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An Ongoing Phase 1–2a Study of EO1001, an Oral Brain-Penetrant Pan-ErbB Inhibitor, in Patients with Advanced ErbB-Driven Solid Tumors Including CNS Disease

Sophia Frentzas[1], Malaka Ameratunga[2,3], Amy L. Body[1], Daphne Day[1], Richard Kelly[2], Penny Macquire[1], Yasmin Malik[2], Lauren Murphy[1], Jeremy Neeman[1], Siang Tan[1], Jeffrey A. Bacha[5], Sarath Kanekal[5], Mike T. Li[5], Ian Nisbet[4], Neil Sankar[5], Kathy Skoff[4], Dennis M. Brown[5]

[1]Monash Health, Melbourne, Australia; [2]The Alfred, Melbourne, Australia; [3]School of Translational Medicine, Monash University, Melbourne, Australia; [4]Senz Oncology Pty Ltd; [5]Edison Oncology Holding Corp.

BACKGROUND

Central nervous system (CNS) metastases and primary brain tumors remain a major cause of morbidity and mortality in patients with ErbB-driven malignancies, particularly as improved systemic therapies prolong survival. Aberrations in the ErbB family of receptor tyrosine kinases—including EGFR, HER2, and HER4—are frequently associated with CNS progression, therapeutic resistance, and poor outcomes across multiple tumor types. In glioblastoma and other CNS malignancies, specific EGFR extracellular domain (ECD) alterations, including EGFRvIII and recurrent ECD missense variants, have been previously reported to promote ligand-independent signaling, invasive tumor biology, and resistance to currently available EGFR-targeted therapies.

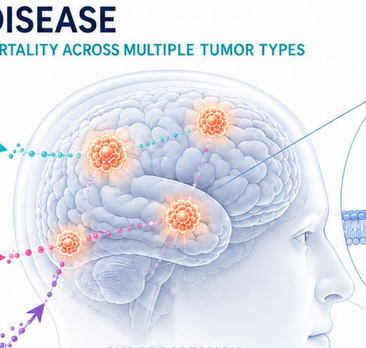
ErbB-DRIVEN CNS DISEASE

A MAJOR DRIVER OF MORBIDITY AND MORTALITY ACROSS MULTIPLE TUMOR TYPES

LUNG CANCER
Up to 30–40% of EGFR-mutant NSCLC patients develop brain metastases[1]

BREAST CANCER
Up to 30–40% of HER2+ breast cancers develop brain metastases[2]

GBM & OTHER CNS MALIGNANCIES
EGFR alterations (EGFRvIII, ECD missense variants) are common and drive aggressive, therapy-resistant disease[3]



DRIVER ALTERATIONS IN CNS TUMORS

EGFRvIII	Ligand-independent signaling and invasive biology
ECD missense variants	Therapeutic resistance and poor outcomes

UNMET NEED:
CNS metastases and primary brain tumors remain a major cause of morbidity and mortality in ErbB-driven malignancies.

~30–40%
Brain metastases in EGFR-mutant NSCLC and HER2+ breast cancer[1,2]

EGFR alterations (EGFRvIII, ECD variants) are frequent in GBM and other CNS tumors[3]

Current EGFR therapies have limited CNS penetration and durable responses

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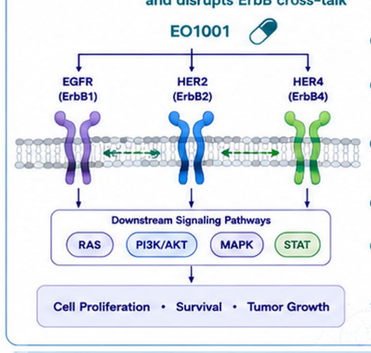
EO1001: A next-generation CNS-penetrant panErbB inhibitor designed to overcome treatment resistance

