Trials in Progress: Phase 1a/b study of ELVN-002 in solid tumors with HER2 mutations, amplification, or overexpression

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KEY POINTS

ELVN-002 is a first-in-human, phase 1, open-label, multicenter, dose escalation and expansion study to evaluate the safety, tolerability, PK, and preliminary antitumor activity of HER2-overexpressed monotherapy and in combination with T-DXd or TDM1 in patients with solid tumors with HER2 alterations, including HER2-mutant NSCLC and HER2-overexpressed MBC

OBJECTIVES AND ENDPOINTS

Phase 1a Monotherapy and Combination Dose Escalation

Primary Endpoints
- Tumor response assessed by RECIST v1.1
- Safety and tolerability
- Pharmacokinetics
- Pharmacodynamics
- Clinical activity

Secondary Objectives
- Antitumor activity in combination with T-DXd or TDM1
- Biologic mechanisms of action
- Tumor profiling
- Clinical activity with or without brain metastases in patients with HER2-overexpressed MBC

Phase 1b Monotherapy Dose Expansion

Primary Objective
- Evaluate the safety and tolerability of ELVN-002 in patients who have previously received T-DXd or TDM1
- Assess preliminary antitumor activity of ELVN-002 alone and in combination with T-DXd or TDM1

Secondary Objectives
- Evaluate the PK profile of ELVN-002
- Assess preliminary antitumor activity of ELVN-002 in HER2-overexpressed MBC with or without brain metastases
- Evaluate post-treatment biologic changes

INCLUSION/EXCLUSION CRITERIA

Inclusion Criteria
- Patients with HER2-overexpressed (IHC3+ or IHC2+/ISH+) breast cancer, and who have previously received T-DXd or TDM1, who have no prior HER2-targeted therapy
- Patients with brain metastases (treated or untreated) are not excluded unless requiring immediate local therapy

Exclusion Criteria
- Patients with HER2-mutant NSCLC
- Patients with activating HER2 alterations, including BRAF V600E
- Patients with YVMA-mutant NSCLC
- Patients with brain metastases, alone or in combination with HER2-overexpressed MBC
- Patients with brain metastases, alone or in combination with HER2-mutant NSCLC
- Patients with HER2-mutant NSCLC

PHASE 1A TRIALS IN PROGRESS

ELVN-002-001 (NCT05650879)

Trials in Progress: Phase 1a/b study of ELVN-002 in solid tumors with HER2 mutations, amplification, or overexpression

ELVN-002-001 (NCT05650879) is a First-in-Human Study With 2 Objectives

Objectives
- Evaluate the safety, tolerability, and pharmacokinetics of ELVN-002 in patients with HER2-overexpressed or HER2-mutant breast cancer
- Evaluate the antitumor activity of ELVN-002 in patients with HER2-overexpressed or HER2-mutant breast cancer

Study Design
- Phase 1a Dose Escalation
- Phase 1b Dose Expansion

Phase 1a Dose Escalation

Eligible patients will be randomized into 4 dose cohorts: ELVN-002 at RD1 in combination with a fixed dose of T-DXd or TDM1

Phase 1b Dose Expansion

Patients will be randomized to a dose-escalation cohort or a fixed dose cohort

STUDY DESIGN

ELVN-002 is in phase 1, randomized, multicenter, dose escalation and expansion study.

Phase 1a Combination Dose Escalation

Successive cohorts of patients with HER2-overexpressed advanced solid tumor will receive escalating doses of ELVN-002 in combination with a fixed dose of T-DXd or TDM1

Phase 1b Monotherapy Dose Expansion

Successive cohorts of patients with HER2-overexpressed MBC will receive escalating doses of ELVN-002 (in combination with a fixed dose of T-DXd or TDM1)

Phase 1b Monotherapy Dose Expansion

- Patients with HER2-overexpressed MBC will be included between 2 dose levels of ELVN-002 each

Table 1: ELVN-002 Selectivity and Potency in Her2 and Her2 Mutants While Sparring Egrf

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<th>Potency</th>
<th>EGRF Potency</th>
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<tr>
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<td>64</td>
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<tr>
<td>HER2-Mutant NSCLC</td>
<td>1.8</td>
<td>58</td>
<td>32</td>
</tr>
</tbody>
</table>

Table 1: ELVN-002 Selectivity and Potency in Her2 and Her2 Mutants While Sparring Egrf

Figure 1: ELVN-002 Mechanism of Action (MOA)

Figure 2: ELVN-002 Demonstrated Antitumor Activity, Including an Intracranial Model, and Additive Activity in Combination With T-DXd at Well-Tolerated Doses

Figure 3: ELVN-002-001 Study Design

Figure 4: Clinical Trial Sites

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