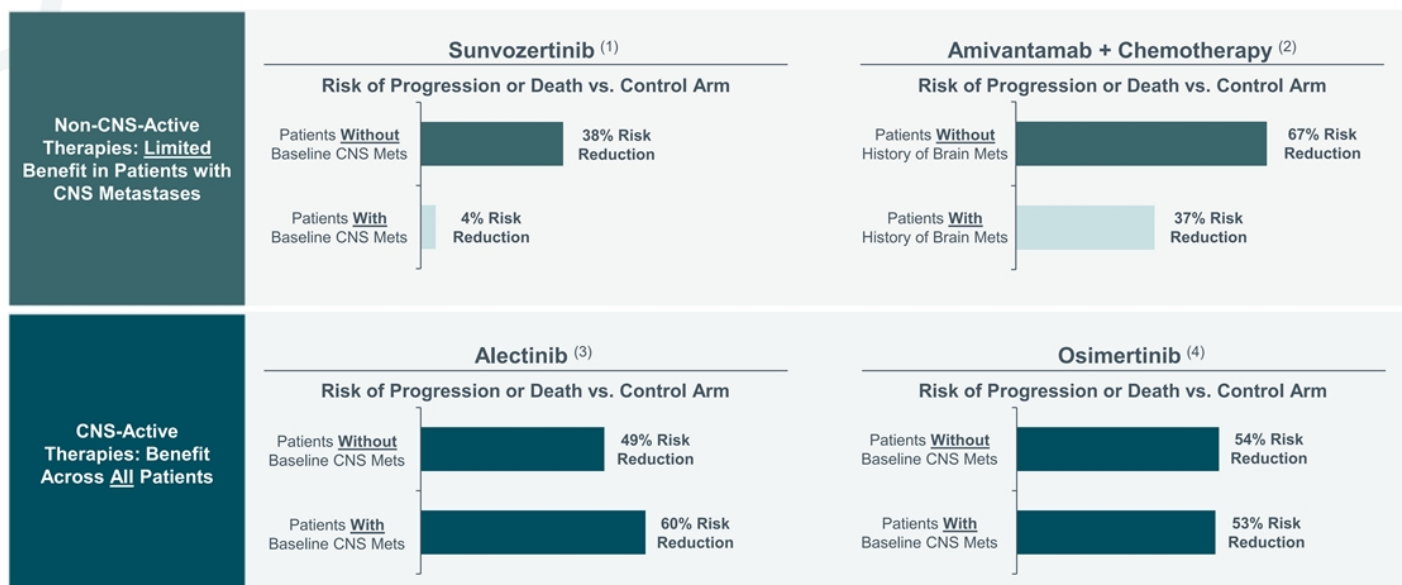
	Afatinib (Approved)	Osimertinib (NCCN Guidelines)	Investigational Therapies (Late-Stage)	Enozertinib
ENROLLMENT				
Mutations included	Only S768I, L861Q, G719X	Only S768I, L861Q, G719X	PACC +/- L861Q	PACC + L861Q
% Baseline CNS mets	NR	25%	≤32%	65%
Untreated CNS mets allowed	No	Yes	Mixed	Yes
CLINICAL ACTIVITY				
Systemic ORR	66%	50%	57% to 68%	84%^{INV} / 80%^{BICR}
CNS ORR	NR	40%	NR to 29%	70%^{INV} / 67%^{BICR RANO-BM}
6-month PFS	~65%	~65%	~75%	88%
SAFETY				
Significant off-target toxicities	Yes	Yes	Yes	None
Discontinuations due to TRAE	14%	13%	0% to 24%	0%

Enozertinib demonstrated potential best-in-class systemic and CNS response rates in a population with more than double the rate of baseline CNS disease as competitor datasets



Source: Giotrif (afatinib) label, 14% discontinuation rate per LUX-Lung 3; Tagrisso (osimertinib) label, 13% discontinuation rate per FLAURA; Cho et al. (2020); Yang et al. (2015); Le et al. WCLC (2025); Neal et al. ASCO (2026); Le et al. Cancer Cell (2026); Ahn et al. ESMO (2026).
Note: Investigational therapies include amivantamab + lazertinib and firmonertinib.