POTENT, SELECTIVE, AND CNS-PENETRANT PAN-ErbB INHIBITOR

EO1001 potently inhibits EGFR, HER2, and HER4 and disrupts ErbB cross-talk

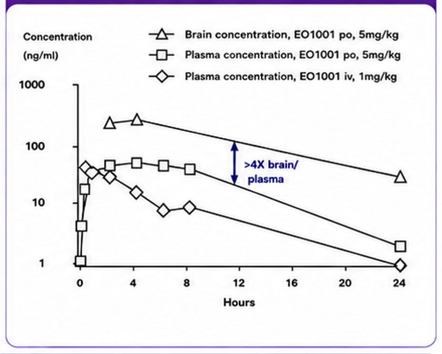


- Irreversible pan-ErbB inhibitor
- Potent inhibition of activating mutations in EGFR, HER2, and HER4
- Blocks ErbB receptor cross-talk and downstream signaling
- Active against ErbB ECD mutants
- Designed for enhanced CNS penetration

EO1001 exhibits activity vs approved EGFR-TKIs in multiple *in vivo* models with no observed toxicity at therapeutic dose

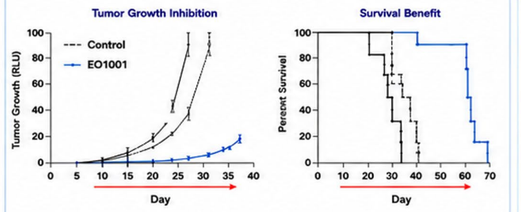
Model	ErbB Status	Control/ Reference	Outcome
H1975 NCSLC FLANK	EGFR T790M+	Untreated; erlotinib; afatinib	Superior activity vs. erlotinib, equivalent vs. afatinib
N87 Gastric FLANK	HER2+	Untreated; lapatinib	Superior activity vs lapatinib
GBM39 Intracranial	EGFRvIII	Untreated	p>.001 survival vs control
GBM12 Intracranial	EGFR+	Untreated; erlotinib; lapatinib	p>.0001 survival vs control at 10/mg/kg Superior activity compared to lapatinib
GBM12 Intracranial	EGFR+	Untreated; lapatinib	p>.001 survival EO1001 vs lapatinib
GBM12 Intracranial	EGFR+	Untreated; erlotinib	p>.05 survival E01001 vs. erlotinib
U87 Intracranial	EGFRvIII transfected	Untreated; erlotinib	Superior activity compared to erlotinib

EO1001 achieves rapid CNS penetration and sustained tumor exposure following oral administration in vivo



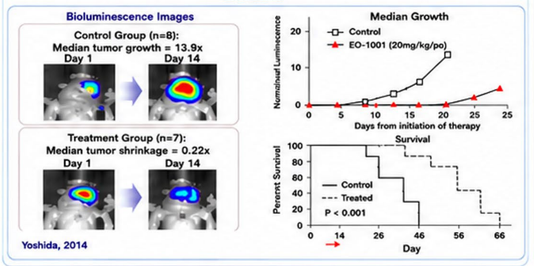
ANTITUMOR ACTIVITY IN PRECLINICAL MODELS

EGFR+



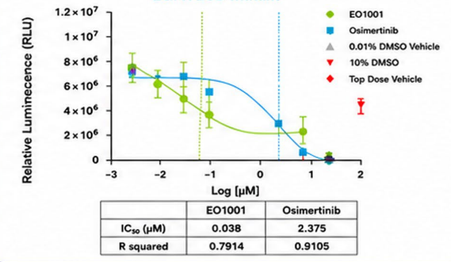
EO1001 significantly inhibited intracranial GBM12 (EGFR+) tumor growth and prolonged survival compared with both untreated controls and lapatinib-treated animals.

EGFRvIII



EO1001 treatment inhibited intracranial tumor growth and significantly prolonged survival in orthotopic EGFRvIII-driven glioblastoma xenograft models compared with vehicle-treated controls.

