A Phase 1/2 Study of VRN110755 in Patients with Epidermal Growth Factor Receptor (EGFR) Mutant Non-small Cell Lung Cancer (NSCLC)

#LB-A006

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BACKGROUND

- Despite meaningful advances with EGFR TKIs (e.g., osimertinib), most patients with EGFR-mutant NSCLC ultimately develop acquired resistance—frequently via EGFR C797S—and CNS progression remains a major clinical limitation, underscoring a continued unmet need.
- VRN110755 is a brain-penetrant, highly potent, and mutant-selective EGFR inhibitor designed to spare wild-type EGFR while retaining activity across common drivers (Del19, L858R), C797S-mediated resistance (Del19/C797S, L858R/C797S), and several uncommon variants.
- In preclinical models, VRN11 demonstrated sub-nanomolar potency against key mutant EGFR targets, robust intracranial exposure, and antitumor activity—including in intracranial xenografts—while showing marked selectivity over EGFR wild type.
- The ongoing Phase 1, multicenter, open-label study evaluates VRN110755 as once-daily once-daily oral monotherapy using a standard 3+3 dose-escalation followed by global expansion cohorts.
- Pharmacodynamic assessments incorporate serial liquid-biopsy ctDNA to track EGFR driver and resistance allele dynamics and explore exposure-response and mechanism-of-resistance signals alongside clinical efficacy
- As of the draft TIP poster cut, sequential cohort enrollment through higher dose levels has progressed without dose-limiting toxicities at the reported tiers, supporting continued escalation and backfill; overall, safety has been monitorable with predominantly low-grade, on-mechanism events to date.
- Collectively, the preclinical profile (mutant selectivity, CNS penetration) and emerging clinical tolerability/PD readouts provide the rationale to advance VRN11 into dose expansion and future combination strategies in EGFR-mutant NSCLC with resistance and/or CNS involvement.

ELIGIBILITY CRITERIA

Key Inclusion Criteria

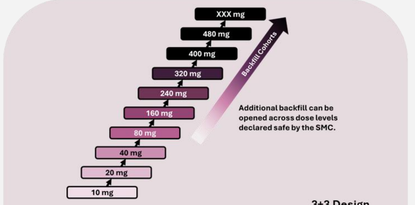
- Age ≥18 years
- Diagnosis of advanced (Stage IIIB/IV or recurrent) NSCLC, harboring EGFR mutation
- Measurable disease per RECIST v1.1
- Prior EGFR TKI treatment with disease progression
- ECOG PS 0-1

Key Exclusion Criteria

- CNS metastases or spinal cord compression that is associated with progressive neurological symptoms or requires increasing does of corticosteroids
- History of interstitial lung disease or drug or radiation induced pneumonitis, Grade ≥2 or requiring steroid treatment
- Have a documented additional validated targetable oncogenic driver mutation or alteration

STUDY DESIGN

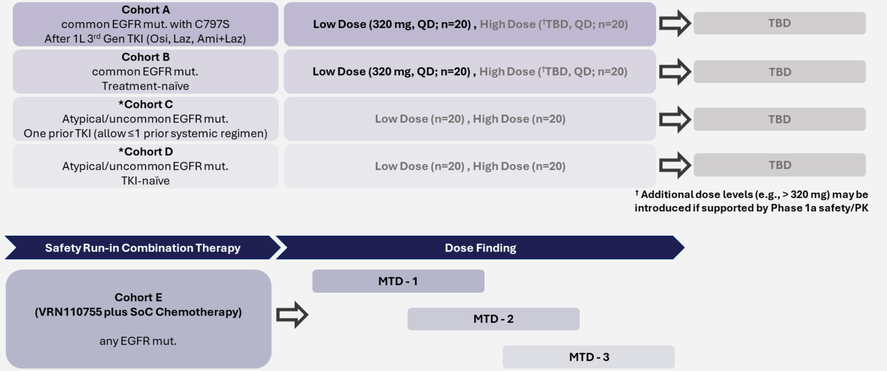
Phase 1a



3+3 Design

Dose Levels	Number of Patients Enrolled
Dose level 1 / 10mg QD	3
Dose level 2 / 20 mg QD	4
Dose level 3 / 40mg QD	3
Dose level 4 / 80mg QD	12
Dose level 5 / 160mg QD	13
Dose level 6 / 240 mg QD	14
Dose level 7/ 320mg QD	4
Dose level 8/ 400mg QD	3
Total	**56**

Phase 1b/2



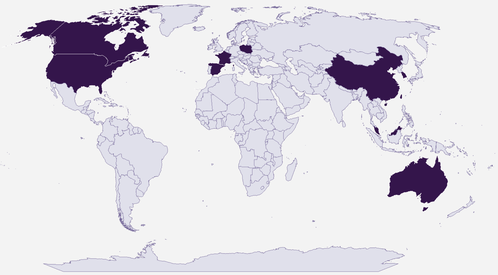
OBJECTIVES/ENDPOINTS

Phase 1a	Phase 1b/2
Objectives	
• To evaluate the safety and tolerability of VRN110755 in patients with EGFR mutant NSCLC • To determine the maximum tolerated dose (MTD) of VRN110755 in Phase 1a of the study	• To evaluate the safety and tolerability of VRN110755 in NSCLC patients with disease progression after first-line treatment with third-generation EGFR TKIs and confirmed C797S resistance mutation • To determine the recommended Phase 2 dose (RP2D) of VRN110755
Primary Endpoints	
• Incidence of DLTs • Incidence of adverse events (AEs)/serious AEs (SAEs)	• Incidence of AEs/SAEs
Secondary Endpoints	
• PK, ctDNA evaluation • ORR, DOR, DCR, PFS and intracranial ORR if brain metastatic lesions are present • PFS2 (PFS after next line of treatment) per RECIST v1.1 by investigator assessment • Patient-reported outcomes	• PK, ctDNA evaluation • ORR, DOR, DCR, PFS and intracranial ORR if brain metastatic lesions are present • PFS2 (PFS after next line of treatment) per RECIST v1.1 by investigator assessment • Patient-reported outcomes

PHASE 1B/2 PD ANALYSIS PLAN

Pharmacodynamic (PD) assessments are planned through liquid biopsy, which will enable the non-invasive monitoring of circulating tumor DNA (ctDNA) dynamics at Baseline, C2D1 or C3D1, and at the end of treatment (EOT). Sequential ctDNA measurements during the study will provide insights into treatment response, mutation clearance, and potential mechanisms of resistance.

STUDY SITES



40 study sites in 13 countries globally

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