Given the High Rate of CNS Metastases in NSCLC Patients with Oncogenic Drivers, CNS-Active Agents Benefit All Patients Regardless of Baseline CNS Disease



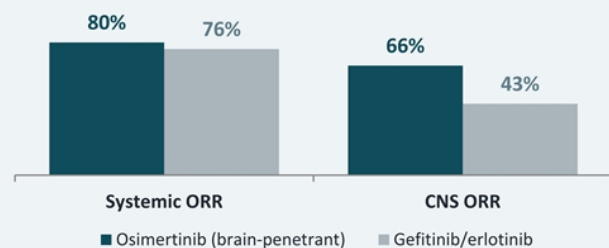
An effective CNS-penetrant therapy can potentially drive long-term outcomes and extend survival by treating existing CNS metastases and preventing the development of new CNS lesions

Targeted Therapies with Robust CNS Activity Have Been Associated with Prolonged Clinical Benefit in NSCLC Patients

Importance of CNS Activity with Targeted Therapies for NSCLC

Osimertinib vs gefitinib/erlotinib

FLAURA Phase 3 Trial | 1L EGFR-mutant NSCLC

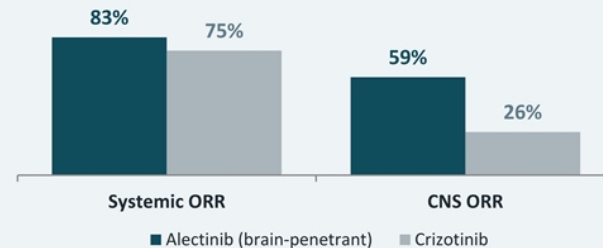


Median PFS

18.9 months vs **10.2** months **1.9_x**

Alectinib vs crizotinib

ALEX Phase 3 Trial | 1L ALK-positive NSCLC



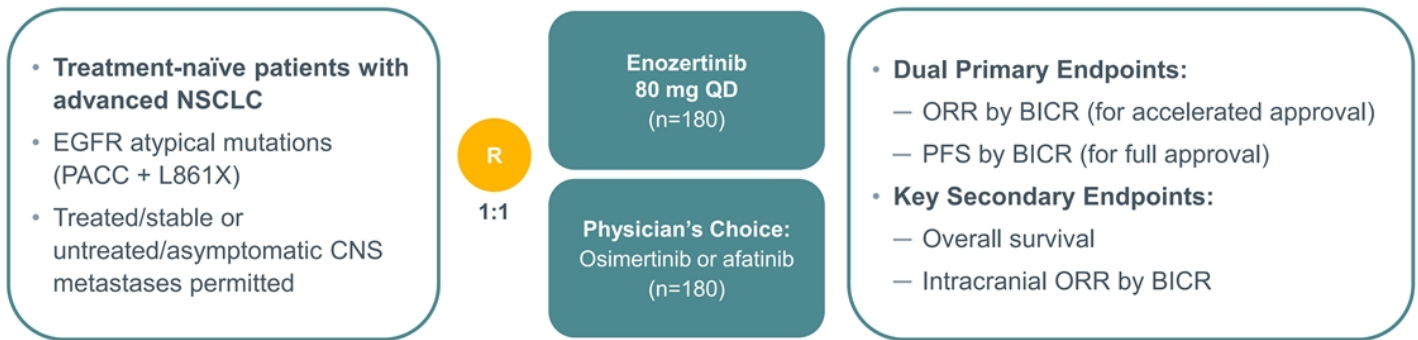
Median PFS

34.8 months vs **10.9** months **3.2_x**

CNS-active agents demonstrate that modestly improved systemic ORR and significantly improved CNS ORR are associated with dramatically longer progression-free survival in Phase 3 head-to-head trials

End-of-Phase 1 FDA Interactions Completed to Support Redwood-1, a Global Phase 3 Trial of Enozertinib in 1L NSCLC Patients with EGFR Atypical Mutations