EGFR ECD Mutant



	EO1001	Osimertinib
IC_{50} (μM)	0.038	2.375
R squared	0.7914	0.9105

EO1001 demonstrates greater potency than osimertinib at Day 5 in an EGFR ECD mutant (R108K) GBM tumor model

KEY TAKEAWAYS

- Potent, irreversible inhibition of EGFR, HER2, and HER4 with activity against activating mutations and ECD mutants
- Designed for CNS penetration with rapid brain exposure and sustained target engagement
- Demonstrates robust antitumor activity and survival benefit in preclinical models
- Supports development in patients with ErbB-driven solid tumors, including CNS disease

EO1001 Phase 1–2a Study

First-in-Human, Multicenter, Open-Label Study of Once-Daily Oral EO1001

EDISON ONCOLOGY | SenzOncology development that makes sense

STUDY DESIGN

PHASE 1 DOSE ESCALATION
Accelerated titration design
↓
Transition to standard 3+3 schema following ≥Grade 2 treatment-related toxicity

PHASE 2 EXPANSION
Enrolling patients at or below the recommended Phase 2 dose (RP2D)

DAILY ORAL EO1001
Once daily dosing in 28-day cycles

Following initial single-dose pharmacokinetic assessment

ELIGIBLE PATIENTS

- Adults with advanced or metastatic ErbB–expressing solid tumors
- Progressed following standard therapy
- Patients with treated or untreated CNS disease are eligible

STUDY LOCATIONS

Monash Health and The Alfred
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Monash Health | theAlfred

STUDY OBJECTIVES

PRIMARY OBJECTIVES
- Evaluate safety and tolerability
- Determine RP2D

SECONDARY OBJECTIVES
- Characterize pharmacokinetic profile
- Assess preliminary antitumor activity using RECIST v1.1 and/or RANO criteria, as appropriate

EXPLORATORY OBJECTIVES
- Evaluate pharmacodynamic and molecular biomarkers in available tissue
- Optional cerebrospinal fluid sampling to further assess CNS exposure and pathway modulation

This Phase 1–2a study is evaluating the safety, pharmacokinetics, and preliminary antitumor activity of EO1001 in patients with advanced ErbB-driven solid tumors, including those with CNS involvement.

CURRENT STATUS

- Dose escalation completed across multiple dose levels
- Phase 2 expansion enrollment ongoing
- Active evaluation of safety, PK, and CNS antitumor activity at biologically active dose levels

Clinical Trial Identifier: ANZCTR ACTRN12620000583943

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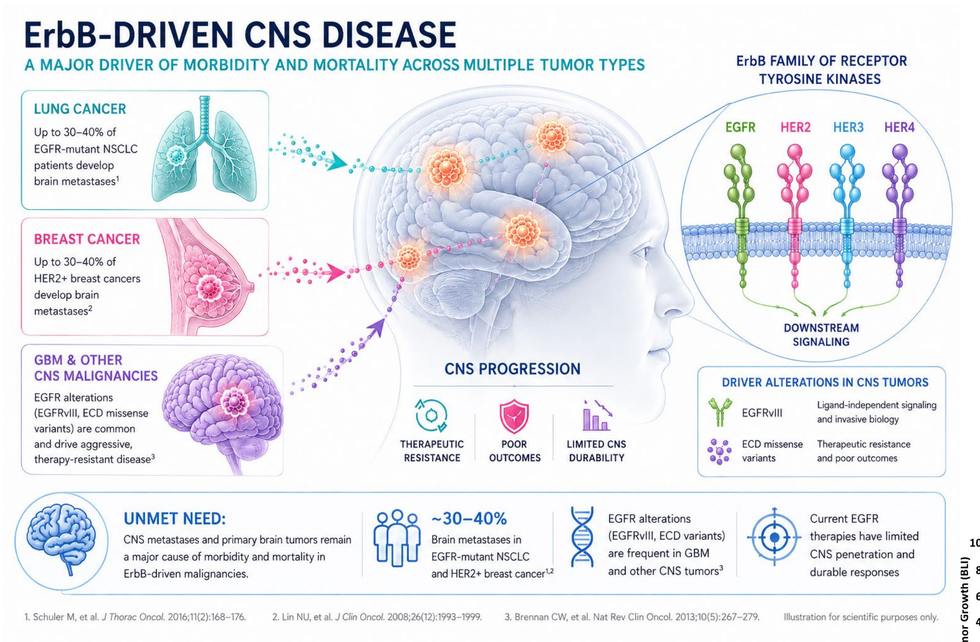
EO1001 is a novel, oral, irreversible pan-ErbB inhibitor designed to achieve sustained CNS exposure and broad ErbB pathway inhibition, demonstrating potent activity in intracranial xenograft models of EGFR-altered primary brain tumors —including EGFR+ (GBM12) and EGFRvIII-amplified/high-expressing (GBM39, U87) glioblastoma models — as well as across distinct EGFR extracellular domain (ECD) mutation classes, with greater or more sustained activity relative to FDA-approved ErbB inhibitors in preclinical studies.



