EGFRChannel | OncLive

EGFR-DRIVEN SOLID TUMORS · PRECLINICAL DATA

A new way to target *EGFR*—without the usual limits.

EPI-326 degrades *EGFR* across mutation types, spares healthy tissue, and shows activity where current therapies fail.

PROBLEM 1

Current agents are mutation-dependent.

EPI-326 is mutation-independent and active across *EGFR*-mutant and wild-type tumors.

PROBLEM 2

Resistance mechanisms limit single-agent activity.

Receptor degradation removes downstream signaling entirely, generating durable monotherapy activity.

PROBLEM 3

Current agents can't distinguish tumor *EGFR* from healthy-tissue *EGFR*.

EPI-326 uses tissue-selective degrader receptors to spare normal tissue and minimize off-target toxicity.

Preclinical efficacy across tumor types

In cell line–derived and patient-derived xenograft models, EPI-326 demonstrated robust tumor regressions across *EGFR*-mutant and wild-type settings, including disease states where standard therapies had already failed.

90%

COMPLETE RESPONSE RATE IN AN *EGFR*-MUTANT NSCLC MODEL

First-in-human phase 1 trial now enrolling

The first patient has already been dosed. Here's what the trial looks like.

Trial ID	NCT07462377
Phase	Phase 1, dose escalation
Design	Open-label, multicenter
Treatment	EPI-326 monotherapy
Tumor types	*EGFR*-mutated NSCLC and HNSCC
Disease stage	Locally advanced or metastatic
Expected enrollment	110 patients
Active sites	5 centers in the United States
Status	Enrolling – first patient dosed

NSCLC

- Active in exon 19 deletions
- Active in exon 21 L858R/T790M mutations
- Active in exon 20 C797S mutations

HNSCC

- Active in exon 19 deletions
- Active in exon 21 L858R/T790M mutations
- Active in exon 20 C797S mutations

Colorectal cancer (CRC)

- Active in wild-type *EGFR* models
- Superior antitumor activity vs amivantamab in PDX models
- Synergistic activity with KRAS inhibitors (eg, sotorasib)

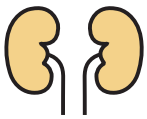
Comparators included cetuximab (Erbitux) and amivantamab-vmjw (Rybrevant). Both are standard *EGFR*-blocking antibodies.

Eligible patients must be

Age 18 or older

Life expectancy >12 weeks

ECOG performance status 0–2



Adequate organ function

EXCLUDED: PATIENTS WITH SYMPTOMATIC BRAIN METASTASES

Trial is assessing:

- Safety and tolerability
- Pharmacokinetics and pharmacodynamics
- Preliminary antitumor activity (ORR and duration of response)

Takeaway

EPI-326 is one of the first agents designed to degrade *EGFR* rather than simply block it—and to do so regardless of mutation status. If early clinical signals match the preclinical data, it could expand treatment options across NSCLC, HNSCC, and CRC, including in patients who have already progressed on osimertinib or cetuximab.

David R. Spigel, MD, Chief Scientific Officer, Sarah Cannon Research Institute · 2026 AACR Annual Meeting, San Diego