Phase 3 Trial of Enozertinib in 1L NSCLC with EGFR Atypical Mutations



Following EOP1 FDA interactions, alignment received on:

✓ RP3D

✓ Patient population

✓ Endpoints

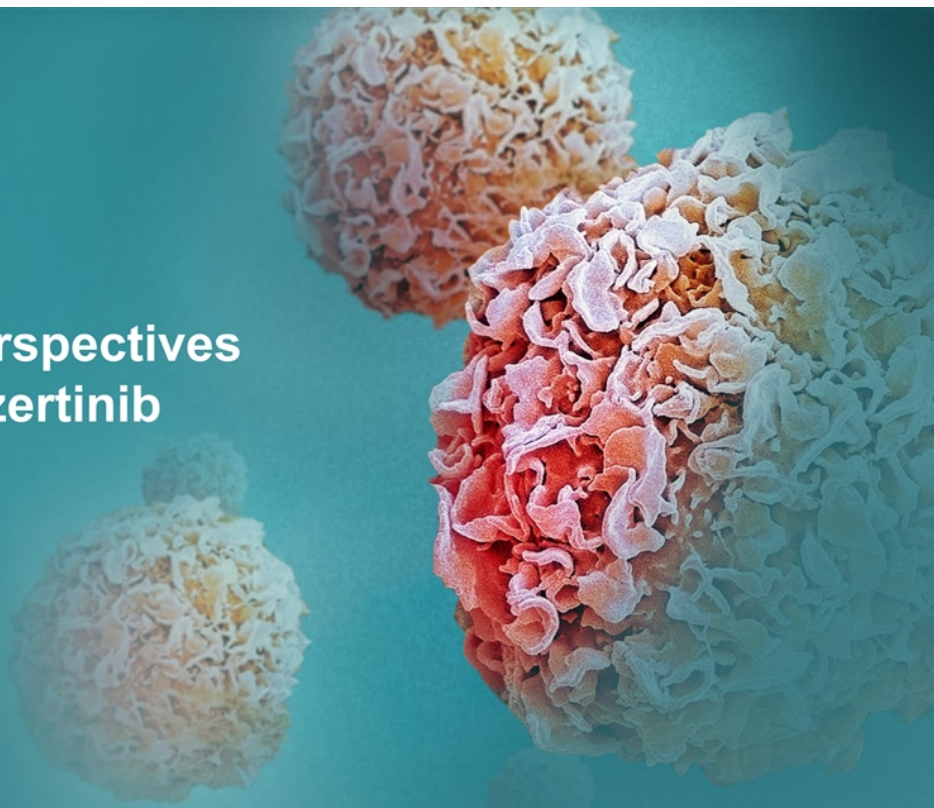
✓ Control arm

✓ Statistical methodology

ORIC has completed End-of-Phase 1 FDA interactions to support the Redwood-1 Phase 3 trial, expected to initiate in 1H 2027



KOL Perspectives on Enozertinib



KOL Perspectives on Enozertinib

Discussion with Dr. Joshua Sabari, Enozertinib Trial Investigator

Guest KOL Biography

Joshua Sabari, MD

- Thoracic medical oncologist at NYU Langone Health and Assistant Professor of Medicine at NYU Grossman
- Investigator across multiple clinical trials evaluating targeted therapies and immuno-therapies
- Author or co-author on over 70 peer-reviewed publications
- After receiving his MD from Rutgers, Dr. Sabari completed his Internal Medicine Residency at Montefiore Medical Center, and a Medical Oncology Fellowship at Memorial Sloan Kettering Cancer Center



Topics of Discussion

- Unmet need in the EGFR atypical landscape
- Experience with enozertinib and commentary on Phase 1b data
- Enozertinib in the context of the current development landscape
- Next steps for enozertinib development



Commercial Potential

Enozertinib Is Initially Pursuing a Significant Addressable Market in 1L EGFR Atypical NSCLC