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N87 Gastric FLANK	HER2+	28 days	15 & 30	Untreated; lapatinib	Superior activity vs lapatinib
GBM39 Intracranial	EGFRvIII	14 days	20	Untreated	p>.001 survival vs control
GBM12 Intracranial	EGFR+	7 days	20 & 10	Untreated; erlotinib; lapatinib	p>.0001 survival vs control at 10/mg/kg Superior activity compared to lapatinib
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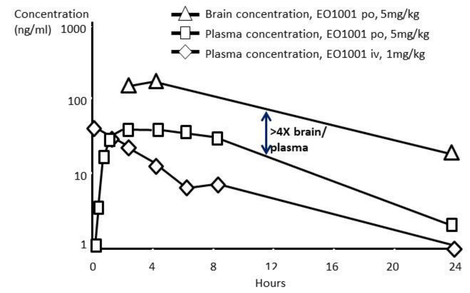
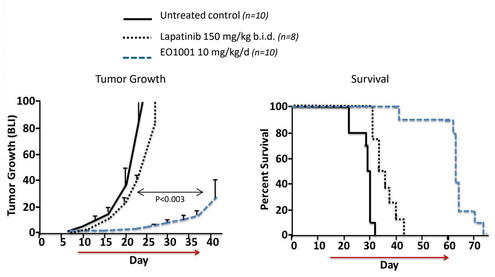
EO1001 achieves rapid CNS penetration and sustained tumor exposure following oral administration in vivo.



EGFR+



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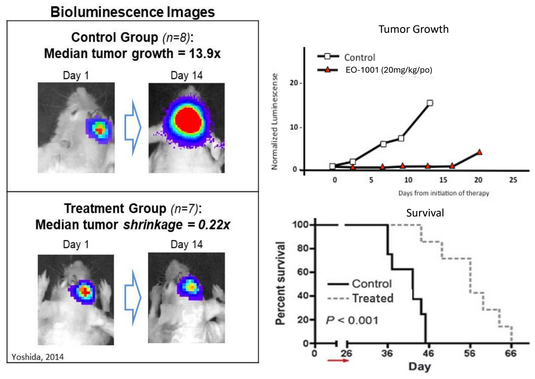
EGFRVIII



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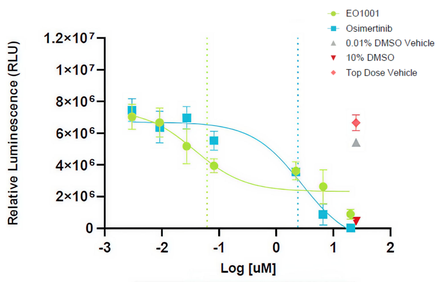

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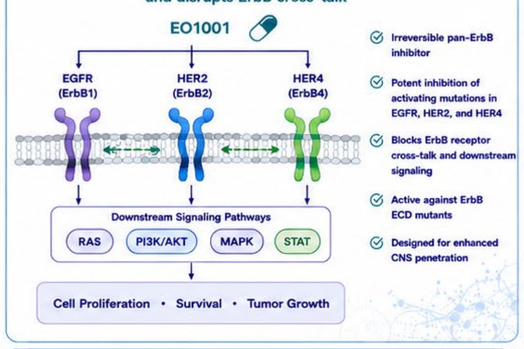