Enozertinib Total Addressable Market in 1L EGFR Atypical NSCLC



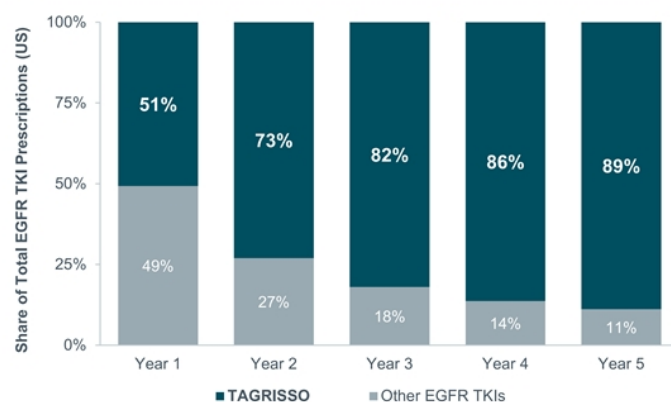
1L EGFR atypical NSCLC is an attractive market opportunity for a CNS-penetrant agent that extends durability; Enozertinib is positioned to potentially capture substantial market share with a best-in-class profile

Best-in-Class Targeted Therapies for NSCLC Rapidly Capture Majority Share

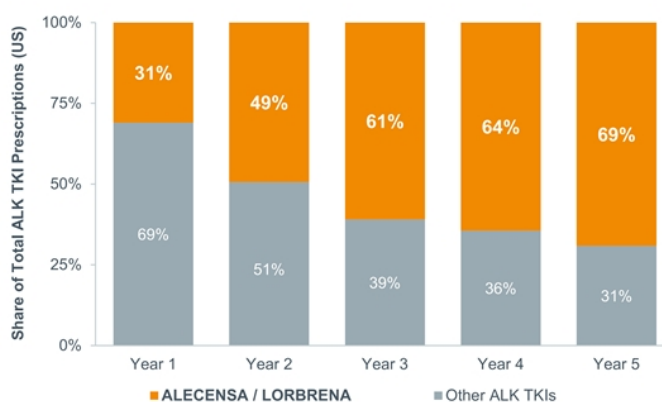
Case Study: Market Share of Best-in-Class Targeted Therapies for NSCLC



- Best in class systemic ORR, CNS activity and PFS
- 4th EGFR inhibitor to market, >12 years after Iressa (gefitinib)



- Best in class systemic ORR, CNS activity and PFS
- 3rd and 5th ALK inhibitors to market, >4 years after Xalkori (crizotinib)



Best-in-class therapies with strong CNS activity rapidly take the majority market share of their class



Source: Symphony Health US prescription data.

Note: Year 1 represents year of launch in 1L NSCLC for Tagrisso (2018) and Alecensa (2017). Other EGFR TKIs includes gefitinib, erlotinib, afatinib and dacomitinib. Other ALK TKIs include crizotinib, ceritinib and brigatinib. TKI – tyrosine kinase inhibitor.

Independent Physician Market Research Supports Enozertinib Having Best-In-Class Potential in 1L EGFR Atypical NSCLC

Key Insights from Independent Market Research Testing Blinded Target Product Profiles (TPPs)

Overview of US Prescriber Survey

Oncologists (n=75) surveyed across academic and community settings were shown two blinded TPPs:

	Product X (Next-Gen EGFR TKI)	Product Y (enozertinib)
Efficacy	Competitor EGFR atypical data	Improved systemic and CNS efficacy
Safety		No significant off-target and similar EGFRwt toxicity

Key Takeaways

Surveyed physicians estimated that Product Y would capture **~60% share of 1L EGFR atypical market**

“... **80% of patients responding**, very high percent of those **with CNS** ... **This is a very promising therapy** ...”

“... **This efficacy data is really robust** ... effective in the brain in the same way that it's effective extracranially ...”

“... **Treating CNS metastases matter, and preventing development of CNS metastases is also important** ... Quite a few patients will develop CNS metastases throughout the course of their disease ...”

Market research indicates that a therapy consistent with enozertinib's target product profile may achieve substantial share



Source: ORIC market research 2026.
Note: Product Y reflects the tested target product profile for enozertinib.