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PC-9/GR NSCLC	EGFR Exon 19 del (Osimertinib-resistant)	Oxnard GR, et al. JCI Insight. 2017;2:e88947.	TGI = 86%	Osimertinib TGI = -17%
WZ4002 NSCLC	EGFR L858R/T790M/C797S	Huang SY, et al. Clin Cancer Res. 2018;24: 1898–1907.	TGI = 90%	Osimertinib TGI = -14%
U87MGvIII GBM	EGFRvIII	Hegi ME, et al. Clin Cancer Res. 2012;18: 487–496.	TGI = 88%	Erlotinib TGI = -6%
HCC827 NSCLC	EGFR Exon 19 del	Yun CH, et al. Mol Cancer Ther. 2007;6: 3113–3121.	TGI = 93%	Erlotinib TGI = -9%
A431 Xenograft	EGFR Wild Type (Overexpression)	Gazdar AF, et al. Cancer Res. 1980;40: 1731–1737.	TGI = 85%	Gefitinib TGI = -12%
NCI-H1975 Brain Metastasis	EGFR L858R/T790M	Lockman PR, et al. Clin Cancer Res. 2010;16: 5144–5152.	TGI = 91%	Osimertinib TGI = 11%

TGI – Tumor Growth Inhibition

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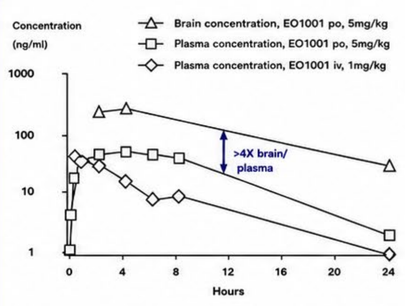
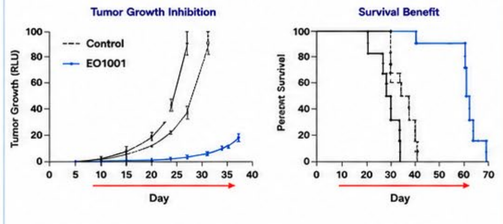
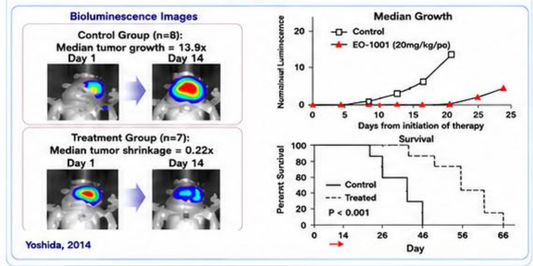


EGFR+



EGFRvIII



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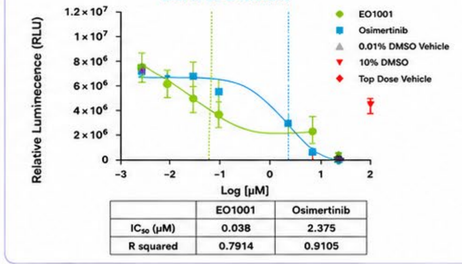

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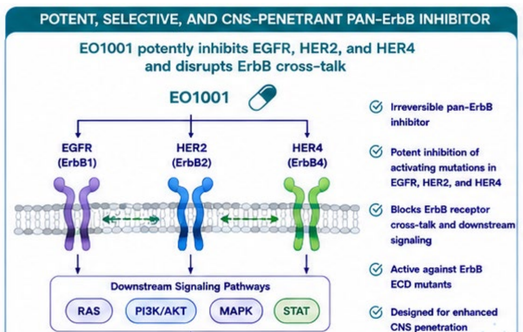

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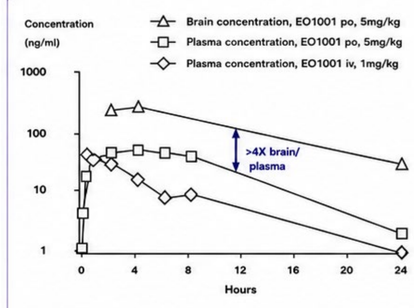

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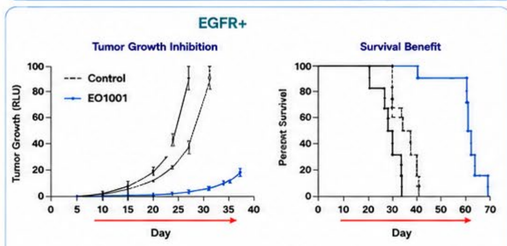

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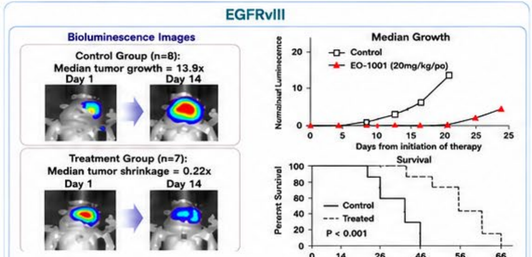

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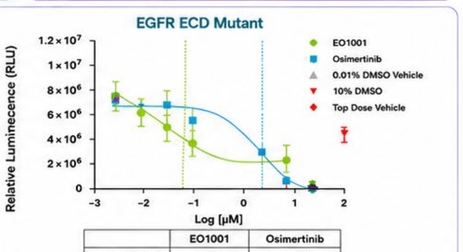

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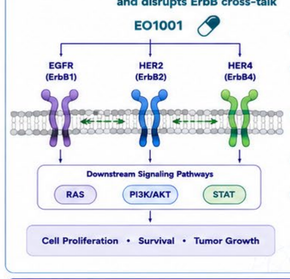

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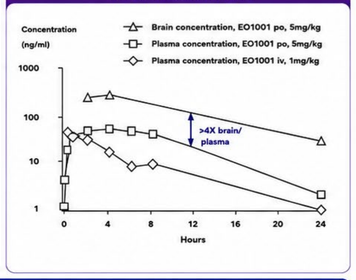
U87MGvIII GBM	EGFRvIII	Hegi ME, et al. Clin Cancer Res. 2012;18: 487–496.	TGI = 88%	Erlotinib TGI = -6%
HCC827 NSCLC	EGFR Exon 19 del	Yun CH, et al. Mol Cancer Ther. 2007;6: 3113–3121.	TGI = 93%	Erlotinib TGI = -9%
A431 Xenograft	EGFR Wild Type (Overexpression)	Gazdar AF, et al. Cancer Res. 1980;40: 1731–1737.	TGI = 85%	Gefitinib TGI = -12%
NCI-H1975 Brain Metastasis	EGFR L858R/T790M	Lockman PR, et al. Clin Cancer Res. 2010;16: 5144–5152.	TGI = 91%	Osimertinib TGI = 11%

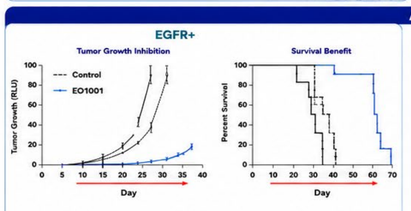
TGI = Tumor Growth Inhibition

EO1001 achieves rapid CNS penetration and sustained tumor exposure following oral administration in vivo

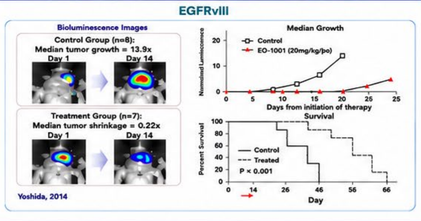


ANTITUMOR ACTIVITY IN PRECLINICAL MODELS

EGFR+

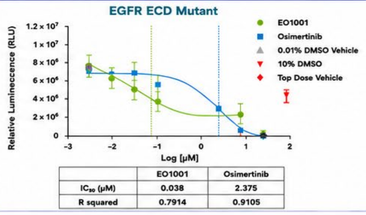


EGFRvIII



Yoshida, 2014

EGFR ECD Mutant



	EO1001	Osimertinib
IC_{50} (μM)	0.038	2.375
R squared	0.7914	0.9105

KEY TAKEAWAYS

- Potent, irreversible inhibition of EGFR, HER2, and HER4 with activity against activating mutations and ECD mutants
- Designed for CNS penetration with rapid brain exposure and sustained target engagement
- Demonstrates robust antitumor activity and survival benefit in preclinical models
- Supports development in patients with ErbB-driven solid tumors, including CNS disease

EO1001: A next-generation CNS-penetrant panErbB inhibitor designed to overcome treatment resistance