Executive Summary and Next Steps

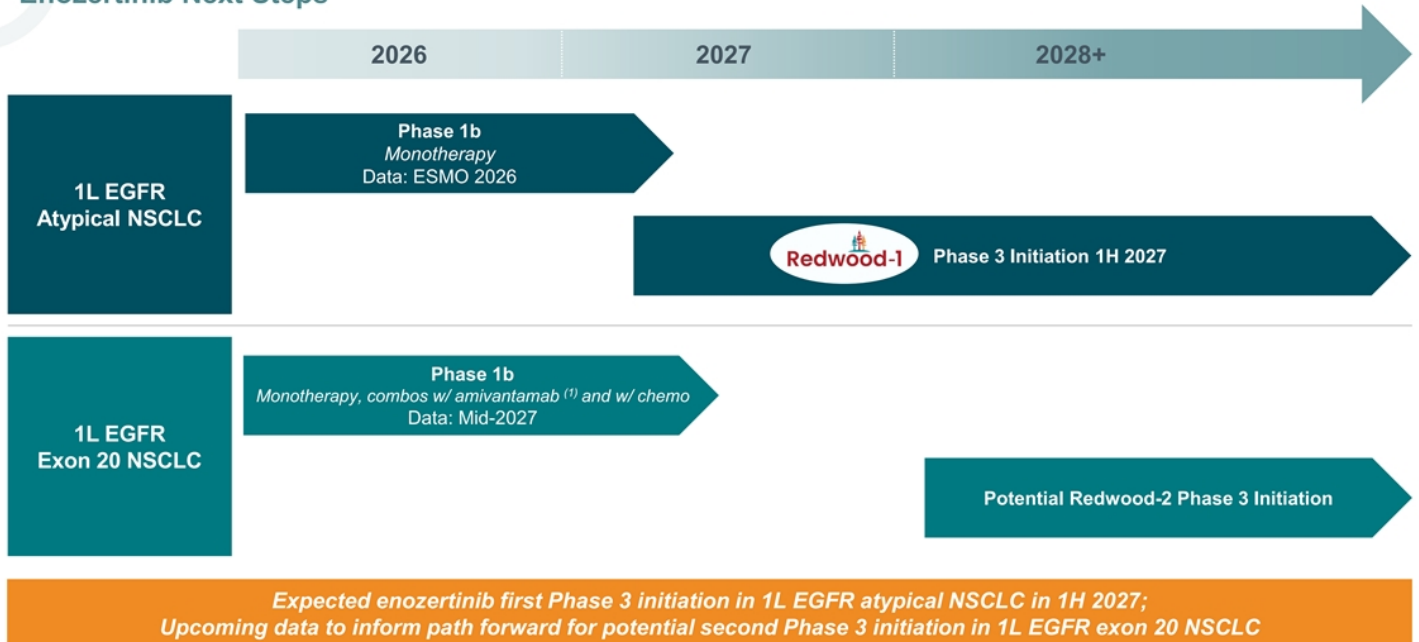
Enozertinib Establishes Potential Best-in-Class Profile in 1L EGFR Atypical NSCLC, with Data Supporting Rapid Advancement to Phase 3

Executive Summary

- 1L EGFR Atypical NSCLC is a **>\$2.5bn market opportunity in the US alone** and lacks a best-in-class therapy with meaningful systemic efficacy, compelling CNS activity, and favorable tolerability
- In a global 1L EGFR Atypical population with **over double the rate of baseline CNS disease** as competitor datasets, including untreated CNS metastases, enozertinib raises the efficacy benchmarks by achieving:
 - **84% confirmed systemic ORR**
 - **70% confirmed CNS ORR**, with **multiple complete responses**
 - **88% 6-month landmark PFS**
- Competitive safety profile: **no significant off-target toxicity** and **no treatment-related discontinuations**
- ORIC plans to **initiate Redwood-1, a global Phase 3 trial** in 1L EGFR Atypical NSCLC, in 1H 2027

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

Enozertinib Next Steps





Thank You

